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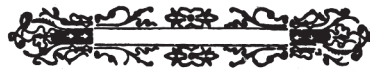
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Fundada el 13 de marzo de 1893

por el

DR. LUIS RAZETTI

Organo de la Academia Nacional de Medicina
y del Congreso Venezolano de Ciencias Médicas



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Dr. Luis Razetti

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La revista Gaceta Médica de Caracas (GMC) es una publicación periódica, órgano oficial de la Academia Nacional de Medicina y del Congreso Venezolano de Ciencias Médicas. Se publica cuatro veces al año y recibe manuscritos inéditos que de ser aceptados por el Comité Redactor, no podrán ser publicados parcial o totalmente en otra parte, sin el consentimiento del Comité Redactor de la GMC.

La GMC sigue las Recomendaciones para la realización, informe, edición y publicación de trabajos académicos en revistas médicas, del Comité Internacional de Editores de Revistas Médicas conocidas como Recomendaciones ICMJE [www.ICMJE.org, Gac Méd Caracas. 2020;128(1): 77-111]. Las unidades deben presentarse de acuerdo con el Sistema Internacional de Unidades (SI) [Gac Méd Caracas. 2015;123(1):46-71].

En la GMC se dará cabida a los trabajos realizados por profesionales de la medicina o especialidades conexas, presentados en la Academia, en los Congresos de Ciencias Médicas y los que sugiera la Corporación a través del Comité Científico, y aceptación final por la Dirección-Redacción. Los manuscritos enviados a la GMC —escritos en español o en inglés—, serán revisados por el Comité Editorial y — si reúnen la calidad científica y cumplen con las normas de presentación necesarias— serán sometidos a un proceso de arbitraje externo, doble ciego, por personas con competencias similares a las de los productores del trabajo (pares) para su debida evaluación. Una vez recibida la opinión de los árbitros, el Comité Editorial tomará la decisión final de su aceptación para publicación. Queda entendido que el Comité Editorial puede rechazar un manuscrito, sin necesidad de acudir al proceso de arbitraje, si se incumple con lo establecido en las normas.

Todos los trabajos deberán ser enviados por Internet en Microsoft Word, a doble espacio, letra Times New Roman tamaño 12.

La GMC solicitará bajo la modalidad de Donación a la Fundación Rísquez de la Academia Nacional de Medicina, una cuota que será establecida e indicada al autor luego de ser aceptado su artículo. Esta donación permitirá cubrir los requerimientos del pago de producción, publicación y asignación de DOI. Quedarán exentos de esta Donación los miembros de la Academia Nacional de Medicina, los Docentes de Universidades Nacionales y los Miembros de Sociedades Científicas, de estas instituciones localizadas en Venezuela. Los manuscritos para números especiales, encomendados por el Comité Editorial a los Editores Ejecutivos, no serán arbitrados; serán solamente supervisados por el Comité Editorial. Las

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La GMC considerará contribuciones para las siguientes secciones:

- Artículos de revisión
- Artículos originales
- Artículos especiales
- Casos clínicos
- Historia y filosofía de la medicina
- Información epidemiológica
- Bioética
- Comunicaciones breves
- Perlas de observación
- Noticias y cartas al editor
- Varios

Los trabajos enviados deberán cumplir con los requisitos que se describen a continuación.

EDITORIALES

Esta sección estará dedicada al análisis y la reflexión sobre los problemas de salud de la población, los distintos enfoques preventivos y terapéuticos, así como los avances logrados en el campo de la investigación biomédica y otros que considere la Dirección-Redacción.

ARTÍCULOS ORIGINALES

Deberán contener en la página frontal, el título conciso e informativo del trabajo; nombre(s) y apellido(s) de cada autor; grados académicos de los autores e institución en la cual se realizó el trabajo; nombre y dirección actual del autor responsable de la correspondencia; un título corto de no más de 40 caracteres (contando espacios y letras) y las palabras clave.

Los trabajos originales, revisiones sistemáticas y metanálisis deben tener un resumen estructurado, como se indica a continuación:

Debe contener un máximo de 250 palabras, y los siguientes segmentos:

- Introducción: ¿Cuál es el problema principal que motivó el estudio?
- Objetivo: ¿Cuál es el propósito del estudio?
- Métodos: ¿Cómo se realizó el estudio? (selección de la muestra, métodos analíticos y observacionales).
- Resultados: ¿Cuáles son los aspectos más importantes? (datos concretos y en lo posible su significancia estadística)
- Conclusión: ¿Cuál es la más importante que responde al objetivo?

Al final se anotarán 3 a 6 palabras clave.

Resumen en inglés

Debe corresponderse con el resumen en español. Se sugiere que este sea revisado por un traductor experimentado, a fin de garantizar la calidad del mismo.

Introducción

Incluir los antecedentes, el planteamiento del problema y el objetivo del estudio en una redacción libre y continua debidamente sustentada por la bibliografía.

Método

Señalar claramente las características de la muestra, el o los métodos empleados con las referencias pertinentes, de forma que se permita a otros investigadores, realizar estudios similares.

Resultados

Incluir los hallazgos importantes del estudio, comparándolos con las figuras estrictamente necesarias y que amplíen la información vertida en el texto.

Discusión

Relacionar los resultados con lo reportado en la literatura y con los objetivos e hipótesis planteados en el trabajo.

Conclusión

Describir lo más relevante que responda al objetivo del estudio.

Agradecimientos

En esta sección se describirán los agradecimientos a personas e instituciones así como los financiamientos.

Referencias

Se presentarán de acuerdo con las Recomendaciones ICMJE.

Indicarlas con números arábigos entre paréntesis en forma correlativa y en el orden en que aparecen por primera vez en el texto, cuadros y pie de las figuras. En las citas de revistas con múltiples autores (más de seis autores), se deberá incluir únicamente los 6 primeros autores del trabajo, seguido de et al.,

- a. Artículos en revistas o publicaciones periódicas: apellido(s) del autor(es), inicial del nombre(s). Título del artículo. Abreviatura internacional de la revista: año; volumen: páginas, inicial y final. Ejemplo: Puffer R. Los diez primeros años del Centro Latinoamericano de la Clasificación de Enfermedades. Bol. Of San Pam. 1964;57:218-229.
- b. Libros: apellido(s) del autor(es), inicial(es) del nombre(s). Título del libro. Edición. Lugar de publicación (ciudad): casa editora; año. Ejemplo: Plaza Izquierdo F. Doctores venezolanos de la Academia Nacional de Medicina. Caracas: Fundación Editorial Universitaria, 1996. (No lleva "Edición" por tratarse de la primera).
- c. Capítulo de un libro: apellido(s) del autor(es), inicial(es) del nombre. Título del capítulo. En: apellido(s) e

inicial(es) del editor(es) del libro. Título del libro. Edición. Lugar de publicación (ciudad): casa editora; año.p. página inicial y final. Ejemplo: Aoün-Soulie C. Estado actual de la salud en Venezuela. En: Aoün-Soulie C, Briceño-Iragorry L, editores. Colección Razetti Volumen X. Caracas: Editorial Ateproca; 2010.p.87-124- (No lleva "Edición por tratarse de la primera).

Fotografías

Las fotografías de objetos incluirán una regla para calibrar las medidas de referencia.

En las microfotografías deberá aparecer la ampliación microscópica o una barra de micras de referencia.

CONGRESO DE CIENCIAS MÉDICAS

Se publicarán únicamente trabajos originales de presentaciones en Congresos de Ciencias Médicas. Serán enviados a la Gaceta por los coordinadores, quienes se responsabilizarán de la calidad, presentación de los manuscritos, secuencia y estructura, incluyendo un resumen general en español y en inglés, en formato libre y que no excedan de 250 palabras. Cada contribución no excederá de 10 cuartillas y deberá apegarse a lo señalado en estas instrucciones a los autores.

ARTÍCULOS DE REVISIÓN

Versarán sobre un tema de actualidad y de relevancia médica. El autor principal o el correspondiente deberá ser una autoridad en el área o tema que se revisa y anexará una lista bibliográfica de sus contribuciones que avale su experiencia en el tema.

Las secciones y subtítulos serán de acuerdo con el criterio del autor. Incluir un resumen general en español y en inglés que no exceda de 150 palabras. La extensión máxima del trabajo será de 20 cuartillas. Las ilustraciones deberán ser las estrictamente necesarias, no siendo más de seis, la bibliografía suficiente y adecuada y en la forma antes descrita.

ARTÍCULOS ESPECIALES

Son aquellas contribuciones que por su importancia el Comité Redactor considere su inclusión en esta categoría.

CASOS CLÍNICOS

Deberán constar de resumen en español e inglés (máximo 100 palabras) en formato libre. Constará de introducción, presentación del caso, discusión, ilustraciones y referencias, con una extensión máxima de 10 cuartillas y apegadas a las instrucciones a los autores.

HISTORIA Y FILOSOFÍA DE LA MEDICINA

En esta sección se incluirán los artículos relacionados con aspectos históricos, filosóficos, bases conceptuales y éticas de la medicina. Aunque su estructura se dejará a criterio del autor, deberá incluir resúmenes en español e inglés (máximo 100 palabras) en formato libre, referencias bibliográficas citadas en el texto y en listadas al final del

NORMAS PARA LOS AUTORES

manuscrito, siguiendo los lineamientos citados para los manuscritos de GMC.

ACTUALIDADES TERAPÉUTICAS

Se informará sobre los avances y descubrimientos terapéuticos más recientes aparecidos en la literatura nacional e internacional y su aplicación en nuestro ámbito médico. La extensión máxima será de cuatro cuartillas y con un máximo de cinco referencias bibliográficas. Deberá incluir resúmenes en español en inglés, en formato libre (máximo 100 palabras).

INFORMACIÓN EPIDEMIOLÓGICA

Será una sección de información periódica sobre los registros epidemiológicos nacionales e internacionales, destacando su importancia, su comparación con estudios previos y sus tendencias proyectivas. La extensión máxima será de cuatro cuartillas y deberá incluir resúmenes en español en inglés (máximo 100 palabras), en formato libre.

COMUNICACIONES BREVES

Serán considerados en esta sección, los informes preliminares de estudios médicos y tendrán la estructura formal de un resumen como se describió previamente (máximo 150 palabras). Se deberán incluir 10 citas bibliográficas como máximo.

BIOÉTICA

Se plantearán los aspectos éticos del ejercicio profesional y aquellos relacionados con los avances de la investigación biomédica y sus aplicaciones preventivas y terapéuticas. Su extensión máxima será de cuatro cuartillas y cuatro referencias bibliográficas, deberá incluir resúmenes en español e inglés (máximo 100 palabras) en formato libre.

EL MÉDICO Y LA LEY

Esta sección estará dedicada a contribuciones tendientes a informar al médico acerca de las disposiciones legales, riesgos y omisiones de la práctica profesional que puedan conducir a enfrentar problemas legales. Su máxima extensión será de cuatro cuartillas y no más de cinco referencias bibliográficas. Deberá incluir resúmenes en español e inglés (máximo 100 palabras).

NOTICIAS Y CARTAS AL EDITOR

Cartas al editor son breves informes de observaciones clínicas o de laboratorio, justificadas por los datos controlados pero limitado en su alcance, y sin suficiente profundidad de investigación para calificar como artículos originales. Al igual que los artículos originales, estos manuscritos están sujetos a arbitraje. Las cartas al editor son accesible para búsquedas bibliográficas, y citadas como

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Las migraciones y su impacto en la salud pública

Enrique Santiago López-Loyo

El fenómeno migratorio ha sido descrito desde tiempos inmemoriales, se registran las descripciones bíblicas de desplazamientos forzados de poblaciones enteras, hasta los fenómenos inducidos en tiempos de guerra y crisis socio-políticas y económicas como la ocurrida en nuestro propio país. La Comisión Económica para América Latina y el Caribe (CEPAL) define la migración como el cambio de residencia que implica el traspaso de algún límite geográfico o administrativo debidamente definido, estableciendo que si el límite que se cruza es de carácter internacional o que implica frontera entre países, la migración pasa a denominarse “migración internacional” y si este límite corresponde a algún tipo de demarcación dentro de un país la migración se denomina como “migración interna” (1).

Un concepto más dinámico es aquel que considera las migraciones como un fenómeno de adaptación social en el cual los grupos poblacionales generan olas masivas de movilizaciones a favor de un gradiente de mejores condiciones de vida, que incluye

desarrollo de capacidades intelectuales por acceso a la educación como factor de movilidad social, acceso a las tecnologías de punta como elemento de progresión en tiempos de desarrollo de habilidades de inteligencia artificial, seguridad social con la provisión de empleos de calidad para proveer recursos en el fomento del progreso de la familia y la disponibilidad de servicios de salud eficientes que pongan a otro nivel las potencialidades de supervivencia de las poblaciones, que logran superar el espacio geográfico dominado por endemias recurrentes que diezman consecutivamente a sus habitantes. Muchas conceptualizaciones han dado solo preponderancia a la migración simplemente como una consecuencia de los impactos climáticos al describirla como una forma de adaptación humana, sin embargo, para otros conduce a una mayor vulnerabilidad y a una espiral de pobreza, llevando finalmente a una reducción de la capacidad de esa misma adaptación de los grupos humanos. Analizando la evidencia sobre las diversas circunstancias y resultados de la migración solo en el contexto del cambio climático, distinguimos entre migración reactiva y proactiva, que supone una diferenciación precisa en el debate académico. Pero la realidad es que la migración no conduce necesariamente a una mayor capacidad de adaptación de los hogares en todos los contextos, sino que también puede tener consecuencias perjudiciales, lo que lleva a un mayor empobrecimiento y a vulnerabilidades más profundas (2).

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Los migrantes humanitarios son los que se desplazan en busca de seguridades de todo tipo y aunque existen declaraciones de principios que manifiestan los países receptores como comprensibles a este fenómeno, en la práctica se enfrentan a la coexistencia de una brecha de protección y a una brecha de cumplimiento de las condiciones de permanencia de estos grupos, muchos de los cuales simplemente utilizan los cruces de fronteras como estancias transitorias en la búsqueda de destinos definitivos con la mira puesta en puntos finales de llegada (3). La brecha de protección implica que la noción legal de “refugiado” excluye a muchos tipos de migrantes humanitarios de la protección legal y esta ha sido la situación particular de los migrantes venezolanos, que bajo la declaración de Emergencia Humanitaria Compleja de la Organización de Naciones Unidas (ONU) emprendieron la huida masiva del país, con cifras que de acuerdo con algunos organismos multilaterales alcanza a más de 8 millones de desplazados, sin embargo, antes de esta declaración los migrantes superaban cifras de más de 3 millones de personas. Este estado de protección descrito convencionalmente no es igual a grupos que salen huyendo, por ejemplo, de las guerras de Ucrania y Gaza en comparación con el fenómeno venezolano, el cual numéricamente supera a todo proceso migratorio conocido hasta ahora.

Muchos venezolanos salieron por las fronteras para lograr la superación de problemas de salud, tanto propios como de familiares con requerimientos de tratamientos médicos o quirúrgicos y estos volúmenes poblacionales han llevado a la saturación de servicios públicos en los países que los han recibido, incluyendo a los servicios de prestación de salud. Esa situación no superada, lo que ha hecho es trasladar nuestra condición de miseria social a otras regiones y ha repercutido negativamente en la aceptación de nuestros connacionales, los cuales finalmente son tratados de manera discriminatoria, máxime cuando muchos han incurrido en la práctica de la delincuencia organizada.

Este fenómeno se ha caracterizado en un estudio de la situación de salud de las migrantes venezolanas irregulares embarazadas que residen en el Caribe colombiano en las ciudades de Barranquilla y Riohacha. Esta investigación

incluyó 520 gestantes encuestadas entre 2018 y 2019 atendidas en hospitales públicos, evaluando su estado nutricional, seguridad alimentaria, presencia de síntomas depresivos y accesibilidad/satisfacción con los servicios de salud. Se confirmó un estado de inseguridad alimentaria, anemia en más del 51 % de las pacientes, síntomas depresivos en un tercio de los casos, violencia de pareja en casi la totalidad de ellos y la falta de atención prenatal significativa. Esto es un ejemplo de atención a una población de migrantes vulnerables y de un manejo responsable de un país que asume como propios los problemas de este particular segmento de migrantes que aportarán nuevos ciudadanos a esa nación que los ha recibido (4).

Otro estudio sobre la migración venezolana realizado en Perú, investigó la asociación entre la discriminación percibida y la posibilidad de recibir tratamiento adecuado para sus enfermedades crónicas. Evaluaron a 865 migrantes con edad promedio de 36 años, siendo el 58 % mujeres. Más de la mitad (54,8 %) manifestaron trato discriminatorio y el 89,2 % de ellos no recibieron el tratamiento adecuado para sus enfermedades crónicas. Esto demuestra la situación real del migrante en todo el mundo, dado que la discriminación está implícita en la consideración de personas que llegan a otro país y que son percibidas como una real competencia o amenaza para la provisión de servicios sanitarios en relación con los ciudadanos de naciones receptoras (5).

Estas investigaciones son contrastantes en cuanto al trato aplicable a los migrantes y al estado de vulnerabilidad constante en su nuevo entorno de vida. La respuesta de países receptores también está influenciada por el papel de los migrantes, sabiendo que no es lo mismo lo que ocurre con un profesional de alta calificación que es un recurso humano captado para los planes de desarrollo de su nuevo país de destino y lo que ocurre con aquellos grupos socialmente comprometidos sin un soporte profesional o financiero que puedan ofrecer a su nuevo asiento territorial.

Un aspecto fundamental de la migración es su relación con la epidemiología. Es inevitable que los grupos poblacionales se trasladen con sus problemas de salud. Históricamente se han implementado procesos de “aislamiento”

y “asimilación” de estos grupos en su proceso adaptativo. Sin embargo hay casos bien definidos de epidemias asociadas a grupos poblacionales desplazados. Bien identificadas están patologías como tuberculosis, dengue, malaria, fiebre amarilla y hasta VIH/SIDA. Los países receptores están en el deber de implementar procesos de vigilancia epidemiológica. Protocolos similares aplican para productos agrícolas y pecuarios para la prevención de desequilibrios sanitarios (6).

Los fenómenos migratorios han caracterizado parte de los procesos de dinámica poblacional y deben ser debidamente ponderados en la aplicación de políticas efectivas de salud pública y en la adecuación de las respuestas por parte de los estados, a fin de afrontarlos con las mínimas consecuencias que lleven a un desequilibrio de su propia realidad nacional.

REFERENCIAS

1. Boletín de la Comisión Económica para América Latina y el Caribe (CEPAL). Migraciones. Noviembre 2023. Publicación Electrónica. Consultado 06-11-2023. Disponible en: <https://www.cepal.org/es/subtemas/migracion#>
2. Vinke K, Bergmann J, Blocher J, Upadhyay H, Hoffmann R. ¿La migración como adaptación? Estudios Sobre Migración. 2020;8(4):626-634.
3. van Houte M, Kaşlı Z, Leerkes A. Introducción: Migrantes humanitarios irregulares: políticas, fundamentos y búsqueda de soluciones más duraderas. J Refugee Studies. 2023;36(3):315-336.
4. Fernández-Niño JA, Rojas-Botero ML, Bojórquez-Chapela I, Giraldo-Gartner V, Sobczyk RA, Acosta-Reyes J, et al. Situación de salud de las migrantes venezolanas embarazadas en el Caribe colombiano: primer informe para una respuesta rápida en salud pública. Rev Univ Indust Santander. 2019;51(3):208-219.
5. Delgado-Flores C, Soto Cutire O, Cvetkovic-Vega A, Nieto-Gutiérrez W. La discriminación percibida como barrera para el tratamiento adecuado de enfermedades crónicas en migrantes venezolanos provenientes del Perú. Rev Bras Epidemiol. 2021;24: E210029.
6. Margaret A Handley, James Grieshop, Migración globalizada y epidemiología transnacional. Revista Internacional de Epidemiología. 2007;36(6):1205-1206.

Migrations and their impact on public health

Enrique Santiago López-Loyo

The migratory phenomenon has been described since immemorial time, biblical descriptions of forced displacements of entire populations are recorded as the phenomena induced in times of war and socio-political and economic crises such as the one that occurred in our own country. The Economic Commission for Latin America and the Caribbean (ECLAC) defines migration as the change of residence that implies the transfer of some duly defined geographical or administrative limit, establishing that if the limit crossed is international or that involves a border between countries, migration is now called “international migration” and if this limit corresponds to some type of demarcation within a country, the migration is called “internal migration” (1).

A more dynamic concept considers migrations as a phenomenon of social adaptation in which population groups generate massive waves of mobilization in favor of a gradient of better living conditions, which includes the development of intellectual capacities through access to education

as social mobility factor, access to cutting-edge technologies as an element of progression in times of development of artificial intelligence skills, social security with the provision of quality jobs to provide resources to promote family progress and the availability of services efficient health systems that raise the survival potential of populations to another level, which manage to overcome the geographic space dominated by recurrent endemic diseases that consecutively decimate its inhabitants. Many conceptualizations have given prominence to migration simply because of climate impacts by describing it as a form of human adaptation, however, for others it leads to greater vulnerability and a spiral of poverty, ultimately leading to a reduction in the capacity of that same adaptation of human groups. Analyzing the evidence on the various circumstances and outcomes of migration only in the context of climate change, we distinguish between reactive and proactive migration, which represents a precise differentiation in the academic debate. But the reality is that migration does not necessarily lead to greater adaptive capacity of households in all contexts, but can also have detrimental consequences, leading to greater impoverishment and deeper vulnerabilities (2).

Humanitarian migrants are those who move in search of security of all kinds and although there are declarations of principles that the receiving countries show as being understandable to this phenomenon, in practice they face the coexistence

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of a protection gap and a compliance gap of the conditions of permanence of these groups, many of whom simply use border crossings as temporary stays in the search for definitive destinations with an eye toward final points of arrival (3). The protection gap implies that the legal notion of “refugee” excludes many types of humanitarian migrants from legal protection and this has been the particular situation of Venezuelan migrants, who under the declaration of Complex Humanitarian Emergency of the United Nations Organization (UN) undertook the massive flight from the country, with figures that according to some multilateral organizations reach more than 8 million displaced people, however, before this declaration the migrants exceeded figures of more than 3 million people. This conventionally described state of protection is not the same as groups fleeing, for example, the wars in Ukraine and Gaza compared to the Venezuelan phenomenon, which numerically surpasses any migratory process known until now.

Many Venezuelans left across the borders to overcome health problems, both their own and those of their families requiring medical or surgical treatment, and these population volumes have led to the saturation of public services in the countries that have received them, including those in the health provision services. This situation has not been overcome, what it has done is transfer our condition of social misery to other regions and has had a negative impact on the acceptance of our fellow citizens, who are finally treated in a discriminatory manner, especially when many have engaged in the practice of organized crime.

This phenomenon has been characterized in a study of the irregular health situation of pregnant Venezuelan migrants residing in the Colombian Caribbean in the cities of Barranquilla and Riohacha. This research included 520 pregnant women surveyed between 2018 and 2019 and treated in public hospitals, evaluating their nutritional status, food security, presence of depressive symptoms, and accessibility/satisfaction with health services. A state of food insecurity was confirmed, anemia in more than 51 % of the patients, depressive symptoms in a third of the cases, intimate partner violence in almost all of them, and the lack of significant prenatal care. This is an example of attention to a population of vulnerable migrants and responsible

management of a country that assumes as its own the problems of this particular segment of migrants who will bring new citizens to the nation that has received them (4).

Another study on Venezuelan migration carried out in Peru investigated the association between perceived discrimination and the possibility of receiving adequate treatment for chronic diseases. They evaluated 865 migrants with an average age of 36 years, 58 % being women. More than half (54.8 %) reported discriminatory treatment and 89.2 % of them did not receive adequate treatment for their chronic diseases. This demonstrates the real situation of migrants throughout the world, given that discrimination is implicit in the consideration of people who arrive in another country and who are perceived as a real competition or threat to the provision of health services concerning citizens of that country receiving nations (5).

These investigations are contrasting in terms of the treatment applicable to migrants and the state of constant vulnerability in their new living environment. The response of receiving countries is also influenced by the role of migrants, knowing that what happens with a highly qualified professional who is a human resource recruited for the development plans of their new destination country is not the same as what occurs with those socially committed groups without the professional or financial support that they can offer to their new territorial seat.

A fundamental aspect of migration is its relationship with epidemiology. Population groups inevitably move with their health problems. Historically, processes of “isolation” and “assimilation” of these groups have been implemented in their adaptive process. However, there are well-defined cases of epidemics associated with displaced population groups. Pathologies such as tuberculosis, dengue, malaria, yellow fever, and even HIV/AIDS are well-identified. Recipient countries have the duty to implement epidemiological surveillance processes. Similar protocols apply to agricultural and livestock products to prevent health imbalances (6).

Migration phenomena have characterized part of the population dynamics processes and must be duly considered in the application of effective

public health policies and in the adaptation of responses by states, to face them with the minimum consequences that lead to an imbalance of its national reality.

REFERENCES

1. Boletín de la Comisión Económica para América Latina y el Caribe (CEPAL). Migraciones. Noviembre 2023. Publicación Electrónica. Consultado 06-11-2023. Disponible en: <https://www.cepal.org/es/subtemas/migracion#>
2. Vinke K, Bergmann J, Blocher J, Upadhyay H, Hoffmann R. ¿La migración como adaptación? Estudios Sobre Migración. 2020;8(4):626-634.
3. van Houte M, Kaşlı Z, Leerkes A. Introducción: Migrantes humanitarios irregulares: políticas, fundamentos y búsqueda de soluciones más duraderas. *J Refugee Studies*. 2023;36(3):315-336.
4. Fernández-Niño JA, Rojas-Botero ML, Bojórquez-Chapela I, Giraldo-Gartner V, Sobczyk RA, Acosta-Reyes J, et al. Situación de salud de las migrantes venezolanas embarazadas en el Caribe colombiano: primer informe para una respuesta rápida en salud pública. *Rev Univ Indust Santander*. 2019;51(3):208-219.
5. Delgado-Flores C, Soto Cutire O, Cvetkovic-Vega A, Nieto-Gutiérrez W. La discriminación percibida como barrera para el tratamiento adecuado de enfermedades crónicas en migrantes venezolanos provenientes del Perú. *Rev Bras Epidemiol*. 2021;24: E210029.
6. Margaret A Handley, James Grieshop, Migración globalizada y epidemiología transnacional. *Revista Internacional de Epidemiología*. 2007;36(6):1205-1206.

Outcomes of Lightweight Mesh Sacrocolpopexy for Pelvic Organ Prolapse Repair

Resultados de la Sacrocolpopexia con Malla Ligera para la Reparación del Prolapso de Órganos Pélvicos

Roman Banakhevych^{1*}, Klavdiia Akymova², Kateryna Pariienko³, Vsevolod Nechaiev⁴

SUMMARY

Objective: The research objective is to present and evaluate 3 years of experience in sacrospinal fixation using polypropylene mesh in the surgical treatment of genital prolapse in women. **Methods:** This retrospective study evaluated perioperative and mid-term outcomes in 68 women who underwent transvaginal sacroscopic cervicocolpopexy with lightweight polypropylene mesh for stage II-IV prolapse with apical involvement. Anatomical outcomes, complications, and symptoms were assessed using POP-Q staging and validated questionnaires preoperatively and at 12 and 36 months postoperatively. **Results:** No intraoperative complications were observed. In the long-term postoperative period, the following were observed: vaginal wall erosion in transvaginal Mesh-systems placement along the postoperative suture line at 2.9 % (2/68), and chronic pelvic pain at 2.9 % (2/68). The percentage of anatomical success in restoring

the position of the apical vaginal segment was 98.5 % (67/68) 12 months after surgery and remained unchanged after 36 months of follow-up. There were symptoms of recurrence in the anterior segment of the vagina (cystocele) in 8.8 % (6/68) of patients in the form of cystocele of I-II degree, and an isolated recurrence of rectocele of II degrees was observed in 1.5 % (1/68) of 68 patients in the posterior segment of the vagina. A significant level of elimination of pathological symptoms in the functioning of the pelvic organs and improvement in quality of life, as assessed by questionnaires, was established: PFDI-20 ($76.4 \pm 8.6 - 4.3 \pm 0.6$; $p < 0.05$), PFIQ-7 ($41.0 \pm 5.8 - 8.3 \pm 1.1$; $p < 0.05$) before surgery and at the final stage of the study. **Conclusion:** Transvaginal sacroscopic cervicocolpopexy with lightweight mesh demonstrated favorable anatomical and functional outcomes at 3 years for apical prolapse repair, with low complication rates. Further comparative trials are warranted to establish long-term effectiveness versus other surgical techniques.

Keywords: Transvaginal sacrospinal cervicopexy, pelvic organ prolapse, vaginal surgery, lightweight polypropylene mesh, recurrence.

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RESUMEN

Objetivo: El objetivo de la investigación es presentar y evaluar 3 años de experiencia en fijación sacroespinal mediante malla de polipropileno en el tratamiento quirúrgico del prolapso genital en la mujer. **Métodos:** Este estudio retrospectivo evaluó los resultados perioperatorios y a mediano plazo en 68 mujeres que se sometieron a cervicocolpopexia sacroscópica transvaginal con malla liviana de polipropileno para prolapso en estadio II-IV con afectación apical. Los resultados anatómicos, las complicaciones y los síntomas se evaluaron mediante estadificación POP-Q y cuestionarios validados antes de la operación y a los 12 y 36 meses del postoperatorio. **Resultados:** No se observaron complicaciones intraoperatorias. En el período postoperatorio a largo plazo, se observó lo siguiente: erosión de la pared vaginal en la colocación de sistemas de malla transvaginal a lo largo de la línea de sutura postoperatoria en un 2,9 % (2/68) y dolor pélvico crónico en un 2,9 % (2/68). El porcentaje de éxito anatómico en la restauración de la posición del segmento vaginal apical fue del 98,5 % (67/68) a los 12 meses de la cirugía y se mantuvo sin cambios a los 36 meses de seguimiento. Hubo síntomas de recurrencia en el segmento anterior de la vagina (cistocele) en el 8,8 % (6/68) de las pacientes en forma de cistocele de grado I-II, y se observó una recurrencia aislada de rectocele de grado II en el 1,5 % (1/68) de 68 pacientes en el segmento posterior de la vagina. Se estableció un nivel significativo de eliminación de síntomas patológicos en el funcionamiento de los órganos pélvicos y mejora en la calidad de vida, evaluada mediante cuestionarios: PFDI-20 (76,4±8,6-4,3±0,6; $p<0,05$), PFIQ- 7 (41,0±5,8-8,3±1,1; $p<0,05$) antes de la cirugía y al final del estudio. **Conclusión:** La cervicocolpopexia sacroscópica transvaginal con malla liviana demostró resultados anatómicos y funcionales favorables a los 3 años para la reparación del prolapso apical, con bajas tasas de complicaciones. Se necesitan más ensayos comparativos para establecer la efectividad a largo plazo versus otras técnicas quirúrgicas.

Palabras clave: Cervicopexia sacroespinal transvaginal, prolapso de órganos pélvicos, cirugía vaginal, malla ligera de polipropileno, recidiva.

INTRODUCTION

Genital prolapse (GP) continues to be an urgent problem in modern gynecology and occurs in one-third of all women regardless of age (1-3). Epidemiological studies show that

up to 50 % of women in the United States have signs of genital prolapse at the age of over 40 and 11.1 % of them will be operated on, and some will even have more than one operation in their lifetime (4). The great interest in the problem of internal genital organ prolapses and prolapse is caused by the consistently large number of patients with GP and many recurrences after almost all types of surgical treatment. GP creates both gynecological and social problems, namely: disability (permanent or temporary), social maladjustment, and reduced quality of life (5). Following various authors, depending on the profile of the gynecological hospital and the specialization of the department's gynecologists, 6.1-38.9 % of women receive inpatient treatment of all patients with gynecological pathology requiring surgical treatment (2-5).

Over the past 30 years, the understanding of the etiology and pathogenesis of GP has significantly expanded, and several theories have been put forward. However, none of the many theories provides a complete explanation of all the causes of its development. The existence of the theory of systemic connective tissue dysplasia, under which GP is only one of the signs of multiorgan connective tissue insufficiency at the level of the reproductive system, partially answers most of the questions (4,5). As a result, the lack of a complete theoretical justification for the pathogenesis of all types of GP has led to the fact that hundreds of types of operations have been described to date aimed at surgical treatment of GP, correction of the position of the pelvic organs (PO) and supporting structures of the pelvic floor. However, most reputable experts note many recurrences in the treatment of GP and insufficient functional effect in restoring the normal position of the genitals and PO. Following the authors, the recurrence rate of GP ranges from 33 to 61.7 % (6). Of these, approximately 12.1 % of patients undergo reoperation for recurrence.

Transvaginal sacrospinal cervicopexy using the PROLIFT system has been an effective surgical method for the treatment of apical genital prolapse (7). Nevertheless, certain criticism regarding transvaginal access in the reconstructive treatment of GP using transvaginal Mesh-systems (TVM) exists (8,9) due to the relatively high incidence and severity of complications associated with the use of TVM.

It is extremely important to balance the positive effects with the potential complications when surgery is performed for a disease that affects a woman's quality of life. One of the most recent randomized clinical trials compared the results of surgical treatment of hernia using lightweight mesh (35 g/m², TiMesh®) and medium weight mesh (75 g/m², Parietex®) (9,10). There was a decrease in postoperative pain in patients, which contributed to a faster recovery of performance (routine activities) when using lightweight mesh, without any increase in the 2-year risk of hernia recurrence. However, very few clinical trials have been published on the results of using lightweight TVM for the treatment of GP using transvaginal access.

The research objectives are to analyze the frequency of intra- and postoperative complications; to assess anatomical results 12 and 36 months after surgery; to assess the level of elimination of pathological symptoms in the functioning of the pelvic organs and improvement of quality of life, using questionnaires in the application of lightweight polypropylene TVM (46 g/m²), used in transvaginal access for surgical treatment of complete or incomplete uterine prolapse.

The purpose of this study is to analyze the frequency of intra- and postoperative complications, assess anatomical results, and evaluate the elimination of pathological symptoms and improvement in quality of life using lightweight polypropylene transvaginal mesh for surgical treatment of complete or incomplete uterine prolapse.

MATERIALS AND METHODS

This retrospective multicenter cohort study was conducted between January 2017 and December 2020 at two unspecified medical centers in Ukraine and included a 36-month follow-up period. The study enrolled 68 women with complete or incomplete uterine prolapse who underwent transvaginal sacrospinal cervicopexy. Informed consent was obtained from each participant regarding the retrospective design, data collection, and long-term follow-up. Comprehensive data was gathered preoperatively, intraoperatively, and postoperatively at 12 months and 36 months.

Before the research, it was established that all the involved surgeons had experience using polypropylene TVM for transvaginal access in the treatment of GP. The preoperative assessment consisted of an interview, urogynecological examination, and quantitative assessment of prolapse using the simplified pelvic organ prolapse quantification (POP-Q) stage assessment system (measuring the total vaginal length at rest TVL and Ba, C, C/D, and Bp at maximum, performing a Valsalva test, and GH size) (4). Patients underwent a standardized examination before the planned surgical intervention. Special urodynamic tests were performed only in patients with existing urodynamic disorders. Patients with decubitus ulcers received special treatment until complete epithelialization of the vaginal wall.

Between 2017 and 2020, 68 patients were enrolled in the research, all of whom gave consent. After 36 months, 68 patients completed the research. The average age of the patients was 57.1±7.2 years (range 47-79) years, the average body mass index (BMI) was 29.3±2.1 kg/m², and the average parity was 2.1±1.1. The number of patients with a history of supravaginal uterine amputation was 7.4 % (5/68), and 2.9 % (2/68) patients received SUI surgical treatment.

Inclusion criteria: signs of incomplete or complete uterine prolapse with a predominance of prolapse in the apical segment of the vagina, no contraindications for the use of TVM, and no signs of cervical, uterine, and ovarian pathology. Exclusion criteria: refusal to participate in the study, contraindications for TVM placement, need for uterine removal, refusal to use TVM, use of TVM in previous surgeries. To fix the cervix, a polypropylene implant (TVM) of the author's design was used, which contained a round-shaped base with a round cutout and a fixation part in the form of a sleeve 200 mm long and 15 mm wide. Other technical characteristics: macroporous mesh with a pore size of 2.0×2.4 mm (class 1), lightweight, non-absorbable, fiber thickness 0.34 mm, fiber diameter 0.1 mm, porosity 73.7 % (9,10).

The surgery was performed under regional (spinal) anesthesia or general anesthesia. The patient was placed in the lithotomy position. The bladder was not catheterized. The surgical field was treated with a 10 % antiseptic solution

of Povidone-Iodine. Hydropreparation was performed with 0.9 % NaCl solution up to 100 mL with the addition of Epinephrine (Adrenaline) hydrochloride 0.24 %-2.0 mL. A circular incision of the vaginal wall was made at the level of the fold indicating the position of the lower border of the bladder. The incision was made to the depth of the cervical stroma for easy access to the anterovaginal and retrocervical spaces. From the area of the posterior vaginal vault, the right parametrium was dissected laterally towards the place of departure of the right sacrospinal ligament from the spinous process of the ischial bone. The diameter of the tunnel was up to 30 mm. A pre-prepared mesh of the proposed shape was placed around the cervix. The implant sleeve was passed through the right sacrospinal ligament and placed freely. The main part of the mesh was fixed in three points to the cervical wall around the internal pharynx using non-absorbable sutures (Polyester with silicone coating 2-0). The vaginal wall was restored with sutures (Polyglycolide 1-0). The cervix was set at the level of the interspinal line by pulling the TVM sleeve.

Perioperative parameters and intraoperative complications were analyzed. The safety of TVM use and surgical outcomes were evaluated 12 and 36 months after surgery. The evaluation aimed at the safety of TVM use, which included the timing of pressure ulcer formation around TVM placement on the vaginal wall, pain in the area of TVM placement, or pain during physical activity. Signs of dyspareunia were not assessed. In addition, the anatomical results and the development of de novo pathology were evaluated. Anatomical outcomes after surgery were assessed using the POP-Q system for the anterior, apical, and posterior vaginal segments (C, TVL, Ba, C/D, Bp, GH). The outcome was considered anatomically successful at C -1 or less. Pelvic organ function was assessed by the MHU (urinary handicap measurement), PFDI-20 (Pelvic Floor Distress Inventory), and PFIQ-7 (Pelvic Floor Impact Questionnaire) questionnaires, which included an assessment of symptoms of stress urinary incontinence (SUI), and overactive bladder (OAB) (10). Satisfaction was assessed using a four-point system (++ , + , +/- , -). Quantitative changes were statistically evaluated by frequency in the sample. Qualitative

changes were evaluated as means and standard deviations. The nonparametric Wilcoxon test was used to compare POP-Q values and pelvic organ function (11).

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. A study was approved by the National Ethics Commission of the Ministry of Health of Ukraine on July 10, 2023, No 3113-C.

RESULTS

In the studied patients, most women had signs of a combination of cystocele ($Ba+4.8\pm 2.8$ cm) with signs of complete or incomplete uterine prolapse ($C+3.8\pm 1.9$ (+1 - +8)). Before the operation, more often, in 58.8 % of cases, the degree of prolapse was diagnosed as 3-4 according to POP-Q, which was indicated by the results of measuring the position of points C, Va, and Vr. Signs of rectocele were observed in every third patient (33.8 %) and were less clinically pronounced ($Bp+0.6\pm 2.4$ (-3 to +10)). Measurement of the vaginal length showed almost the same value in all patients of the study group ($TVL 8.0\pm 2.0$ (7 to 9)). The results of the preoperative anatomical assessment according to the POP-Q system and the postoperative assessment of the results of the operation are shown in Table 1.

No intraoperative complications were observed in the research group. The surgical interventions performed under regional anesthesia were 67/68 (98.5 %), general anesthesia – 1/68 (1.5 %), and the average operation time was 38.2 ± 10.7 minutes (range (20-70 minutes)). Additionally, pre-rectal plication was performed in 65/68 patients (95.6 %), and perineorrhaphy – in 63/68 (92.6 %). In 68/68 (100 %) cases, antibiotics (Cefazolin 2.0 g. IV) were prescribed immediately before surgery. No antibiotic therapy was prescribed after surgery. Minor bleeding from the area of pararectal dissection occurred in 3 out of 68 (4.4 %) cases. In these cases, prolonged antibiotic therapy was also not prescribed. So, surgery

Table 1

Results of Measuring the Vaginal Profile of Patients with Uterine Prolapse Before and After Surgical Treatment (N±N, cm)

POP-Q	Initial (N=68)	12 months (N=68)	Pa	36 months (N=68)	Pb
TVL	8.0±2.0 (7 - 9)	10.3±1.8 (7 - 11)	0.24	9.7±1.9 (7 - 11)	0.24
Ba	+4.8±2.8 (+1 - +6)	+4.5±1.9 (+2 - +5)	<0.01	+4.6±1.4 (+1 - +6)	<0.01
C/D	1.6±1.1 (1 - 10)	0.8±0.3 (1 - 2)	<0.01	0.9±0.1(1 - 2)	<0.01
C	+3.8±1.9 (+1 - +8)	- 6.6±0.1 (-7 - 1)	<0.01	-4.1±0.2 (-6 - -1)	<0.01
Bp	+0.6±2.4 (-3 - +5)	-2.7±1.1 (-3 - +1)	<0.01	-1.6±1.0 (-3 - +1)	<0.01
GH	6.1±1.1 (5 - 8)	3.6±0.4 (4 - 5)	<0.01	4.1±0.5 (2 - 5)	<0.01

Note: data are shown as standard deviations N±n; TVL – total vaginal length; a – comparison of initial and 12-month results; b – comparison of initial and 36-month results.

did not cause statistically significant changes in intraoperative hemodynamic and complete blood count.

After the operation, a tight vaginal tamponade was performed with a gauze tampon. The tampon was removed 18-24 hours after surgery. Complications in the form of hematomas in the pararectal spaces were not observed in patients. There were 46/68 (67.6 %) cases of subcutaneous hematomas in the ischio-rectal area at the site of the prosthesis sleeve through the skin. Diffuse hematomas did not require additional treatment. A fixed urinary catheter was installed after surgery in 68/68 cases (100 %). The average duration of bladder catheterization was 0.9±0.1 days. In 5/68 (7.4 %) women, urinary retention of more than 1 day was observed, which required additional non-permanent bladder catheterization for 1.1±0.4 days in the range of (1-3) days. The average duration of pain in the postoperative period was 7.2±1.4 (5-14) days with a visual analogue scale (VAS) of 5.2±2.1 due to perineal pain. The average length of hospital stay was 1.9±0.5 days, a range of 1-4 days. The main reason for the delay in discharge from the hospital was the need for bladder catheterization in case of bladder hypotension. Postoperative perineal discomfort was assessed at 12 and 36 months. Women defined the outcome of the operation as satisfactory (+, +/-) or very satisfactory (++) in 66/68 (97.1 %) cases, and unsatisfactory (-) – in 2/68 (2.9 %) cases. Assessment of the level of discomfort after 36 months showed a statistically

significant difference compared to the initial assessment before surgery ($p>0.05$).

The results of the POP-Q vaginal profile assessment after surgery at 12 and 36 months are shown in Table 1. A positive anatomical result, as assessed by point C, was obtained in all cases at 36 months of follow-up. The results of the POP-Q assessment were statistically significantly different at 36 months of follow-up from the initial assessment of anatomical parameters before surgery ($p>0.01$). A significant decrease in the size of the vaginal entrance after surgery from 6.1±0.4 cm to 4.1±0.5 cm, respectively, was determined ($p>0.01$). This is caused by most surgical interventions ending in standard perineoplasty. After 36 months, the study patients showed a tendency to increase the size of the vaginal entrance over time (from 3.6±0.4 cm to 4.1±0.5 cm) and did not differ significantly from the mean values 12 months after surgery ($p<0.05$), while the mean values of the Ba measurement results did not show any dynamics of changes 12 and 36 months after surgery. Functional disorders of the pelvic organs associated with genital prolapse and MHU, PFDI, and PFIQ were assessed before and after surgery. The results of the assessment of pathological symptoms are shown in Table 2.

The analysis of the pelvic function assessment results showed a significant reduction in the symptoms of urinary disorders and pathology of the act of defecation after surgery in 36 months. The results of the safety evaluation of TVM are

OUTCOMES OF LIGHTWEIGHT MESH SACROCOLPOPEXY

Table 2

Results of Measuring the Vaginal Profile of Patients with Uterine Prolapse Before and After Surgical Treatment (N±N, cm)

Average values	Initial (N=68)	12 months (N=68)	Pa	36 months (N=68)	Pb
PFDI					
UDI-6/100	30.4±3.1	7±2	<0.05	3±1.1	<0.05
CRADI-8/100	13.8±2	4.1±1.3	<0.05	5.5±1.8	<0.05
POPDI-6-100	31.5±1.7	3.8±1.1	<0.05	5.6±0.9	<0.05
PFDI-20/300	76.4±8.6	13.9±1.4	<0.05	4.4±0.6	<0.05
PFIQ					
UIQ-7/100	21±5.4	2.5±0.7	<0.05	4.4±1	<0.05
CRAIQ-7/100	6.8±1.4	1.5±0.6	<0.05	1.8±0.4	<0.05
POPIQ-7/100	11±2.3	1±0.2	<0.05	2±0.7	<0.05
PFIQ-7/300	41±5.8	4.9±0.8	<0.05	8.3±1.1	<0.05

Note: UDI – Urinary Distress Inventory; CRADI – Colorectal-Anal Distress Inventory; POPDI – Pelvic Organ Prolapse Distress Inventory; UIQ – Urinary Impact Questionnaire; CRAIQ – Colorectal-Anal Impact Questionnaire; POPIQ – Pelvic Organ Prolapse Impact Questionnaire; a – comparison of initial and 12-month results; b – comparison of initial and 36-month results; c – comparison of initial and 36-month results.

shown in 68 patients who were re-examined after 12 and 36 months, respectively. The formation of leakage around TVM placement on the vaginal wall was found in 2/68 (2.9 %) patients. No additional cavities or cysts were found around TVM plication during ultrasound examinations, and the TVM was completely integrated into the surrounding tissues. Twisting of the TVM with the formation of gross fibrosis did not cause additional discomfort to patients. There were no cases of pressure ulcers in the rectal wall in the long-term postoperative period.

Satisfaction with the surgery results after 36 months of surgery follow-up was expressed by 66/68 (97.1 %) patients. A negative result was observed in two patients, one of whom performed heavy physical work after surgery, which affected the outcome of the operation. Aseptic inflammation around the implant sleeve could have led to tunnel formation at the sleeve site, causing the apical segment to move toward the vaginal entrance. This resulted in loss of the primary outcome 12 months after surgery and at 36 months follow-up. The patient did not insist on reoperation. In another patient, the cause

of the negative result could not be established. The probable cause was a violation of the sleeve insertion technique through the sacrospinal ligament, the so-called prespinal sleeve insertion. Regarding pain after surgery, the results of the survey are shown in Table 3, only 4/68 (5.8 %) patients reported persistent or spontaneous pain after 36 months, with a mean VAS score of 2.8/10. Induced pain during a physical examination at 36 months was observed in 6/68 (8.8 %) patients with a mean VAS score of 3.1/10. No patient required mesh dissection in the vaginal vault area.

Another surgery for cystocele was performed in 1/68 (1.5 %) patients before the end of the 36-month follow-up period. None of the patients underwent cervical amputation for cervical elongation (Galban's syndrome) during the 3 years of follow-up. Partial excision of the mesh along with granulation polyps was performed in 1/68 (1.5 %) patients after 12 months of follow-up. In two patients, 2/68 (2.9 %) were treated for stress urinary incontinence that formed de novo after surgery. In 8/68 (11.8 %) patients, symptoms of urge urinary incontinence were observed 36 months after surgery.

Table 3

Evaluation of the Results of Surgery in Patients with Genital Prolapse Using TVM for Sacrospinal Fixation (N, %)

Mark	Initial (N=68)		12 months N=68)		Pa	36 months (N=68)		Pb
	N	%	N	%		N	%	
SUI	6	8.8	6	8.8	>0.05	8	11.8	>0.05
OAB	19	27.9	7	10.3	<0.05	8	11.8	<0.05
Urinary retention	24	35.3	1	1.5	<0.05	0	0	<0.05
Defecation disorders	8	11.8	1	1.5	<0.05	1	1.5	<0.05
Pathological secretions	56	82.4	4	5.9	<0.05	2	2.9	<0.05
Vaginal wall erosion	-	-	1	1.5	<0.05	2	2.9	<0.05
Chronic pelvic pain	-	-	5	7.4	<0.05	4	5.9	<0.05
Pain during palpation	3	4.4	8	11.8	<0.05	6	8.8	<0.05
Result satisfaction	-	-	67	98.5	<0.05	67	98.5	<0.05

Note: a – comparison of initial and 12-month results; b – comparison of initial and 36-month results.

DISCUSSION

It has been convincingly demonstrated that TVM has better anatomical results than autoplasty in the surgical treatment of GP. A review of 58 studies in the Cochrane database confirmed that the risk of recurrence is higher with autoplasic repair than with TVM (risk ratio (RR) = 3.15, 95 %; confidence intervals (CI) = 2.50-3.96). However, these studies failed to demonstrate any significant difference in terms of the risk of reoperation or functional aspects, especially because TVM is associated with the risk of specific complications (wrinkling, exposure, pain, dyspareunia) (10,12,13).

In the research, 68 cases out of 68 treated patients were fully analyzed, which amounted to 100 % of the studied patients. The research results show that a positive anatomical result was achieved in 67/68 (98.5 %) cases after 36 months of follow-up, and 98.5 % (67/68) of patients were satisfied with the result of the surgical intervention at the end of the study. A significant level of elimination of pathological symptoms in the functioning of the pelvic organs and improvement in quality of life was found. These indicators were evaluated before surgery and at the final stage of the study, 36 months after surgery, using questionnaires: PFDI-20 (76.4±8.6-4.4±0.6; p<0.05), PFIQ-7 (41.0-8.4; p<0.05). Patients reported a slight improvement

in the act of defecation, without changes in the state of the rectal continence.

The results indicate that the baseline level of assessment of the position of point C (n=68) by POP-Q was +3.8±1.9 cm (+1 – +8). The result of measuring point C (n=68) assessed after 12 months was: -6.6±0.1 (-7 – -1) and was statistically significantly different from the results of measurement before surgery (p<0.01). Subsequently, the result of the point C assessment by POP-Q after 36 months of follow-up did not change significantly: -4.1±0.2 (-6 – -1) (p<0.01), indicating a minimal risk of recurrence when using the proposed technique of fixing the apical segment of the vagina to the right sacrospinal ligament using TVM in long-term follow-up. In total, 2/68 (2.9 %) patients underwent surgery for recurrence in the anterior vaginal segment, and 2/68 (2.9 %) patients underwent surgical correction of stress urinary incontinence, which was established de novo by repeated examination 12 months after surgery. Partial excision of TVM along with granulation polyps was performed in 1/68 (1.5 %) patients.

In the Kulkarni et al. study, the rates of repeat surgery for recurrent apical prolapse (4 %) and mesh exposure (2 %) using lightweight mesh were low and comparable to the authors' study (2.9 % mesh exposure, 0 % recurrent prolapse) (14). This further supports the use of lightweight over heavier mesh to reduce complications requiring

reoperation. However, the mesh exposure rate remained substantial. Modifications like selective trimming of mesh arms may help reduce erosions while maintaining efficacy. Comparative data on authors' technique versus sacrocolpopexy would better delineate the risks and benefits of each approach.

In the Deng et al. study, the mesh exposure rate was 5.7 % with VALS (15). This is comparable to the 2.9 % erosion rate in this study using lightweight transvaginal mesh. The rates of postoperative fever (2.8 % vs. 0 %) and wound infection (0.9 % vs. 0 %) were slightly higher with VALS compared to the authors' technique, though the overall infectious complication rates were low. This suggests the transvaginal approach may reduce surgical site infections, though laparoscopic sacrocolpopexy also has low infection rates. Larger studies directly comparing the techniques are warranted to elucidate potential differences in complications.

A review by Schachar and Matthews found the rate of prolapse recurrence after sacrocolpopexy is consistently around 10 %, regardless of surgical approach (16). The 2.9 % recurrence rate in the authors' study using transvaginal mesh fixation is lower than this benchmark reported for sacrocolpopexy. This suggests the transvaginal approach may provide better apical support durability, though direct comparative data is lacking. Schachar and Matthews also noted ancillary factors like advanced preoperative prolapse stage adversely affect outcomes. The authors' technique achieved a high success rate despite including patients with stage III-IV prolapse, further supporting its efficacy for advanced prolapse. However, a longer follow-up in this study is needed to determine if the 0 % apical recurrence rate is maintained beyond 3 years and how it compares to sacrocolpopexy over the long term.

Following the research results, when applying the suggested technique, no signs of recurrence in the apical segment of the vagina were recorded. The anatomical and functional results of this research are consistent with recent literature (12,17). In addition, studies have shown that the use of lightweight mesh is safer and with fewer complications than the PROLIFT system and medium-weight and heavyweight

propylene mesh (18,19-21). As for the anatomical results of this study concerning the Ba point following the POP-Q, they can be considered unsatisfactory in the medium and long term. This fact can be explained by the fact that the surgical technique excludes the additional use of TVM in the anterior vaginal segment in grade III cystocele (22,23). Based on this experience, using TVM in the anterior vaginal segment should be considered an additional operation. Its need should be discussed individually for each patient if signs of cystocele are seen at Va +2.0 on Valsalva testing. A potential disadvantage of this technique is the lack of effectiveness and the risk of recurrence of prolapse in the posterior segment of the vagina in case of hidden defects in the facial structures and the formation of de novo GP signs in this segment (24-27).

Considering the safety and advantages of using highly porous lightweight TVMs, a good integration of TVMs in the surrounding tissues without the formation of pathological cavities and postoperative infectious complications at the pleating site has been demonstrated. The research results are in line with the results of another study that analyzed the results of the treatment of 154 patients who were followed for at least 24 months, the success rate of the operation was 97.4 %, and the number of complications with TVM was 0.7 % (28,29). On the other hand, an evaluation of the results of using TVM based on the proposed method showed fewer complications compared to the results of using the PROLIFT system to restore the apical segment of the vagina (19,30,31).

The study by Korahanis et al. (32) compared the use of the PROLIFT system and laparoscopic sacrocolpopexy. This study showed that each technique has fundamental differences in the methodology of the operation and specific complications, which makes it impossible to fully compare these two techniques. In addition, the specific characteristics of the TVMs used, which include not only their weight but also their textile properties, make the results of such a comparison questionable. A study by Feola et al. (33) on the use of sacrocolpopexy in monkeys showed that the mechanical properties of the vagina were significantly worse with medium-weight mesh than with light mesh. The study by Liang et al. (34) and Feola et al. (35) showed that vaginal

tissue degeneration was significantly more pronounced with medium-weight TVM, which is associated with increased cell apoptosis and decreased collagen and elastin content in the tissues. The study described by the authors is the first to prospectively evaluate the safety and efficacy of lightweight mesh after 36 months used for the transvaginal treatment of complete and incomplete uterine prolapse.

CONCLUSIONS

The surgical technique studied for repairing prolapsed vaginal walls in cases of partial and complete uterine prolapse showed successful long-term results in restoring the position of the top part of the vagina. Based on the research findings, the rates of specific complications using lightweight surgical mesh were 2.9 % for vaginal wall erosion, 5.9 % for chronic pelvic pain, and 2.9 % for new onset stress urinary incontinence. This surgical approach can be recommended to patients as an alternative treatment option for isolated complete or partial uterine prolapse.

The results of the gynecological prolapse treatment research indicate the sacrospinal cervicopexy with lightweight mesh has advantages for better preserving the elasticity and strengthening the fascial and ligament structures of the pelvis by creating a non-ligamentous support. Despite these positive findings, the use of transvaginal mesh cannot be the only choice for treating complete or partial uterine prolapse, and it should be discussed with each patient when no other pelvic pathology is identified before surgery.

The study demonstrates the potential benefits and safety of using lightweight mesh via a transvaginal approach for treating uterine prolapse, with a high anatomical success rate, low apical segment recurrence, and acceptable complication rate. However, limitations exist including a lack of a comparison group and independent postoperative evaluations. Further research with comparison groups, longer follow-up, and independent assessments is recommended to validate findings. Optimal lightweight mesh properties and surgical techniques to minimize complications like erosion should be explored.

Adding anterior mesh placement could improve cystocele outcomes. Comparing this technique to laparoscopic sacrocolpopexy would elucidate the advantages and disadvantages of each approach. Within the limitations of this initial study, the transvaginal sacrospinal cervicopexy technique shows promise as an effective option for treating uterine prolapse with an acceptable safety profile. Further research is warranted to optimize the technique and better characterize long-term outcomes.

REFERENCES

1. Belayneh T, Gebeyehu A, Adefris M, Rortveit G, Gjerdje JL, Ayele TA. Pelvic organs prolapse surgery and health-related quality of life: A follow-up study. *BMC Women's Health*. 2021;21(1):2-11.
2. Takacs EB, Kreder KJ. Sacrocolpopexy: Surgical technique, outcomes, and complications. *Current Urology Reports*. 2016;17(12).
3. Brown HW, Rogers RG. Female pelvic medicine and reconstructive surgery: Where are we in 2021? *Obstetrics Gynecol Clin*. 2021;48(3):15-16.
4. Maher C, Feiner B, Baessler K, Schmid C. Surgical management of pelvic organ prolapse in women. *Cochrane Database System Reviews*. 2013;30(4).
5. Banakhevykh RM, Akimova KB, Pariienko KO. Prevention of complications after surgical treatment of cystocele. *Med Perspectivi*. 2018;23(2):92-97.
6. Kasyan G, Abramyan K, Popov AA, Gvozdev M, Pushkar D. Mesh-related and intraoperative complications of pelvic organ prolapse repair. *Cent Eur J Urol*. 2014;67(3):296-301.
7. Gigliobianco G, Roman Regueros S, Osman NI, Bissoli J, Bullock AJ, Chapple CR, MacNeil S. Biomaterials for pelvic floor reconstructive surgery: How can we do better? *BioMed Research Int*. 2015;2015.
8. Solà Dalenz V, Pardo Schanz J, Ricci Arriola P, Guiloff Fischer E. Prolift system in the correction of female genital prolapse. *Actas Urológic España*. 2007;31(8):850-857.
9. Inge U, Klosterhalfen B, Müller M, Ottinger AP, Schumpelick V. Shrinking of polypropylene mesh *in vivo*: An experimental study in dogs. *Eur J Surg*. 1998;164(12):965-969.
10. de Tayrac R, Brouziyne M, Priou G, Devoldère G, Marie G, Renaudie J. Transvaginal repair of stage III-IV cystocele using a lightweight mesh: Safety and 36-month outcome. *Int Urogynecology J*. 2015;26(8):1147-1154.

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11. Antomonov MY. Mathematical processing and analysis of biomedical data. Kyiv: Vidavnistvo Maliy Druk; 2006.
12. Moreno-Egea A, Carrillo-Alcaraz A, Soria-Aledo V. Randomized clinical trial of laparoscopic hernia repair comparing titanium-coated lightweight mesh and medium-weight composite mesh. *Surgical Endoscopy*. 2013;27(1):231-239.
13. Ostrzenski A. Pelvic Organ Prolapse Quantification (POP-Q) system needs revision or abandonment: The anatomy study. *Eur J Obstet Gynecol Reprod Biol*. 2021;267:42-48.
14. Kulkarni M, Rolnik DL, Alexander J, McGannon F, Liu YA, Rosamilia A. Outcomes following sacrocolpopexy using ultralight and lightweight mesh. *Int Urogynecol J*. 2022;33(9):2475-2483.
15. Deng T, Wang S, Liang X, Chen L, Wen Y, Zhang X, et al. Medium- to long-term outcomes of vaginally assisted laparoscopic sacrocolpopexy in the treatment of stage III–IV pelvic organ prolapse. *BMC Women's Health*. 2022;22:503.
16. Schachar JS, Matthews CA. Robotic-assisted repair of pelvic organ prolapse: A scoping review of the literature. *Transl Androl Urol*. 2020;9(2):959-970.
17. Stanford EJ, Mattox TF, Pugh CJ. Outcomes and complications of transvaginal and abdominal custom-shaped light-weight polypropylene mesh used in the repair of pelvic organ prolapse. *J Minimal Invasive Gynecol*. 2011;18(1):64-67.
18. Milani AL, Heidema WM, van der Vloedt WS, Kluivers KB, Withagen MI, Vierhout ME. Vaginal prolapse repair surgery augmented by ultra-lightweight titanium-coated polypropylene mesh. *Eur J Obstet Gynecol Reprod Biol*. 2008;138(2):232-238.
19. Bezhenar VF, Ailamazyan EK, Rulev MV, Bogatyreva EV, Rusina EI, Kvetnoy IM, et al. Efficiency of “Profit Total” system implementation for surgical treatment of decompensated forms of pelvic organ prolapse in women. *J Obstetrics Women's Diseases*. 2011;60(1):21-30.
20. Navruzov SN, Polatova DSh, Gafoor-Akhunov MA, Gabdikarimov KH. The value of marker proteins p53, bcl-2, and Ki-67 in predicting the effectiveness of treatment for osteogenic sarcoma of tubular bones. *Vopr Onkol*. 2012;58(5):691-693.
21. Sahalevych AI, Sergiychuk RV, Ozhohin VV, Khrapchuk AY, Dubovyi YO, Frolov OS. The Modified Procedure of Totally Tubeless PNL. *Int J Biol Biomed Engin*. 2022; 16:82-89.
22. Svyatova GS, Zh Abil'Dinova G, Berezina GM. The frequency, dynamics, and structure of congenital malformations in populations under long-term exposure to ionizing radiation. *Genet*. 2001;37(12):1696-1704.
23. Aktaeva LM, Mirzakhmetova DD, Padaiga Z. Extragenital pathologies of pregnant women in the southern regions of the Republic of Kazakhstan. *Sys Rev Pharm*. 2020;11(4):405-412.
24. Svyatova G, Mirzakhmetova D, Berezina G, Murtazaliyeva A. Immunogenetic aspects of idiopathic recurrent miscarriage in the Kazakh population. *J Med Life*. 2021;14(5):676-682.
25. Lukyanenko NS, Imanmadiyeva DM, Dolinnaya VT, Spaska A. “Clinical masks” of congenital malformations of the urinary system in children of early age. *Int J Health Sci*. 2021;5(3):244-251.
26. Grishin A, Spaska A, Kayumova L. Correction of overactive bladder with botulinum toxin type A (BTX-A). *Toxic*. 2021;200:96-101.
27. Fathi R. Optimization of urolithiasis treatment and diagnosis in the Turkestan region. *J Med Life*. 2022;15(3):344-349.
28. Deffieux X, de Tayrac R, Huel C, Bottero J, Gervaise A, Bonnet K, et al. Vaginal mesh erosion after transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft in 138 women: A comparative study. *Int Urogynecology J Pelvic Floor Dysfunction*. 2007;18(1):73-79.
29. Dobrovanov O, Králinský K, Kovalchuk VP. Ethiological agents of urinal infections and microbial resistance: Retrospective study. *Lek Obz*. 2019;(7):186-190.
30. Nuradilova D, Kaliyeva L, Vaitkiene D, Kalimoldayeva S, Issenova S. Urogenital mixed infections in reproductive-aged women with pelvic inflammatory disease. *Georg Med News*. 2021;(312):114-118.
31. Mamed-Zade GT. Congenital development disorder: The system of data collection. *Georg Med News*. 2009;(166):21-25.
32. Korahanis N, Goron A, Farache C, Panel L, Courtieu C. Transvaginal repair of genital prolapse using a lightweight mesh by the vaginal route. *Progres en Urologie*. 2014;24(8):518-525.
33. Feola A, Abramowitch S, Jallah Z, Stein S, Barone W, Palcsey S, et al. Deterioration in biomechanical properties of the vagina following implantation of a high stiffness prolapse mesh. *BJOG*. 2013a;120(2):224-232.
34. Liang R, Abramowitch S, Knight K, Palcsey S, Nolfi A, Feola A, et al. Vaginal degeneration following implantation of synthetic mesh with increased stiffness. *BJOG: An Internat J Obstet Gynaecol*. 2013;120(2):233-243.
35. Feola A, Barone W, Moalli P, Abramowitch S. Characterizing the ex vivo textile and structural properties of synthetic prolapse mesh products. *Int Urogynecology J*. 2013b;24(4):559-564.

Comparison of Kato Katz and Quantitative Polymerase Chain Reaction Methods in Diagnosing Helminth Infection in Pregnant Women in Enrekang District, Indonesia

Comparación de los Métodos de Kato Katz y de la Reacción en Cadena de la Polimerasa Cuantitativa en el Diagnóstico de la Infección por Helmintos en mujeres embarazadas del Distrito de Enrekang, Indonesia

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SUMMARY

Background: Pregnant women are very vulnerable to diseases, one of which is worm infection. Worm infections in pregnant women affect the fetus's condition, such as the risk of prematurity, low birth weight, and perinatal mortality. The *STH* target set by the World Health Organization (WHO) to be achieved by 2030 is to establish an efficient *STH* control program in adolescents, pregnant, and lactating women in the context of elimination, so a sensitive diagnostic is needed to detect worm infections. This study aims to determine the comparison of examination using

the Kato Katz (KK) and Quantitative Real-Time Polymerase Chain Reaction (qPCR) methods in pregnant women in Enrekang Regency. **Method:** The study was conducted using a cross-sectional design. Samples were selected using a purposive sampling technique according to the criteria set by the researcher as many as 84 respondents. Fecal specimens were collected and examined using the Kato Katz and qPCR methods. Analysis was used to determine the value of sensitivity and specificity with diagnostic tests and kappa values for the value of suitability with a confidence interval of 95 %. **Results:** From the fecal examination, the sensitivity value of Kato Katz and qPCR for Hookworm was 41.67 % and 45.45 %. And for the specificity of Kato Katz and qPCR for

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Hookworm of 91.67 % and 90.41 %. **Conclusion:** qPCR is more sensitive than Kato Katz, so Kato Katz should be used for screening while qPCR is used to assess elimination status.

Keywords: STH, Kato Katz, qPCR.

RESUMEN

Antecedentes: Las mujeres embarazadas son muy vulnerables a las enfermedades, una de las cuales es la infección parasitaria. Las infecciones parasitarias en las embarazadas afectan al estado del feto, como el riesgo de prematuridad, el bajo peso al nacer y el riesgo de mortalidad perinatal. El objetivo fijado por la Organización Mundial de la Salud (OMS) para 2030 es establecer un programa eficaz de control de las enfermedades parasitarias en adolescentes, embarazadas y mujeres lactantes en el contexto de la eliminación, por lo que se necesita un diagnóstico sensible para detectar las infecciones parasitarias. El objetivo de este estudio es determinar la comparación del examen mediante los métodos Kato Katz (KK) y Reacción en Cadena de la Polimerasa en Tiempo Real Cuantitativo (qPCR) en mujeres embarazadas de la regencia de Enrekang. **Método de investigación:** El estudio se llevó a cabo mediante un diseño transversal. Las muestras se seleccionaron mediante la técnica de muestreo intencional, de acuerdo con los criterios establecidos por el investigador, hasta un total de 84 encuestados. Se recogieron muestras fecales y se examinaron mediante los métodos Kato Katz y qPCR. Se utilizaron análisis para determinar el valor de sensibilidad y especificidad con pruebas diagnósticas y valores kappa para el valor de idoneidad con un intervalo de confianza del 95 %. **Resultados:** A partir del examen fecal, el valor de sensibilidad de Kato Katz y qPCR para *Anquilostoma* fue de 41,67 % y 45,45 %. Y para la especificidad de Kato Katz y qPCR para *Anquilostoma* de 91,67 % y 90,41 %. **Conclusión:** la qPCR es más sensible que el Kato Katz, por lo que el Kato Katz debería utilizarse para el cribado, mientras que la qPCR se utiliza para evaluar el estado de eliminación.

Palabras clave: STH, Kato Katz, qPCR.

INTRODUCTION

Soil Transmitted Helminth (STH) infections are transmitted through soil contaminated with human feces. Transmission of intestinal worm infections commonly occurs in areas with poor

hygiene and sanitation. Human infection can occur after coming into contact with contaminated soil, objects, or surfaces, or by ingesting food or drink contaminated with parasite eggs or larvae (1). Worm infections affect food intake, digestion, absorption, and metabolism. Cumulatively, worm infections can result in loss of nutritional requirements due to calorie and protein depletion and blood loss. This can hinder physical development, intelligence, and work productivity and reduce the body's immunity, making it vulnerable to other diseases (2).

Another loss due to worm infections is productive time calculated using the Daily Adjusted Life Years (DAILY) method. Based on the DAILYs calculation, the productive time lost for worm infections caused by *Ascaris lumbricoide* was between 1.2 and 10.5 million, between 1.8 and 22.2 million for *Trichuris trichiura* and between 1.6 and 6.4 million for *Necator americanus* and *Ancylostoma duodenale* (3).

Pregnant women are highly susceptible to diseases, one of which is worm infection. Worm infections in pregnant women affect the fetus's condition, such as the risk of prematurity, low birth weight, and perinatal death. This is because pregnant women experience anaemia due to iron loss which results in the disruption of haemoglobin formation due to decreased food intake and malabsorption of nutrients (Apriyadi, Umasugi and Fitriyani, 2022). The STH target set by the World Health Organization (WHO) to be achieved by 2030 is to establish an efficient STH control program in adolescents, pregnant and lactating women.

Determining the prevalence of helminthiasis infection is done through fecal examination. Kato Katz is a very cost-effective diagnostic method in identifying where to conduct mass drug administration (MDA), the frequency of MDA and assessing the progress of program goals, but compared to the molecular testing method qPCR, the sensitivity of Kato Katz is lower (5)

The microscopic Kato-Katz technique is a relatively simple and low-cost method recommended by the WHO for the detection of STH and other helminth eggs in faecal samples (6,7). Consequently, it is widely used in randomized controlled trials (RCTs),

epidemiological surveys, and surveillance studies to determine the impact of STH interventions. Yet, the technique has considerable shortcomings. There is substantial variation in the readings, resulting from uneven distribution of eggs within a single stool sample (within sample variation), day-to-day fluctuations of egg excretion (between sample variations), and ultimately results depending on the readers' skills and experience (1,4,8). Most importantly, the Kato-Katz method may particularly miss low-intensity infections leading to underestimation of the actual prevalence, but in the case of efficacy trials artificially inflated cure rates (CRs) from undetected residual low-egg count infections post-treatment (8). Moreover, expertise in microscopy is increasingly rare (9,10).

A study conducted by Heredia et al. showed that qPCR showed significantly greater sensitivity ($p < 0.05$) with the ability to detect at least 5 EPGs for all three STH species, compared to 50 EPGs by KK and FF. These results suggest that the diagnostic performance of qPCR should be considered for use in confirmation of transmission interruption and discontinuation of preventive chemotherapy/MDA in areas with low STH prevalence (11).

METHODS

Design

This study was conducted in the working areas of Baroko, Baraka, and Malua Health Centers with the consideration that Baroko Health Center (Puskesmas) with a high endemicity level (66.67%), Barako Health Center with a moderate endemicity level (25%) and Health Center Malua free (0%) based on the results of the 2018 survey in June - July 2023. The research used a cross-sectional study design.

Sample Size Calculation

The population in this study were pregnant women who were registered at the Arok, Baraka, and Malua Health Centers in the period January - April 2023 as men 165. Sample calculation using the formula:

$$\frac{Z^2 \cdot \frac{\alpha P(1-P)N}{1-\frac{\alpha}{2}}}{d^2(N-1) + Z^2 \cdot \frac{\alpha P(1-P)}{1-\frac{\alpha}{2}}}$$

$$= \frac{(1,96)^2(0,47)(0,53)(165)}{(0,05)^2(165) + (1,96)^2(0,47)(0,53)}$$

n = 115

The sample selection was carried out by purposive random sampling according to the criteria made by the researcher, the exclusion criteria were not returning the distributed pots. The number of samples collected was 84 respondents (Figure 1).

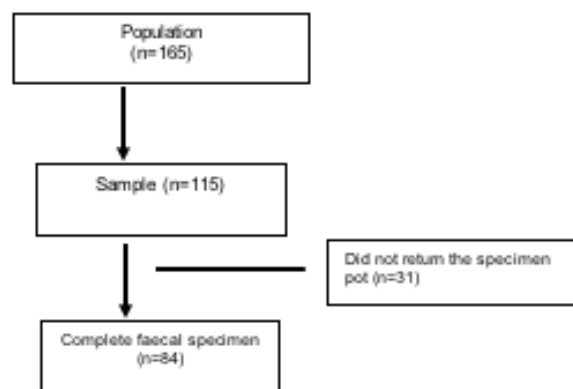


Figure 1. Sample Flowchart.

Data collection on respondent characteristics and faecal samples

An explanation of the study was given during the distribution of the stool pots to pregnant women. The collection of women's faeces was done independently after receiving directions given by the research team assisted by the village midwife. The requirement for specimen collection was that the faeces were not contaminated with liquid materials and soil. Faeces were collected using equipment prepared by the researcher,

namely a screw cap plastic container equipped with a spatula. Fecal samples were collected by respondents by bringing them to the village midwife or the community health center. When the fecal pots were returned, data were collected, and consent was signed. Data collected included characteristics of age, education, occupation, gestational age, number of pregnancies, and Hb levels.

This research involves the examination of stool samples using the Kato-Katz and qPCR methods on the respondents. The steps include meetings with relevant parties for research purposes, distributing stool collection containers, and explaining to pregnant women. The next steps involve village midwives distributing the stool containers to pregnant women, and providing explanations about the purpose of stool sample collection, the collection procedure, storage, and the return schedule. Respondents return the stool containers to the village midwife or the local health center, indicating their consent to participate and signing an informed consent form.

Kato Katz examination

Preparation of Kato Katz specimens was carried out by researchers at the Baroko and Baraka Health Center laboratories. Examination of specimens using the Kato Katz method was carried out by laboratory personnel from the Health Centers of Baroko, Baraka, and Malua and cross-checked directly by the FilCa Program Manager of the South Sulawesi Provincial Health Office.

The Kato-Katz Solution involves the assembly of materials, namely 100 mL of aquadest, 100 mL of glycerol, and 1 mL of either a 3 % malachite green or 3 % methylene blue solution. The 3 % malachite green or methylene blue solution is prepared by meticulously weighing 3 grams of malachite green, introducing it into a glass beaker, gradually adding aquadest, and stirring until a homogeneous 3 % solution is achieved. Subsequently, the Kato-Katz solution is formulated by pouring 100 mL of aquadest into a small plastic container, incrementally introducing 100 mL of glycerol, and 1 mL of the 3 % malachite green or 3 % methylene blue

solution, followed by thorough stirring to yield a 201 mL Kato-Katz solution.

The process of Soaking and Applying Cellophane begins with the preparation of a small plastic container, approximately 15x15x15 cm in size, where the Kato-Katz solution is poured. Cellophane tape, measuring 30x25 mm, is then submerged in the Kato-Katz solution for a duration exceeding 24 hours. When ready for use, tweezers are employed to delicately position the soaked cellophane onto the fecal smear. It is noteworthy that cellophane soaked in the Kato-Katz solution can be utilized over an extended period, provided it remains in a suitable condition and is stored within a sealed container.

The Preparation of Faecal Smears involves the utilization of personal protective equipment (PPE) to minimize the risk of infection. Identification of the sample is marked on a microscope slide using a waterproof marker, ensuring it corresponds with the information on the fecal container. A sheet of wax paper, measuring 10x10 cm, is placed on the table, and a small quantity of feces is deposited on it. Straining of the feces is achieved by positioning a sieve wire on top of the feces and applying pressure with a spatula until the feces has been sufficiently strained. Using a spatula, the strained feces are gathered. A perforated cardboard or plastic piece is placed on a slide, and the strained feces is inserted into the perforation. Carefully lifting the perforated cardboard, the feces is covered with the cellophane that has been soaked in the Kato-Katz solution. Uniform flattening is then performed with a rubber bottle cap, and the slide is allowed to rest for approximately 20 to 30 minutes.

The Microscopic Examination of Intestinal Parasites entails positioning the prepared fecal smear on a microscope slide, ensuring it rests on a level surface. Examination is conducted using a light microscope with either a 10x or 40x objective lens. A comprehensive evaluation of the entire field of view is undertaken, with the counting of eggs by species. This counting facilitates the determination of eggs per gram (EPG) for each identified species, by the appropriate formula.

Eggs

$$EPG = \text{-----} \times 1\,000 \text{ (mg)}$$

Fecal Weight (41,7 grams)

qPCR examination

Specimen preparation with the qPCR method was carried out by Rise Laboratory Staff of the Faculty of Public Health, Hasanuddin University, and the examination was carried out by Rise Laboratory Staff of the Faculty of Public Health, Hasanuddin University at the Makassar Health Laboratory Centre (BBLK) using Biorad CFX 96 equipment. In the DNA extraction process, 250 mg of fresh feces is taken into an Eppendorf tube. Then, 200 μ L of GT buffer and 20 μ L of Proteinase K are added, followed by the disruption of tissue using a Microprestel, and subsequent incubation at 60°C for 30 minutes. After that, 200 μ L of GB buffer is added and vortexed for 5 seconds, followed by another incubation at 60°C for 20 minutes to ensure complete lysis. Following this, 200 μ L of absolute ethanol is added, and the mixture is vortexed for 10 seconds. The next step involves preparing a GD column and transferring all the lysate into it, followed by centrifugation at 16,000 G for 2 minutes. The liquid collected in the collection tube is discarded, and 400 μ L of W1 buffer is added to the GD column, then centrifuged again at 16,000 G for 30 seconds.

The liquid in the collection tube is once more discarded, and 600 μ L of Wash buffer is added to the GD column, followed by centrifugation at 16,000 G for 30 seconds. The GD column is then centrifuged at 16,000 G for 3 minutes to dry it. Subsequently, the GD column is moved to a new Eppendorf tube. Next, 100 μ L of preheated elution buffer is added directly to the matrix. This is allowed to stand for 5 minutes, after which it is centrifuged at 16,000 G for 30 seconds. The eluted DNA in the Eppendorf tube is now ready for PCR analysis.

Data Analysis

The study data were analyzed using Stata Version 14 (StataCorp, 4905 Lakeway Drive College Station, Texas 77845 USA) serial number: 1069939313. The type of test for sensitivity and specificity with the diagnostic test and the suitability value using the kappa coefficient value. Each test used has a Confidence interval (CI) value of 95 % and a p-value <0.05.

RESULTS

Univariate Analysis

Table 1 shows that the largest age group of respondents in this study was the age group 20–30 years as many as 60 respondents (71.43 %) and the lowest at the age of <20 years as many as 4 respondents (4.76 %). Respondents based on the latest education had more high school education as many as 48 respondents (57.14 %) and the lowest percentage of education levels were at the elementary level as many as 1 respondents (1.19 %). Respondents based on occupation, more as housewives namely 73 respondents (86.90 %) and the lowest profession as civil servants (PNS) as many as 5 respondents (5.95 %).

Table 1
Frequency Distribution Based on Demographic Characteristics of Pregnant Women in Enrekang Regency in 2023

Demographic Characteristics	n=84	%
Age Group		
< 20 Years	4	4.76
20 - 30 Years	60	71.43
> 35 Years	20	23.81
Education		
SD	1	1.19
SECONDARY SCHOOL	14	16.67
HIGH SCHOOL	48	57.14
D3	4	4.76
S1 / Equivalent	17	20.24
Jobs		
Housewife	73	86.90
Civil Servant	5	5.95
Employee	6	7.14

Source: Primary Data, 2023

Based on Table 2, the highest gestational age of respondents was trimester as many as 3 respondents (44.05 %) and the lowest was

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in trimester 1 as many as 12 respondents (14.29 %). The highest number of pregnancies or gravida respondents was multigravida as many as 67 respondents (79.76 %). And respondents with non-anaemia status based on hemoglobin levels were 63 respondents (75 %).

The diagnosis of worm infection in respondents is shown in Table 3 for the types of *Ascaris lumbricoides* (roundworm) and *Trichuris trichiura* (whipworm) was not found using either the Kato Katz or qPCR method, only Hookworm (hookworm) was found in the Kato Katz method at 13.10 % and in the qPCR method at 14.29 %.

Table 2

Frequency Distribution Based on Characteristics of Pregnant Women in Enrekang Regency in 2023

Characteristics of Pregnant Women n=84		%
Pregnancy Age		
Trimester 1	12	14.29
Trimester 2	35	41.67
Trimester 3	37	44.05
Gravida		
Primigravida	17	20.24
Multigravida	67	79.76
Anaemia		
Lightweight	16	19.05
Medium	5	5.95
Weight	0	0.00
Not anaemic	63	75.00

Source: Primary Data. 2023

Table 3

Frequency Distribution Based on Diagnosis of Worm Infection by Kato Katz and qPCR Methods in Enrekang District Year 2023

Diagnosis of Worm Infection	Positive		Negative	
	n	%	n	%
Kato Katz				
<i>Ascaris lumbricoides</i>	0	0.00	0	0.00
<i>Trichuris trichiura</i>	0	0.00	0	0.00
Hookworm	11	13.10	73	86.90
qPCR				
<i>Ascaris lumbricoides</i>	0	0.00	0	0.00
<i>Trichuris trichiura</i>	0	0.00	0	0.00
Hookworm	12	14.29	72	85.71

Source: Primary Data. 2023

Bivariate Analysis

In this study. the STH species *Ascaris lumbricoides* and *Trichuris trichiura* were not found so the sensitivity and specificity values were only for Hookworm. Using the Kato Katz method the sensitivity was 42 % (95 % CI) and specificity was 92 % (95 % CI) for Hookworm. While the estimated Positive Predictive Value (PPV) was 45 % (95 % CI) and the Negative Predictive Value (NPV) was 90 % (95 % CI) for

Hookworm. While using the qPCR method; the sensitivity was 45 % (95 % CI) and the specificity was 90 % (95 % CI) for Hookworm; while the estimated Positive Predictive Value (PPV) was 42 % (95 % CI) and Negative Predictive Value (NPV) was 92 % (95 % CI).

The kappa value of 0.34 (p-value=0.0008) indicates that the strength of agreement/ reliability between the Kato Katz and qPCR methods in the diagnosis of Hookworm infection in pregnant women is minimal.

Table 4
Diagnostic Value of Kato Katz and qPCR Method Test in Pregnant Women
in Enrekang Regency in 2023

	Kato Katz		qPCR	
	Sensitivity (%) (95% CI)	Specificity (%) 95% CI)	Sensitivity (%) 95% CI)	Specificity (%) (95% CI)
<i>Ascaris lumbricoides</i>	0(0.00)	0(0.00)	0(0.00)	0(0.00)
<i>Trichuris trichiura</i>	0(0.00)	0(0.00)	0(0.00)	0(0.00)
<i>Hookworm</i>	42(31.52)	92(86.98)	45(35.56)	90(84.97)

Source: Primary Data. 2023

Table 5

Kappa values of Kato Katz and qPCR methods for each STH species in pregnant women in the Enrekang district
Year 2023

	qPCR (+)	qPCR (-)	Kappa (p-value)
<i>Ascaris lumbricoides</i>			
Kato Katz (+)	0 (0.00 %)	0 (0.00 %)	
Kato Katz (-)	0 (0.00 %)	0 (0.00 %)	
<i>Trichuris trichiura</i>			
Kato Katz (+)	0 (0.00 %)	0 (0.00 %)	
Kato Katz (-)	0 (0.00 %)	0 (0.00 %)	
<i>Hookworm</i>			
Kato Katz (+)	5 (5.95 %)	6 (7.14 %)	0.34 (0.0008<0.05)
Kato Katz (-)	7 (8.33 %)	66 (78.57 %)	

Source: Primary Data. 2023

DISCUSSION

This study compares the Kato-Katz and qPCR methods for detecting STH infections in a sample of 84 pregnant women. The examination results obtained using both methods revealed a sensitivity of 41.67 % and specificity of 91.67 % for Hookworms when using the Kato-Katz method, as compared to a sensitivity of 45.45 % and specificity of 90.41 % for Hookworms when using qPCR.

qPCR demonstrates higher sensitivity compared to Kato-Katz, albeit with a marginal difference in sensitivity of 3.78 %. In contrast, Kato-Katz exhibits higher specificity than qPCR, with a difference of 1.26 %.

In a study conducted by Benjamin-Chung et al. (5), which detected three STH species, Kato-Katz demonstrated sensitivities of 49 % for *Ascaris lumbricoide*, 52 % for *Trichuris trichiura*, and 32 % for Hookworm. qPCR sensitivities were 79 % for *Ascaris lumbricoide*, 90 % for *Trichuris trichiura*, and 93 % for Hookworm, with specificities of 97 % for *Trichuris trichiura* and Hookworm, and 97 % for *Ascaris lumbricoides* (5) highly sensitive diagnostics are needed to detect STH infection. We compared double-slide Kato-Katz, the most commonly used copromicroscopic detection method, to multi-parallel quantitative polymerase chain reaction (qPCR). Another study by Mationg et al., 2017, reported qPCR sensitivities of 89.9 % for *Ascaris lumbricoides* and 72.3 % for *Trichuris trichiura*,

while Kato-Katz sensitivities were 30.3 % for *Ascaris lumbricoides* and 44.0 % for *Trichuris trichiura* (12).

A study by Keller et al. (8), indicated sensitivities of 45% for Kato-Katz and 100% for qPCR in detecting *Ascaris lumbricoides*, 52.30% for Kato-Katz and 91.61% for qPCR in detecting *Trichuris trichiura*, and 25.30% for Kato-Katz and 100% for qPCR in detecting Hookworm (8). Additionally, in a study by Dunn et al., 2020, combining Kato-Katz and qPCR results to achieve "true positive" outcomes, Kato-Katz sensitivities were 45.45% for *Ascaris lumbricoides*, 52.30% for *Trichuris trichiura*, and 25.30% for Hookworm, with specificities of 100% for qPCR in detecting *Ascaris lumbricoides*, 91.61% for *Trichuris trichiura*, and 100% for Hookworm (13).

The sensitivity of Kato-Katz for Hookworm in this study, at 41.67 %, is higher than the results of Benjamin-Chung et al. (5), at 32 %, and Keller et al. (8) at 25.30 %. The specificity of Kato-Katz for Hookworm is nearly the same as in other studies, consistently exceeding 90 %. These findings suggest that the results of this study align closely with those of other research in assessing helminth infections using Kato-Katz.

Kato-Katz is commonly used for STH surveillance due to its cost-effectiveness and ease of implementation in resource-constrained settings. However, a significant limitation of this method is that samples must be examined within 30 minutes for Hookworm before the eggs disintegrate and become unobservable under a microscope. Moreover, differentiating between *Necator americanus* and *Ancylostoma duodenale*, which are both types of Hookworm, is not feasible using Kato-Katz due to their morphological similarities.

One of the reasons Kato-Katz is still employed in STH diagnostics is the lack of superior alternative diagnostic methods. Although other microscopic techniques like the McMaster method and FLOTAC exist, they, like Kato-Katz, are hampered by low sensitivity (5,11,14,15).

The lower sensitivity and specificity of Kato-Katz compared to qPCR may be attributed to variations in STH prevalence and infection intensity, different laboratory techniques, and the time lapse between fecal sample collection and

Kato-Katz examination. Laboratory technicians' expertise in identifying STH under a microscope also influences the results. In the Enrekang District, the microscopists at community health centers have not received STH examination-related training in the past three years, which significantly impacts the examination results.

In this study, the prevalence of Hookworm was 14.29 % with the Kato-Katz method and 15.48 % with qPCR among pregnant women. This indicates that the prevalence of STH is higher when using qPCR compared to Kato-Katz.

From the examination results using both methods, a sensitivity of 42 % and specificity of 92 % was obtained for Hookworm using Kato Katz while a sensitivity of 45 % and specificity of 90 % for Hookworm using qPCR. The difference in sensitivity and specificity values for Hookworm between the Kato Katz and qPCR methods was not significantly different.

This is different from previous studies with sensitivity and specificity values that are much different between Kato Katz and qPCR and detect all three types of STH with Kato Katz sensitivity values for *Ascaris lumbricoide* by 49 %. *Trichuris trichiura* (52 %) and Hookworm by 32 %. As for qPCR sensitivity for *Ascaris lumbricoide* (79 %). 90 % for *Trichuris trichiura* and 93 % for Hookworm. Kato Katz specificity is 97 % for *Trichuris trichiura* and Hookworm. 97 % for *Ascaris lumbricoides* while qPCR specificity is 97 % for *Ascaris lumbricoides*, *Trichuris trichiura* and Hookworm (5).

Furthermore, other studies also show that the sensitivity of KK to detect *Ascaris lumbricoides* (45 %), *Trichuris trichiura* (52.30 %), and Hookworm (25.30 %) while the sensitivity of qPCR to detect *Ascaris lumbricoides* (100 %), *Trichuris trichiura* (91.61 %) and for Hookworm is (100 %) (8).

The Kato-Katz method is widely used for STH surveillance because it is inexpensive and relatively easy to perform in resource-poor settings. A significant limitation of this method is that samples must be examined within half an hour for Hookworm before the eggs disintegrate and cannot be seen under a microscope (13).

Hookworm in pregnant women is the highest (78.16 %) which can cause pregnant women to

lose blood as much as 0.005-0.1 mL/day and cause anemia. thus affecting pregnancy due to lack of oxygen intake to the fetus which can cause abnormalities in the fetus (16).

In this study, the type of STH detected was *Hookworm* while *Ascaris lumbricoides* and *Trichuris trichiura* were not found. In line with the results of the study, Enrekang District has implemented *Mass Drug Administration* (MDA) since 2018 until now with coverage of > 80 %, so *Ascaris lumbricoides* and *Trichuris trichiura* are no longer found due to the effectiveness of albendazole during MDA.

A single dose of albendazole and mebendazole on days 14-21 had an average Egg erection rate (ERR) of 94 % and 87.4 % in *Ascaris lumbricoides*. 86.8 % and 40.8 % in *Hookworm* and 44.9 % and 23.8 % in *Trichuris trichiura*, respectively (14).

Efforts are needed to treat *Hookworm* infection by selective treatment of positive cases. So, screening is needed in Enrekang District through the ANC program. All pregnant women attending ANC should have their stool examined so that they can be treated with the WHO standard treatment for pregnant women in trimester 2 of pregnancy.

In addition, with low STH prevalence rates (<20 %) based on the results of this study in Enrekang District using both KK (13.10 %) and qPCR (14.29 %), highly sensitive diagnostics are needed before elimination and to detect re-infection. Although qPCR has a higher cost compared to Kato Katz in achieving elimination, the continued use of low-sensitivity diagnostics may hamper efforts to determine when STH transmission is interrupted which may not necessitate prolonging mass deworming. The cost of prolonged MDA likely outweighs the more expensive diagnostics.

CONCLUSIONS

The sensitivity of qPCR is greater than that of Kato Katz, so for screening Kato Katz can be used, for assessing the effectiveness of MDA. It is necessary to examine using the qPCR method in areas with low prevalence rates.

LIMITATIONS

Limited funds in qPCR examination so that the samples examined are not in all pregnant women. For further research to be carried out with 100 % coverage in pregnant women.

ETHICAL APPROVAL

This research has received ethical approval from the Ethics Committee of the Public Health Faculty, Hasanuddin University with ethics number: 4859/UN4.14.1/TP.01.02/2023

REFERENCES

1. Chong NS, Hardwick RJ, Smith SR, Truscott JE, Anderson RM. A prevalence based transmission model for the study of the epidemiology and control of soil-transmitted helminthiasis. *PLoS One*. 2022;17(8 August):1-28.
2. Nundrisari D. The Relationship Between Environmental Sanitation and Personal Hygiene and the Incidence of Soil-Transmitted Helminthes Infection in Garahan Kidul Plantation Workers. Thesis, Faculty of Medicine, Univ Jember. 2019.
3. Montresor A, Mupfasoni D, Mikhailov A, Mwinzi P, Lucianez A, Jamsheed M, et al. The global progress of soil-transmitted helminthiasis control in 2020 and World Health Organization targets for 2030. *PLoS Negl Trop Dis*. 2020;14(8):1-17.
4. Apriyadi KR, Umasugi MT, Fitriyani E. Risk of Helminthiasis in Pregnant Women. *J Multidisipliner Bharasa*. 2022;1(2):82-91.
5. Benjamin-Chung J, Pilotte N, Ercumen A, Grant JR, Maasch JRMA, Gonzalez AM, et al. Comparison of multi-parallel qPCR and double-slide Kato-Katz for detection of soil-transmitted helminth infection among children in rural Bangladesh. *PLoS Negl Trop Dis*. 2020;14(4):1-23.
6. Bosch F, Palmeirim MS, Ali SM, Ame SM, Hattendorf J, Keiser J. Diagnosis of soil-transmitted helminths using the Kato-Katz technique: What is the influence of stirring, storage time, and storage temperature on stool sample egg counts? *PLoS Negl Trop Dis*. 2021;15(1):e0009032.
7. Liu C, Lu L, Zhang L, Bai Y, Medina A, Rozelle S, et al. More poop, more precision: Improving epidemiologic surveillance of soil-transmitted helminths with multiple fecal sampling using the Kato-Katz technique. *Am J Trop Med Hyg*. 2017;97(3):870.

COMPARISON OF KATO KATZ AND QUANTITATIVE POLYMERASE CHAIN REACTION METHODS

8. Keller L, Patel C, Welsche S, Schindler T, Hürlimann E, Keiser J. Performance of the Kato-Katz method and real-time polymerase chain reaction for the diagnosis of soil-transmitted helminthiasis in the framework of a randomised controlled trial: Treatment efficacy and day-to-day variation. *Parasites and Vectors*. 2020;13(1):1-12.
9. Zelger B, Eisendle K, Mensing C, Zelger B. Detection of spirochetal micro-organisms by focus-floating microscopy in necrobiotic xanthogranuloma. *J Am Acad Dermatol*. 2007;57(6):1026-1030.
10. Caplan J, Niethammer M, Taylor IIR, Czymbek KJ. The power of correlative microscopy: multi-modal, multi-scale, multi-dimensional. *Curr Opin Struct Biol*. 2011;21(5):686-693.
11. Heredia PAZ, Colella V, Hii SF, Traub RJ. Comparison of the egg recovery rates and limit of detection for soil-transmitted helminths using the Kato-Katz thick smear, faecal flotation, and quantitative real-time PCR in human stool. 2021:1-18.
12. Mationg MLS, Gordon CA, Tallo VL, Olveda RM, Alday PP, Reñosa MDC, et al. Status of soil-transmitted helminth infections in schoolchildren in Laguna Province, the Philippines: Determined by parasitological and molecular diagnostic techniques. *PLoS Negl Trop Dis*. 2017;11(11):1-16.
13. Dunn JC, Papaiakovou M, Han KT, Chooneea D, Bettis AA, Wyine NY, et al. The increased sensitivity of qPCR in comparison to Kato-Katz is required for the accurate assessment of the prevalence of soil-transmitted helminth infection in settings that have received multiple rounds of mass drug administration. *Parasites and Vectors*. 2020;13(1):1-11.
14. Oliaro PL, Vaillant MT, Diawara A, Speich B, Albonico M, Utzinger J, et al. Egg excretion indicators for the measurement of soil-transmitted helminth response to treatment. *PLoS Neglected Tropical Diseases*. 2022;16: e0010593.
15. Paniker CJ, Ghosh S. *Medical Parasitology*. Seventh Ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2013.
16. Gebrehiwet MG, Medhaniye AA, Alema HB. Prevalence and associated factors of soil-transmitted helminths among pregnant women attending antenatal care in Maytsebri Primary Hospital, North Ethiopia. *BMC Res Notes*. 2019;12(1):4-9.

COVID-19 y la Mentalidad Universitaria: Un Viaje Prospectivo a través de las Creencias y Actitudes en relación con la Vacunación

COVID-19 and the College Mindset: A Prospective Journey Through Beliefs and Attitudes about Vaccination

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RESUMEN

*Se investigaron las creencias y actitudes de estudiantes universitarios sobre la vacunación contra la COVID-19 y su influencia en la decisión de vacunarse. Se identificaron múltiples factores que afectan estas creencias, como la información recibida, experiencias personales, confianza en autoridades de salud y comunicación pública. Las actitudes también se ven influenciadas por la percepción del riesgo y la importancia de la vacuna. **Objetivo:** Analizar las creencias y actitudes en torno a la inmunización de la COVID-19 en los estudiantes universitarios. **Metodología:** Estudio descriptivo de corte transversal con componente correlacional. La población fue de 15 000 estudiantes universitarios y se utilizó un muestreo aleatorio para encuestar a 115 participantes. Se empleó un cuestionario autoadministrado en formato de escala de Likert. **Resultados:** Los resultados mostraron que alrededor del 45,5 % de los estudiantes consideran importante la vacunación para crear una*

*respuesta inmunológica y controlar la propagación del virus. La responsabilidad en la protección de la salud a través de la vacuna fue compartida por el 69,1 %, mientras que el 21,8 % tuvo dudas sobre la seguridad y no completó todas las dosis. Se encontró correlación entre el número de dosis administradas y las percepciones sobre la vacuna, así como la perspectiva de asumir la responsabilidad en la protección de la salud. **Conclusión:** Los resultados enfatizan la necesidad de considerar diversos aspectos al analizar las creencias sobre la vacunación de la COVID-19 que tienen implicaciones importantes para la educación y comunicación pública en este contexto. **Palabras clave:** Vacunación, COVID-19, estudiante, universitario, creencia, percepción, actitud.*

SUMMARY

We investigated college students' beliefs and attitudes about COVID-19 vaccination and its influence on the decision to get vaccinated. Multiple factors affecting these beliefs were identified, such as information

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received, personal experiences, trust in health authorities, and public communication. Attitudes are also influenced by the perception of risk and the importance of the vaccine. Objective. Analyze beliefs and attitudes around COVID-19 immunization in college students. Methodology: Descriptive cross-sectional study with correlational component. The population was 15 000 college students and random sampling was used to survey 115 participants. A self-administered questionnaire in Likert scale format was used. Results: The results showed that about 45.5 % of students consider vaccination important to create an immune response and control the spread of the virus. The responsibility for health protection through the vaccine was shared by 69.1 %, while 21.8 % had doubts about safety and did not complete all doses. A correlation was found between the number of doses administered and perceptions about the vaccine and the prospect of taking responsibility for health protection. Conclusion: The results emphasize the need to consider various aspects when analyzing beliefs about COVID-19 vaccination and have important implications for education and public communication in this context.

Keywords: Vaccination, COVID-19, student, university, belief, perception, attitude.

INTRODUCCIÓN

Las creencias y percepciones de los estudiantes universitarios sobre la vacunación contra la COVID-19 desempeñan un papel fundamental en su decisión de aceptar o rechazar la vacunación.

Estas creencias y percepciones están influenciadas por una variedad de factores, incluyendo la información que reciben, sus experiencias personales, la confianza en las autoridades de salud y la comunicación pública sobre las vacunas (1-3). Comprender estas creencias y percepciones es esencial para diseñar estrategias efectivas de promoción de la vacunación, entre las cuales se encuentran, por ejemplo, la percepción de riesgo que influye en las creencias estudiantiles acerca de la vacuna contra la COVID-19. Algunos pueden minimizar el riesgo y optar por no vacunarse, mientras que otros consideran la gravedad de la enfermedad como motivo suficiente para vacunarse (4,5). La desconfianza en la ciencia, los efectos secundarios y la transparencia de las autoridades de salud pueden impactar en la elección de

no vacunarse (6-8). La desinformación y los mitos sobre las vacunas contra la COVID-19 influyen en las creencias estudiantiles, sumado a la exposición de información errónea o falsa que se encuentra en línea y en redes sociales distorsionando la percepción de riesgos y beneficios de la vacunación (2,9). La influencia de amigos, familiares y figuras de autoridad en su entorno puede ser crucial en la decisión de recibir la vacuna (7,10-12). Las creencias sobre las vacunas en general también pueden influir en las actitudes de los estudiantes sobre la vacunación contra la COVID-19 (10,13,14). Las creencias y percepciones de estudiantes universitarios sobre la vacunación contra la COVID-19 son diversas y culturalmente influenciadas (7,15,17,18). Abordar estas creencias implica comunicación clara, respaldada por evidencia científica, y considerar aspectos sociales y psicológicos (7,14-16).

Las actitudes de los estudiantes universitarios hacia la vacunación contra la COVID-19 y las posibles barreras que enfrentan, como la falta de acceso, el miedo a los efectos secundarios y las preocupaciones éticas son un factor determinante para las actitudes frente a la inmunización de manera general y más con la COVID-19, donde al inicio de la pandemia se sabía poco o nada acerca de la enfermedad (3,17-20).

Entre los factores más importantes tenemos disposiciones mentales y emocionales como los desafíos propios propuesto por la vacuna. Algunos estudiantes pueden tener actitudes positivas hacia la vacunación contra la COVID-19 debido a su confianza en la ciencia, la protección personal que creen que la vacuna brindará y su deseo de contribuir a la contención de la pandemia, la cual es una percepción compartida independientemente del país analizado (21). Por otro lado, las actitudes negativas debido a preocupaciones sobre los efectos secundarios de la vacuna, la rapidez con la que se desarrollaron las vacunas o la falta de confianza en las autoridades de salud (17,22,23) donde estas actitudes pueden estar influidas por la desinformación y los mitos en torno a las vacunas.

Es por lo que el presente estudio tuvo como objetivo analizar las creencias y actitudes en torno a la inmunización contra la COVID-19 en los estudiantes universitarios.

METODOLOGÍA

El diseño del estudio fue descriptivo de corte transversal con un componente correlacional. La naturaleza descriptiva de la investigación se ha dirigido a caracterizar tanto el avance del esquema de vacunación contra la COVID-19 como las percepciones y actitudes entre los estudiantes universitarios en relación con la vacuna.

Población y Muestra

La población estuvo conformada por todos los estudiantes de los programas de la Universidad Popular del Cesar, aproximadamente 15 000 estudiantes. Para llevar a cabo el estudio, se utilizó un muestreo aleatorio, en el cual los participantes reclutan a nuevos participantes entre sus conocidos. Esta técnica permitió la participación de 115 sujetos de estudio para completar la encuesta con un nivel de confianza del 99 % y un margen de error del 12 %, representando los 18 programas académicos de la universidad. La técnica de recolección de datos fue una encuesta utilizando un cuestionario autoadministrado en formato de escala de Likert con 14 ítems. Los datos recopilados fueron procesados mediante cálculos de estadísticas descriptivas a través de Microsoft Excel 2016 y el programa SPSS 21®.

RESULTADOS

En relación con la Importancia de la Vacunación versus la Importancia de la Inmunización con la Vacuna SARS-CoV-2, aproximadamente el 45,5 % de los estudiantes universitarios creen que la vacunación es importante porque ayuda a proteger a las personas al crear una respuesta inmunológica. Esto puede considerarse como un porcentaje significativo que valora la inmunización para controlar la propagación del virus. En el componente de Creencias sobre la Vacunación Versus las Percepciones o Creencias acerca de la Vacuna SARS-CoV-2, se observa que existe una variedad de creencias. En este sentido, el 64,5 % de los estudiantes creen en la necesidad de la vacuna para fortalecer las defensas y combatir la propagación del virus. Sin

embargo, un 12,7 % tiene una actitud negativa al no creer en las vacunas implementadas contra la COVID-19. También hay un porcentaje que tiene dudas sobre los efectos secundarios (17,3 %) y un pequeño grupo (5,5 %) que confía en el sistema autoinmune natural para combatir el virus. Desde la perspectiva sobre la Protección de la Salud versus Perspectiva de la Responsabilidad en la Protección de su Salud en Torno a la Vacuna SARS-CoV-2, se observó que el 69,1 % de los estudiantes considera que la responsabilidad es propia y optaron por vacunarse y cumplir su esquema de vacunación. Sin embargo, un 21,8 % expresó haber tenido dudas sobre la seguridad de la vacuna y no haber completado todas las dosis (Cuadro 1).

Respecto al Intervalo de Edad versus las Reacciones Adversas Inmediatas de la Vacuna SARS-CoV-2, se evidenció que el cansancio y las náuseas son las reacciones adversas se presentaron en un porcentaje bajo y similar en todos los intervalos de edad, oscilando entre el 0 % y el 1,8 %. Por otro lado, respecto al Desconocimiento de la Información sobre las reacciones adversas es más alto en el intervalo de edades de 18-24 años con un 8,2 % y en las edades de más de 39 años en un 10,9 %. Esto podría indicar que las personas más jóvenes y mayores pueden tener menos conocimiento sobre las posibles reacciones adversas. En relación con el Dolor de Cabeza y Dolor Muscular, estos parecen ser más comunes en el intervalo de edad entre 18-24 años (6,4 %) y entre 25-31 años" (3,6 %). Al evaluar acerca de los efectos relacionados con los Escalofríos y Fiebre se observó una prevalencia baja en el intervalo de edad entre los 18-24 años 4,5 %. Con la fiebre en el intervalo de edad entre los 25-31 años en 1,8 % y en edades de más de 39 años en 2,7 %. Las edades que no experimentaron ningún tipo de reacción adversas se encontraron entre los 18-24 años en un 6,4 %. Es decir, que las reacciones varían según los intervalos de edad con un valor de $p \leq 0,005$ (Cuadro 2).

Los programas académicos en la institución muestran una mayor presencia de estudiantes de Enfermería en un 5,22 % e Instrumentación Quirúrgica en 29,57 %, programas relacionados con la salud. Dado su conocimiento del ámbito médico, es posible que estos estudiantes tengan actitudes más informadas y positivas hacia la

Cuadro 1

Actitudes y Creencias en Estudiantes Universitarios hacia la Vacunación contra la COVID-19 según Género y Otras Variables

	Género					
	Femenino		Masculino		Total	
Género * Vacunado Contra el SARS-CoV-2	n	%	n	%	n	%
Vacunado Contra el SARS-CoV-2						
No	7	6,4	4	3,6	11	10,0
Si	58	52,7	41	37,3	99	90,0
Total	65	59,1	45	40,9	110	100,0
Valor-p				0,507*		
Género * Vacuna Contra SARS-CoV-2 con la cual se Inmunizó						
	n	%	n	%	n	%
AstraZeneca	4	3,6	5	4,5	9	8,2
He combinado marcas de vacunas en mis tres dosis	12	10,9	8	7,3	20	18,2
Janssen/Ad26.COV2.S	7	6,4	5	4,5	12	10,9
Moderna	7	6,4	3	2,7	10	9,1
No me que vacunado	6	5,5	3	2,7	9	8,2
Pfizer/BioNTech	20	18,2	13	11,8	33	30,0
Sinovac	9	8,2	8	7,3	17	15,5
Total	65	59,1	45	40,9	110	100,0
Valor-p				0,936		
Género * Importancia de la Inmunización de la Vacuna SARS-CoV-2 para Controlar la Propagación del Virus						
	n	%	n	%	n	%
Ayuda a no tener graves afecciones posteriores al SARS-CoV-2	9	8,2	12	10,9	21	19,1
Ayuda a no tener graves afecciones posteriores al SARS-CoV-2	1	0,9	0	0,0	1	0,9
Ayuda a proteger a las personas porque crea una respuesta inmunitaria	29	26,4	21	19,1	50	45,5
Desconozco la importancia	6	5,5	4	3,6	10	9,1
La conozco, pero no estoy de acuerdo	10	9,1	4	3,6	14	12,7
Varias de las anteriores	10	9,1	4	3,6	14	12,7
Total	65	59,1	45	40,9	110	100,0
Valor-p				0,444		

Continúa en la pág. 813...

...continuación Cuadro 1. Actitudes y Creencias en Estudiantes Universitarios hacia la Vacunación contra la COVID-19 según Género y Otras Variables

Género * Reacciones Adversas Inmediatas que Produce la Vacuna SARS-CoV-2	Femenino		Masculino		Total
	n	%	n	%	
Cansancio y náuseas	1	0,9	1	0,9	2
Desconozco esta información	8	7,3	4	3,6	12
Dolor de cabeza y dolor muscular	9	8,2	3	2,7	12
Escalofríos y fiebre	3	2,7	2	1,8	5
Fiebre	2	1,8	1	0,9	3
Ninguno de los anteriores	1	0,9	6	5,5	7
Todos los anteriores	41	37,3	28	25,5	69
Total	65	59,1	45	40,9	110
Valor-p				0,277	
Género * Efectos Secundarios que Produce la Vacuna SARS-CoV-2					
	Femenino		Masculino		Total
	n	%	n	%	
Síntomas digestivos: diarrea y dolor de estómago	0	0,0%	1	0,9	1
Síntomas neurológicos: dificultad para concentrarse, dolores de cabeza, problemas para dormir, mareos	2	1,8%	3	2,7	5
Todos los anteriores	25	22,7	19	17,3	44
Trombosis (del seno venoso cerebral)	1	0,9	0	0,0	1
Desconozco esta información	22	20,0	12	10,9	34
Dolor articular o muscular	10	9,1	5	4,5	15
ninguno de los anteriores	4	3,6	1	0,9	5
Ninguno de los anteriores	1	0,9	4	3,6	5
Total	65	59,1	45	40,9	110
Valor-p				0,346	
Género * Percepciones o Creencias Acerca de la Vacuna SARS-CoV-2					
	Femenino		Masculino		Total
	n	%	n	%	
No creo en las vacunas implementadas para inmunizar el virus que produce el SARS-CoV-2	10	9,1	4	3,6	14
Creo que es necesaria, pero conlleva a					

Continúa en la pág. 814...

...continuación Cuadro 1. Actitudes y Creencias en Estudiantes Universitarios hacia la Vacunación contra la COVID-19 según Género y Otras Variables

Género * Percepciones o Creencias Acerca de la Vacuna SARS-CoV-2	Femenino		Masculino		Total	
	n	%	n	%	n	%
efectos secundarios, por tanto, no estoy seguro de los beneficios	13	11,8	6	5,5	19	17,3
Creo que no es necesaria, el sistema autoinmune natural lucha contra el SARS-CoV-2.	3	2,7	3	2,7	6	5,5
Creo que si es necesaria para fortalecer las defensas ante el SARS-CoV-2 para combatir la propagación del virus	39	35,5	32	29,1	71	64,5
Total	65	59,1	45	40,9	110	100,0
Valor-p				0,516		
Género * Perspectiva de la Responsabilidad en la Protección de su Salud en Torno a la Vacuna SARS-CoV-2						
Perspectiva de la Responsabilidad en la Protección de su Salud en Torno a la Vacuna SARS-CoV-2	Femenino		Masculino		Total	
	n	%	n	%	n	%
Considero que la responsabilidad es propia, por tanto, fue mi decisión NO vacunarme a causa de los efectos adversos a corto y largo plazo que podría presentar.	5	4,5	5	4,5	10	9,1
Considero que la responsabilidad es propia, por tanto, fue mi decisión vacunarme y cumplir por completo mi esquema para cuidarme	43	39,1	33	30,0	76	69,1
Sé que es mi responsabilidad el cuidado de la salud, me vacuné, pero no con todas las dosis porque tengo dudas acerca de mi seguridad por la vacuna.	17	15,5	7	6,4	24	21,8
Total	65	59,1	45	40,9	110	100,0
Valor-p				0,385		

n: Frecuencia. %: Porcentaje

inmunización. Los programas relacionados con las ciencias sociales y humanas, las actitudes de los estudiantes podrían variar debido a su enfoque hacia las implicaciones sociales de aplicarse la

vacuna o no. Mientras que los programas de ingeniería serían los estudiantes un poco más analíticos (Cuadro 3).

Cuadro 2

Distribución de Reacciones Adversas Inmediatas de la Vacuna SARS-CoV-2 según Intervalo de Edad

Intervalo de Edad * Reacciones adversas inmediatas que produce la vacuna SARS-CoV-2	Intervalo de Edad								Total		
	Entre 18-24 años		Entre 25-31 años		Entre 32-38 años		Más de 39 años				
	n	%	n	%	n	%	n	%	n	%	
Reacciones adversas inmediatas que produce la vacuna SARS-CoV-2											
Cansancio y náuseas	0	0,0	2	1,8	0	0,0	0	0,0	2	1,8	
Desconozco esta información	9	8,2	2	1,8	0	0,0	1	0,9	12	10,9	
Dolor de cabeza y dolor muscular	7	6,4	4	3,6	0	0,0	1	0,9	12	10,9	
Escalofríos y fiebre	5	4,5	0	0,0	0	0,0	0	0,0	5	4,5	
Fiebre	1	0,9	0	0,0	0	0,0	2	1,8	3	2,7	
Ninguno de los anteriores	5	4,5	1	0,9	1	0,9	0	0,0	7	6,4	
Todos los anteriores	39	35,5	23	20,9	5	4,5	2	1,8	69	62,7	
Total	66	60,0	32	29,1	6	5,5	6	5,5	110	100,0	
Valor-p						0,005					

n: Frecuencia. %: Porcentaje

Cuadro 3

Distribución de Estudiantes por Programa Académico

Programa	Estudiantes N (%)
Licenciatura en Literatura y Lenguas Castellanas	12 (10,43)
Derecho	8 (6,96)
Ingeniería Electrónica	5 (4,35)
Psicología	6 (5,22)
Contaduría	10 (8,70)
Enfermería	6 (5,22)
Instrumentación Quirúrgica	35 (29,57)
Ingeniería Civil	1 (0,87)
Sociología	3 (2,61)
Comercio Internacional	5 (4,35)
Educación Física y Deporte	4 (3,48)
Ing. Sistemas	3 (2,61)
Ing. Ambiental	5 (4,35)
Microbiología	7 (6,09)
Administración de Empresas	4 (3,48)
Licenciatura en Matemáticas	1 (0,87)
Total	115 (100)

n: Frecuencia. %: Porcentaje

La prueba de correlación de Pearson indicó un valor de r negativo de $-0,406$ con un valor de $p \leq 0,005$, lo que indica que las personas que han recibido menos dosis de la vacuna tienden a estar más dispuestas a vacunarse. La correlación entre número de dosis y percepciones o creencias acerca de la vacuna SARS-CoV-2 fue de $-0,485$ con un p -valor $\leq 0,001$. La correlación entre el número de dosis y su perspectiva de la responsabilidad en la protección de su salud en

torno a la vacuna SARS-CoV-2 fue $-0,329$ con un p -valor $\leq 0,001$. La correlación negativa en ambos casos indica que a medida que aumenta el número de dosis administradas de la vacuna contra el SARS-CoV-2, tiende a haber una disminución en las percepciones o creencias positivas acerca de la vacuna y en la perspectiva de asumir la responsabilidad en la protección de la salud a través de la vacunación (Cuadro 4).

Cuadro 4

Correlación de las creencias y actitudes de los universitarios respecto a la vacunación contra el SARS-CoV-2

Correlación	Se ha vacunado contra el SARS-CoV-2.	Número de Dosis	Cuáles son las reacciones adversas inmediatas que produce la vacuna SARS-CoV-2	Percepciones o creencias acerca de la vacuna SARS-CoV-2.
Número de Dosis	-0,406 (0,00)			
La inmunización de la vacuna SARS-CoV-2 es importante para controlar la propagación del virus	-0,357 (0,00)			
La vacuna SARS-CoV-2 produce reacciones adversas inmediatas	0,259 (0,01)			
Cree usted acerca de los efectos secundarios que produce la vacuna SARS-CoV-2			0,428 (0,00)	
Percepciones o creencias acerca de la vacuna SARS-CoV-2.	0,333 (0,00)			
Su perspectiva de la responsabilidad en la protección de su salud en torno a la vacuna SARS-CoV-2	0,268 (0,01)	-0,485 (0,00)		-0,329 (0,00)

(Valor-p)

DISCUSIÓN

El presente estudio ofrece una visión esclarecedora de la compleja relación que existe entre la vacunación contra la COVID-19 y las actitudes de los estudiantes universitarios. Los resultados destacan una correlación significativa entre el número de dosis administradas y las percepciones individuales sobre la vacuna, así como la perspectiva de la responsabilidad en la protección de la salud. Conforme los estudiantes

reciben más dosis, algunos muestran una disminución en la confianza hacia la vacuna y una menor disposición a asumir la responsabilidad de su bienestar a través de la inmunización. Estos hallazgos respaldan investigaciones previas que han resaltado la influencia crucial de la percepción de la vacuna en la aceptación y el cumplimiento de las pautas de inmunización. Esta contribución proporciona información valiosa para profesionales de la salud pública y científicos interesados en mejorar las tasas de vacunación y abordar las inquietudes de las comunidades en

relación con las vacunas (10,13). En conjunto, estudios en Francia, Egipto o Indonesia resaltan la necesidad de abordar de manera personalizada y precisa las preocupaciones de las poblaciones universitarias al diseñar estrategias de promoción de la vacunación que subrayan la importancia de comprender las percepciones de riesgo, las creencias y las barreras asociadas con la vacilación hacia las vacunas en diferentes contextos. Esto puede ayudar a diseñar estrategias de promoción de la vacunación más efectivas y específicas para abordar las preocupaciones de diversas poblaciones y mejorar las tasas de cobertura de vacunación en todo el mundo (24-26). La variabilidad en las actitudes hacia la vacunación, como se evidencia en los estudios realizados en Indonesia, China entre estudiantes de odontología, sugiere que la formación académica y la información recibida en distintas áreas de estudio pueden influir en cómo los individuos perciben la importancia y seguridad de la vacuna como se encontró en nuestros resultados donde la distribución de estudiantes en función de sus programas académicos también resalta posibles tendencias en las actitudes hacia la vacunación. Por lo tanto, es plausible que la educación en diversos campos juegue un papel clave en la formación de actitudes hacia la vacunación, lo que subraya la necesidad de considerar enfoques específicos para abordar la vacilación y promover la aceptación de las vacunas en diferentes grupos académicos. Esto es especialmente relevante en el contexto de la pandemia de COVID-19, donde la vacunación masiva es esencial para controlar la propagación del virus (4,24-31). El artículo sobre la vacunación contra la COVID-19 en adolescentes y adultos jóvenes con diabetes tipo 1 identifica una correlación entre la edad y las reacciones adversas a la vacuna, lo que sugiere que los jóvenes pueden experimentar efectos secundarios con mayor frecuencia (32). Esta relación puede influir en su disposición a recibir dosis adicionales y en su actitud general hacia la vacunación (24,33,34).

Aunque la mayoría de los encuestados reconoce la importancia de la inmunización para controlar la propagación del virus y prevenir afecciones graves, existe un segmento que desconoce esta importancia o no está de acuerdo. Esto subraya la necesidad de una comunicación más efectiva y precisa acerca de los beneficios de la vacunación.

Las reacciones adversas inmediatas y los efectos secundarios también juegan un papel crucial en las actitudes hacia la inmunización. Aquellos que experimentan reacciones adversas pueden mostrar actitudes más negativas, mientras que aquellos que no las experimentan pueden tener una mayor disposición a continuar con la vacunación (21,34-37).

En síntesis, este estudio pone de manifiesto la compleja interacción entre la percepción de la vacuna, el número de dosis, las reacciones adversas y las actitudes hacia la inmunización entre los estudiantes universitarios. Estos hallazgos resaltan la importancia de considerar una variedad de factores al analizar las creencias y actitudes relacionadas con la vacunación contra la COVID-19. Además, estos resultados tienen implicaciones significativas para la educación y la comunicación pública, particularmente en lo que respecta a la relevancia de la vacunación y la seguridad de las vacunas en el contexto actual.

REFERENCIAS

1. Schäfer M, Stark B, Werner AM, Müller LM, Heller S, Reichel JL, et al. Determinants of university students' COVID-19 vaccination intentions and behavior. *Sci Rep.* 2022;12(1):18067.
2. Niu Q, Liu J, Kato M, Shinohara Y, Matsumura N, Aoyama T, et al. Public opinion and sentiment before and at the beginning of COVID-19 vaccinations in Japan: Twitter analysis. *JMIR Infodemiology.* 2022;2(1):e32335.
3. Abdallah DA, Lee CM. Social norms and vaccine uptake: College students' COVID vaccination intentions, attitudes, and estimated peer norms and comparisons with influenza vaccine. *Vaccine.* 2021;39(15):2060-2067.
4. Kelekar AK, Lucia VC, Afonso NM, Mascarenhas AK. COVID-19 vaccine acceptance and hesitancy among dental and medical students. *J Am Dent Assoc.* 2021;152(8):596-603.
5. Sherman SM, Smith LE, Sim J, Amlôt R, Cutts M, Dasch H, et al. COVID-19 vaccination intention in the UK: Results from the COVID-19 vaccination acceptability study (CoVAccS), a nationally representative cross-sectional survey. *Hum Vaccines Immunother.* 2021;17(6):1612-21.
6. Troiano G, Nardi A. Vaccine hesitancy in the era of COVID-19. *Public Health.* 1 de mayo de 2021;194:245-251.

7. Latkin CA, Dayton L, Yi G, Konstantopoulos A, Boodram B. Trust in a COVID-19 vaccine in the US: A social-ecological perspective. *Soc Sci Med.* 2021;270:113684.
8. Gabay G, Tarabieh M. Science and behavioral intentions among Israeli Jewish ultra-Orthodox males: death from COVID-19 or from the COVID-19 vaccine? A thematic study. *Public Underst Sci.* 2022;31(4):410-427.
9. Shmueli L. Predicting intention to receive COVID-19 vaccine among the general population using the health belief model and the theory of planned behavior model. *BMC Public Health.* 2021;21(1):1-13.
10. Yaqub O, Castle-Clarke S, Sevdalis N, Chataway J. Attitudes to vaccination: A critical review. *Soc Sci Med.* 2014;112:1-11.
11. Larson HJ, Clarke RM, Jarrett C, Eckersberger E, Levine Z, Schulz WS, et al. Measuring trust in vaccination: A systematic review. *Hum Vaccines Immunother.* 2018;14(7):1599-609.
12. Brunson EK. The impact of social networks on parents' vaccination decisions. *Pediatrics.* 2013;131(5):e1397-404.
13. Magadmi RM, Kamel FO. Beliefs and barriers associated with COVID-19 vaccination among the general population in Saudi Arabia. *BMC Public Health.* 2021;21(1):1-8.
14. Jennings W, Stoker G, Bunting H, Valgarðsson VO, Gaskell J, Devine D, et al. Lack of trust, conspiracy beliefs, and social media use predict COVID-19 vaccine hesitancy. *Vaccines.* 2021;9(6):593.
15. Urrunaga-Pastor D, Bendezu-Quispe G, Herrera-Añazco P, Uyen-Cateriano A, Toro-Huamanchumo CJ, Rodríguez-Morales AJ, et al. Cross-sectional analysis of COVID-19 vaccine intention, perceptions and hesitancy across Latin America and the Caribbean. *Travel Med Infect Dis.* 2021;41:102059.
16. Caycho-Rodríguez T, Ventura-León J, Valencia PD, Vilca LW, Carbajal-León C, Reyes-Bossio M, et al. What is the support for conspiracy beliefs about COVID-19 vaccines in Latin America? A prospective exploratory study in 13 countries. *Front Psychol.* 2022;13:1885.
17. Al-Mugheed K, Al Rawajfah O, Bani-Issa W, Rababa M. Acceptance, attitudes, and barriers of vaccine booster dose among nursing students: A multicounty survey. *J Nurs Manag.* 2022;30(7):3360-3367.
18. Gallant AJ, Harding A, Johnson C, Steenbeek A, Curran JA. Identifying H1N1 and COVID-19 vaccine hesitancy or refusal among health care providers: A scoping review. *JBI Evid Synth.* 2023;21(5):913.
19. Ruiz JB, Bell RA. Predictors of intention to vaccinate against COVID-19: Results of a nationwide survey. *Vaccine.* 2021;39(7):1080-1086.
20. Goldenberg MJ. Vaccine hesitancy: Public trust, expertise, and the war on science. University of Pittsburgh Press; 2021.
21. Greyling T, Rossouw S. Positive attitudes towards COVID-19 vaccines: A cross-country analysis. *PLOS ONE.* 2022;17(3):e0264994.
22. Qiao S, Tam CC, Li X. Risk exposures, risk perceptions, negative attitudes toward general vaccination, and COVID-19 vaccine acceptance among college students in South Carolina. *Am J Health Promot.* 2022;36(1):175-9.
23. Campo-Arias A, Pedrozo-Pupo JC. Attitude towards COVID-19 vaccines in Colombian university students: Frequency and associated variables. *Acta Bio Medica Atenei Parm.* 2021;92(6).
24. Khouri C, Larabi A, Verger P, Gauna F, Cracowski JL, Ward JK. Exploring the feelings of being at risk of vaccine-related adverse effects: A cross-sectional survey in France. *J Psychosom Res.* 2023;172:111433.
25. Saied SM, Saied EM, Kabbash IA, Abdo SAEF. Vaccine hesitancy: Beliefs and barriers associated with COVID-19 vaccination among Egyptian medical students. *J Med Virol.* 2021;93(7):4280-91.
26. Efendi D, Rifani SR, Milanti A, Efendi F, Wong CL, Rustina Y, et al. The role of knowledge, attitude, confidence, and sociodemographic factors in COVID-19 vaccination adherence among adolescents in Indonesia: A nationwide survey. *Vaccines.* 2022;10(9):1489.
27. Bai W, Cai H, Liu S, Liu H, Qi H, Chen X, et al. Attitudes toward COVID-19 vaccines in Chinese college students. *Int J Biol Sci.* 2021;17(6):1469.
28. Mascarenhas AK, Lucia VC, Kelekar A, Afonso NM. Dental students' attitudes and hesitancy toward COVID-19 vaccine. *J Dent Educ.* 2021;85(9):1504-10.
29. Berry CN, Walker K, Baker N, Trevor-Wright C. "I See a lot of Crazy Things and I Don't Know What to Believe": Lessons Learned about Health Literacy and Strategies for Communicating with Vaccine-Hesitant College Students. *Healthcare.* enero de 2023;11(15):2212.
30. Akhter H, Abdul Rahman AA, Jafarin N, Mohammad Saif AN, Esha BH, Mostafa R. Investigating the barriers that intensify undergraduates' unwillingness to online learning during COVID-19: A study on public universities in a developing country. *Cogent Educ.* 2022;9(1):2028342.
31. Mahmud S, Mohsin M, Khan IA, Mian AU, Zaman MA. Knowledge, beliefs, attitudes and perceived risk about COVID-19 vaccine and determinants of COVID-19 vaccine acceptance in Bangladesh. *PloS One.* 2021;16(9):e0257096.
32. Piccini B, Pessina B, Pezzoli F, Casalini E, Toni S. COVID-19 vaccination in adolescents and young

- adults with type 1 diabetes: Glycemic control and side effects. *Pediatr Diabetes*. 2022;23(4):469-72.
33. Schäfer M, Stark B, Werner AM, Müller LM, Heller S, Reichel JL, et al. Determinants of university students' COVID-19 vaccination intentions and behavior. *Sci Rep*. 2022;12(1):18067.
 34. Riad A, Pokorná A, Klugarová J, Antalová N, Kantorová L, Koščík M, et al. Side effects of mRNA-based COVID-19 vaccines among young adults (18–30 years old): an independent post-marketing study. *Pharmaceuticals*. 2021;14(10):1049.
 35. François G, Duclos P, Margolis H, Lavanchy D, Siegrist CA, Meheus A, et al. Vaccine safety controversies and the future of vaccination programs. *Pediatr Infect Dis J*. 2005;24(11):953-61.
 36. DeRoo SS, Pudalov NJ, Fu LY. Planning for a COVID-19 vaccination program. *Jama*. 2020;323(24):2458-9.
 37. Schoch-Spana M, Brunson EK, Long R, Ruth A, Ravi SJ, Trotochaud M, et al. The public's role in COVID-19 vaccination: Human-centered recommendations to enhance pandemic vaccine awareness, access, and acceptance in the United States. *Vaccine*. 2021;39(40):6004-6012.

Determinants of Anemia in Adolescent Women at Makassar

Determinantes de la Anemia en Mujeres Adolescentes en Makassar

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SUMMARY

Background: Anemia is one of the most common nutritional deficiency disorders which is a serious global public health problem, especially in developing countries, which is estimated to reach 30 %. Anemia is especially prevalent among adolescent girls. The prevalence of anemia according to the World Health Organization (WHO), 2017 ranges from 40-88 %. The results of Basic Health Research (Riskesdas) data in 2018 indicate that the prevalence of anemia increased from 37.1 % in Riskesdas 2013 to 48.9 % in 2018. The purpose of the study was to assess the determinants of anemia in adolescent girls aged 14-17 years at State High School (SMAN) 9 Makassar, Indonesia. **Methods:** The study was conducted at a State Senior High School in Makassar. With cross-sectional design. A total of 211 adolescent girls were selected by proportional random sampling.

Hemoglobin levels were measured using the Easy Touch GCU tool. Measurements of weight with a digital scale and height with a Microtoise height meter. Intake of fat, carbohydrate, protein, iron, folic acid, cobalamin, and ascorbic acid was obtained by 2x24-hour recall method and then calculated with nutrisurvey. Bivariate analysis used a Chi-Square test and multivariate with multiple logistic regression test. **Results:** Respondents who were anemic were 115 people (54.5 %). The results of the bivariate analysis showed that significant variables with anemia were protein ($P=0.056$; $OR=1.783$), iron ($P=0.003$; $OR=2.386$), cobalamin ($P=0.027$; $OR=2.675$), and ascorbic acid ($P=0.010$; $OR=2.103$). The results of multivariate analysis showed that the most influential variables on the incidence of anemia were Iron and cobalamin. **Conclusion:** Iron and cobalamin intake are the most influential variables in the incidence of anemia in adolescent girls at Senior High School Makassar.

Keywords: Anemia, adolescent girls, macronutrient intake, micronutrient intake.

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RESUMEN

Antecedentes: La anemia es uno de los trastornos por deficiencia nutricional más comunes y supone un grave problema de salud pública mundial, especialmente en los países en desarrollo, que se estima que alcanza el 30 %. La anemia es especialmente frecuente entre las adolescentes. La prevalencia de anemia según la Organización Mundial de la Salud (OMS) 2017 oscila entre el 40 % y el 88 %. Los resultados de los datos de la Investigación Básica en Salud (Riskesdas) en 2018 indican que la prevalencia de anemia aumentó del 37,1 % en Riskesdas 2013 al 48,9 % en 2018. El propósito del estudio fue evaluar los determinantes de la anemia en adolescentes de 14 a 17 años en la Escuela Secundaria Estatal (SMAN) 9, Makassar, Indonesia. **Métodos:** El estudio se realizó en Escuela secundaria superior, distrito de Rappocini. Con diseño transversal. Se seleccionó un total de 211 muestras de mujeres jóvenes por muestreo aleatorio proporcional. Los niveles de hemoglobina se midieron con la GCU Easy Touch, las medidas de peso con una balanza digital y la altura con un medidor de altura Microtoise. La ingesta de grasas, carbohidratos, proteínas, hierro, ácido fólico, cobalamina y ácido ascórbico se obtuvo mediante el método de recordatorio de 2 x 24 horas y luego se calculó mediante una nutriencuesta. El análisis bivariado se realizó mediante la prueba de Chi-Cuadrado y multivariante con pruebas de regresión logística múltiple. **Resultados:** Los encuestados que presentaban anemia fueron 115 personas (54,5 %). Los resultados del análisis bivariado encontraron que las variables fueron significativas con la incidencia de anemia proteica ($P=0,056$; $OR=1,783$), hierro ($P=0,003$; $OR=2,386$), cobalamina ($P=0,027$; $OR=2,675$), y ácido ascórbico ($P=0,01$; $OR=2,103$). Los resultados del análisis multivariado mostraron que las variables que más influyeron en la incidencia de anemia fueron el hierro y la cobalamina. **Conclusión:** La ingesta de hierro y cobalamina es la variable que más influye en la incidencia de anemia en mujeres jóvenes en Escuela Secundaria Superior.

Palabras clave: Anemia, mujeres jóvenes, ingesta de macronutrientes, ingesta de micronutrientes

INTRODUCTION

Nutritional deficiencies and poor eating habits established during adolescence can have long-term consequences, including delayed sexual maturation, loss of final adult height, increased disease susceptibility in adulthood, and the risk

of giving birth to a generation with nutritional problems (1).

Growth failure and micronutrient inadequacy, during childhood and adolescence can delay growth and create a high risk of chronic diseases in adulthood. Inadequate nutritional needs, both macronutrients and micronutrients, can cause sub-optimal physical growth, decreased intelligence, decreased work productivity, and decreased endurance, which can result in high rates of infectious diseases and even death. One of the nutritional problems that is still faced by Indonesian people is anemia, which is one of the most common nutritional deficiency disorders being a serious global public health problem leading to low birth weight including morbidities and mortalities of mothers and children in addition to negative consequences on the cognitive and physical development of children, and poor productivity in adults (2).

One of the six global targets for 2025 is a 50 % reduction in the problem of anemia in women of childbearing age (WUS). Currently, anemia is still a public health issue in Indonesia and the trend is increasing. Intervention for anemia needs to be done early during the period of a teenager's life. Interventions during the pregnancy phase tend to be late (3).

Basic Health Research (RISKESDAS) has shown an increase in the prevalence of anemia in the youth group of 15-24 years, from 18.4 % in 2013 to 32 % in 2018. The World Health Organization (WHO), in 2020, recognized iron deficiency anemia as the most common nutritional deficiency in the world and affects 33 % of non-pregnant women, 40 % of pregnant women, and 42 % of adolescents worldwide (4).

According to Briawan, nutritional anemia is caused by iron deficiency, and also deficiency of vitamin A, ascorbic acid, folic acid, or cobalamin, but it is generally assumed that 50 % of anemia cases are caused by iron deficiency. Iron deficiency in general can occur due to increased demand for iron in the body. Anemia, mainly caused by insufficient intake of food sources of iron, is the most common nutritional disorder and generally occurs in young women (5).

The emergence of anemia can be caused by the depletion of iron stores that may result from blood

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loss, decreased intake, impaired absorption, or increased demand, irregular and unbalanced with the adequacy of the nutritional sources needed by the body including energy intake, protein intake, carbohydrate intake, fat intake, ascorbic acid, and especially lack of food sources that contain iron and folic acid. Additional factors that can cause anemia are deficiency of folic acid, deficiency of vitamins B12 (cobalamin) and vitamin C (ascorbic acid), chronic disease, nutritional status, length of menstruation, educational level of parents, level of knowledge, and economic level (6).

Iron is essential to produce hemoglobin. Intake of macronutrients such as protein plays a role in iron storage and transportation. Apart from iron intake, micronutrients such as folic acid and vitamin B12 are also related to body hemoglobin levels. Food intake needs to be considered related to the amount of nutritional intake that enters the body (7).

Data show the high prevalence of anemia and indicate several factors that cause anemia in young girls such as parents' education, family income, nutritional status, nutritional intake, physical activity, menstrual patterns, and eating patterns. In this regard, little is known about the prevalence of anemia in adolescents in Rappocini District, Makassar City, especially at the Senior High School of Makassar. Based on the Central Bureau of Statistics, Rappocini Subdistrict is one of the subdistricts with the poorest households or middle and lower socioeconomic households. Secondary data from Basic Education Data indicate that Rappocini Subdistrict is the Subdistrict with the highest number of students. Thus, this study aimed to assess the determinants of anemia in adolescent girls aged 14-17 years at State High School (SMAN) 9 Makassar, Indonesia.

METHODS

This research was conducted using the observational method using a cross-sectional design. Was conducted at senior high school Makassar, Rappocini District in August-February 2023. The population was students of class X and XI at Senior High School Makassar. The total number was 449 students. The sample in

this study is representative of the population and meets the inclusion criteria. Sampling was obtained based on the calculation of the Slovin formula (8), and 211 respondents were selected using proportional random sampling. Data collection was performed by 2x24 hour recall which was carried out in no sequence and the value of hemoglobin levels was obtained from venous blood sampling with an easy touch digital device. Bivariate data analysis used the Chi-Square test and multivariate analysis, was performed using multiple linear regression tests.

RESULTS

As shown in Table 1, out of 211 respondents, most adolescent girls were in the age category of 16 years as many as 89 people (42.2 %), and the lowest age value was in the age category of 14 years, as many as 21 people (10.0 %).

Most of the nutritional status of adolescent girls was in the good nutrition category as many as 133 people (63.0 %) and the less nutritional status was in the overnutrition category as many as 8 people (3.8 %).

Meanwhile, adolescent girls who experienced anemia were 115 people (54.5 %) and not anemic as many as 96 people (45.5 %).

Table 1
Table of characteristics of respondents

Age	n	%
14	21	10
15	79	37.4
16	89	42.2
17	22	10.4
Nutritional Status		
Good Nutrition	133	63
Malnutrition	53	25.1
Overnutrition	8	3.8
Obesity	17	8.1
Anemia Incidence		
Anemia (<12 g/dL)	115	54.5
Not Anemia (<12 g/dL)	96	45.5
Total	211	100

Source: Primary Data, 2023

Based on Table 2, the distribution of macronutrient intake in young girls at Senior High School Makassar was, in fat intake 163 (77.3 %) respondents experienced deficient fat intake. For carbohydrates, there were 195 (92.4 %) respondents who experienced deficient intake while 16 (7.6) had a normal intake. The respondents who were deficient in protein were 148 people (70.1 %).

As for micronutrients, for iron intake 133 (63.0 %) respondents were deficient in iron intake. For folic acid, 211 (100 %) respondents had deficient intake. As for Cobalamin, 187 (88.6 %) respondents presented a deficient intake. For Ascorbic acid, there were 141 (66.8 %) respondents whose intake was deficient.

Table 2

Distribution of Macro and Micro Intake in Young Girls at SMAN 9 Makassar

Macronutrients Intake	N	%
Fat		
Less	163	77.3
Enough	48	22.7
Carbohydrate		
Less	195	92.4
Enough	16	7.6
Protein		
Less	148	70.1
Enough	63	29.9
Micronutrients Intake		
Iron		
Less	133	63.0
Enough	64	30.3
Folic Acid		
Less	211	100
Enough	0	0
Cobalamin		
Less	187	88.6
Enough	24	11.4
Ascorbic acid		
Less	141	66.8
Enough	70	33.2
Total	211	100.0

Source: Primary Data, 2023.

According to Table 3, the variables that were statistically significant in the incidence of anemia were protein in macronutrients, and iron, cobalamin, and ascorbic acid for micronutrients. The results of the study showed that from a total of 148 female adolescents with insufficient protein intake, 87 (58.8 %) had anemia, while 61 (41.2 %) did not manifest anemia. The results of the Chi-Square test obtained a $p = 0.056$ (OR: 1.783), $p < 0.05$, which means that H_a is accepted and H_0 is rejected so that it can be concluded that there is a relationship between protein intake and the incidence of anemia. Adolescent girls who have a deficiency in protein intake are 1.783 times more at risk of developing anemia than female adolescents who have sufficient protein intake.

Iron deficiency intake was shown in a total of 133 adolescent girls, from which 83 (62.4 %) experienced anemia and 50 (37.6 %) did not present anemia. In the group with an adequate level of iron intake, 32 people (41.0 %) showed anemia. Chi-Square test results obtained $p = 0.003$ (OR: 2.386), $p < 0.05$, which means H_a is accepted and H_0 is rejected so it can be concluded that there is a relationship between iron intake and the incidence of anemia. Adolescent girls who have deficient iron intake are 2.386 times more at risk of presenting anemia than adolescent girls who have adequate iron intake.

In addition, a total of 187 adolescent girls experienced a deficit of cobalamin intake, and from those 107 (57.2 %) experienced anemia. While from a total of 24 persons with a sufficient level of cobalamin intake, there were 8 people (33.3 %) who presented anemia. Chi-Square test results obtained a of $p = 0.027$ (OR: 2.675) $p < 0.05$ which means H_a is accepted and H_0 is rejected so it can be concluded that there is a relationship between cobalamin intake and the incidence of anemia. Adolescent girls who have less cobalamin intake are 2.675 more at risk of anemia than adolescent girls who have sufficient cobalamin intake.

As for a total of 134 adolescent girls who experienced a deficient intake of ascorbic acid, anemia intake was present in 82 (61.2 %), while in 77 people who had sufficient levels of ascorbic acid intake still 33 people (42.9 %) experienced anemia. Chi-Square test results obtained $p = 0.010$ (OR: 2.103) $p < 0.05$, which means H_a is accepted and H_0 is rejected so it can be concluded

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Table 3
Relationship of independent variables with Anemia Incidence

Variable	Anemia Incident						P-value	OR	95 % CI	
	Anemia n	%	Not Anemia n	%	Total n	%			Lower- Upper	
MACRO-NUTRIENTS										
Fat										
Not Enough	94	57.7	69	42.3	163	100	0.089	1.752	0.915-3.353	
Enough	21	43.8	27	56.3	48	100				
Carbohydrate										
Not Enough	108	55.4	87	44.6	195	100	0.369	1.596	0.571-4.459	
Enough	7	43.8	9	56.3	16	100				
Protein										
Not Enough	87	58.8	61	41.2	148	100	0.056	1.783	0.983-3.232	
Enough	28	44.4	35	56.6	63	100				
MICRO-NUTRIENTS										
Iron										
Not Enough	83	62.4	50	37.6	133	100	0.003	2.386	1.347-4.226	
Enough	32	41.0	46	59.0	78	100				
Cobalamin										
Not Enough	107	57.2	80	42.8	187	100	0.027	2.675	1.091-6.558	
Enough	8	33.3	16	66.7	24	100				
Ascorbic acid										
Not Enough	82	61.2	52	38.8	134	100	0.010	2.103	1.190-3.716	
Enough	33	42.9	44	57.1	77	100				

*Chi-Square Test.

that there is a relationship between ascorbic acid intake and the incidence of anemia. Adolescent girls who have less ascorbic acid intake are 2.103 more at risk of anemia than adolescent girls who have sufficient ascorbic acid intake is sufficient.

The multiple logistic regression results are presented in Table 4. Show that in Step 1, the

variable that has an association with the incidence of anemia in adolescent girls is protein for macronutrient intake ($p = 0.05 < 0.05$). As for micronutrients, there is an association with the incidence of anemia among adolescent girls with iron ($p = 0.003 < 0.05$), vitamin B12 ($p = 0.032 < 0.05$), and ascorbic acid ($p = 0.010 < 0.05$).

Table 4
Results of Multivariate Analysis of the Most Influential Variable with the Incidence of Anemia

Variable	Coef	Std. Err	Wald	P-value	OR	95 % CI	
						Lower	Upper
Step I							
Macronutrient Intake							
Fat	0.561	0.331	2.862	0.091	1.752	0.915	3.353
Protein	0.578	0.304	3.627	0.057*	1.783	0.983	3.232
Micronutrient intake							
Iron	0.870	0.292	8.895	0.003*	2.386	1.347	4.226
Cobalamin	0.984	0.458	4.625	0.032*	2.675	1.091	6.558
Ascorbic acid	0.734	0.291	6.539	0.010*	2.103	1.190	3.716

*Regression Logistik Test

The multiple logistic regression analysis results are shown in Table 5. In Step 2, it can be seen that the variable has a $p < 0.05$ the micronutrient intake variables are iron and cobalamin, so the logistic regression results are considered as the final stage. This means that these variables are considered the most influential variables in the occurrence of anemia in adolescent girls at senior high school in Makassar.

Adolescent girls with insufficient iron intake had a 2.531 times greater risk (95 % CI: 1.396-4.590) of anemia compared to those with sufficient intake. As for cobalamin, adolescent girls with insufficient Vitamin B12 intake had a 2.532 times greater risk (95 % CI: 0.990-6.480) of anemia compared to adolescents with sufficient intake.

Table 5
Results of Multivariate Analysis of Variables Most Influential with the Incidence of Anemia

Variable	Coef	Std. Err	Wald	P-value	OR	95 % CI	
						Lower	Upper
Step II							
Micronutrient- Intake							
Iron	0.929	0.304	9.347	0.002*	2.531	1.396	4.590
Cobalamin	0.929	0.479	3.756	0.053	2.532	0.990	6.480
Cons	-3.189	1.017	9.821	0.002*	0.041		

*Regression Logistic Test.

DISCUSSION

Nutritional status is considered a physiological state of an individual, which results from the relationship between nutrient intake and requirements, and from the body's ability to digest, absorb, and use these nutrients (9). This study was undertaken to assess the relationship between macro- and micronutrient intake and the prevalence of anemia in adolescent girls at a Superior High School. It was found that from a total of 211 adolescent girls, 115 people (54,5 %) experienced anemia, while 96 respondents (45.5 %) did not. Most of the respondents showed deficient categories of nutrient intake (fat, carbohydrates, protein, iron, folic acid, vitamin B12, and vitamin C).

There was no relationship between fat intake and the incidence of anemia. Fat is a source of energy for growth and activity. Low fat intake will result in unfulfilled energy, besides that low

animal fat intake will also affect iron and zinc intake. This is because animal food is a source of iron and zinc (10). This study is in line with research conducted by Kurniasih et al., who found that there is no relationship between fat intake and the incidence of anemia (7).

For carbohydrate intake, the results obtained with the Chi-Square test indicate that there is no relationship between carbohydrate intake and the incidence of anemia. So it is concluded that there is no significant relationship between carbohydrate intake and hemoglobin levels and the higher the carbohydrate content, the lower the hemoglobin level, and vice versa (7). Carbohydrates are the main source of energy for the needs of cells and body tissues. There are some tissues such as the nervous system and erythrocytes that only use carbohydrates as a source of energy (11).

There was a relationship between protein intake and the incidence of anemia. Protein plays an important role in iron transportation

in the body. A deficit of protein intake will cause iron transportation to be inhibited so that iron deficiency will occur. Iron absorption that occurs in the small intestine is assisted by protein transporters, namely transferrin, and ferritin. Transferrin contains ferrous iron which functions to transport iron to the bone marrow for hemoglobin formation (12). This research is in line with research conducted on adolescent girls at SMA Negeri 7 Bengkulu City in 2022, where it was found that of 17 adolescent girls with insufficient protein intake, 14 adolescent girls (82.4 %) suffered from anemia. While out of 18 adolescent girls with sufficient protein intake, there were 2 adolescent girls (11.1 %) suffering from anemia. This data demonstrated that there is a relationship between protein intake and the incidence of anemia (13).

As for iron micronutrients, in the present study, it was shown that there was a relationship between iron intake and the incidence of anemia. Hemoglobin is a complex compound of iron. It is the protein molecule in red blood cells that carries oxygen from the lungs to the body's tissues and returns carbon dioxide from the tissues back to the lungs. It is made up of four protein molecules (globulin chains) that are connected. Some factors that can affect hemoglobin levels in the body include gender, age, diet, and systemic diseases. Hemoglobin levels in the body must be at the threshold of normal values if a person's hemoglobin level decreases (<12 gram/dL) it can lead to anemia (14). Adequate iron stores will fulfill the need for red blood cell formation in the bone marrow.

This study is in line with the study of Rahfiludin et al., who stated that there is a correlation between iron and hemoglobin levels due to the lack of consumption of animal foods that contain iron with higher bioavailability (15). Similarly, Sholicha et al., at SMA 1 Gresik, showed that there is a relationship between iron intake and anemia (16). Furthermore, Azizah, in the Jatinangor area found that respondents who did not meet iron adequacy reached 93.6 % (88 people) and those who met iron adequacy were 6.4 % (6 people) (17).

Since iron is required for a number of diverse cellular functions, a constant balance between iron uptake, transport, storage, and utilization

is required to maintain iron homeostasis. When the amount of iron stores is reduced and the intake of iron consumed is low, the balance of iron is disturbed, as a result, the hemoglobin level drops below the normal value resulting in iron nutritional anemia. Iron deficiency anemia arises when the balance of iron intake, iron stores, and the body's loss of iron are insufficient to fully support the production of erythrocytes. Iron deficiency anemia rarely causes death, but the impact on human health is significant. Iron deficiency anemia symptoms are usually nonspecific. Red blood cells tend to be microcytic and hypochromic, and iron stores are low, as shown by low serum ferritin and low serum iron levels with high serum total iron-binding capacity (10).

It was found that there was a relationship between cobalamin intake and the incidence of anemia with the Chi-Square test of a $p < 0.027$ ($p < 0.05$). These results are in concordance with Ayuningtyas et al., who in a study of 58 female students indicated that there are differences in cobalamin intake based on anemia status ($p = 0.004$) (18). Also, the results are in line with Nasution et al., in their study performed on 116 adolescent girls, in which they concluded that the most dominant factors influencing the incidence of anemia in junior high school girls were the average intake of cobalamin and nutritional knowledge scores. Cobalamin intake and good nutritional knowledge can reduce the incidence of anemia in adolescent girls by 2.04 times and 1.65 times, respectively (19).

Cobalamin has a function that is closely related to folate or folic acid. Cobalamin is needed to convert folate into its active form. Folate deficiency will cause impaired maturation of erythrocyte nuclei, resulting in blood cells of abnormal shape and size. Cobalamin is one of the most essential vitamins in adolescence, as its function is closely related to the formation of red blood cells. Cobalamin deficiency is generally caused by poor absorption. This vitamin deficiency can lead to pernicious anemia, which is the result of poor absorption of cobalamin. The condition of the body with a deficit of cobalamin will cause a disturbance in the bone marrow which causes the bone marrow to be unable to produce erythrocyte cells normally and causes limitations on hemoglobin transport (20). Cobalamin intake

is closely related to the formation of blood cells in the body. The more cobalamin intake in adolescent girls will be directly proportional to the hemoglobin level in their blood, and vice versa, the less cobalamin content in the body will cause low hemoglobin levels in the blood. Cobalamin deficiency in adolescents is generally caused by the lack of cobalamin sources such as liver, meat, shrimp, and shellfish. Minimal intake of animal-source foods will cause a cobalamin deficit because cobalamin is most commonly found in animal-source foods (20).

For ascorbic acid, the Chi-Square test results showed a $p < 0.010$, indicating that there is a relationship between ascorbic acid intake and the incidence of anemia. These results are in concordance with research conducted on 28 students (87.5 %) showing that they did not experience anemia when there was an ascorbic acid intake. Their results showed that there was no relationship between ascorbic acid intake and the incidence of anemia ($p > 0.05$). Ascorbic acid facilitates iron absorption by forming a chelate with ferric iron at an acid pH that remains soluble at the alkaline pH of the duodenum. Absorption of iron in non-heme form increases fourfold in the presence of ascorbic acid because ascorbic acid moves iron from transferrin in the plasma to liver ferritin. This is why ascorbic acid indirectly affects hemoglobin levels. Deficiency of ascorbic acid intake increases susceptibility to infections due to the antioxidant function of ascorbic acid (16).

In the multivariate analysis, it was found that the most influential variables with the incidence of anemia among adolescent girls at senior high school Makassar were Iron and Cobalamin intake.

CONCLUSION

1. There was a relationship between macro-nutrient intake (protein) and the incidence of anemia among adolescent girls at Senior High School Makassar.
2. There was a relationship between the intake of micronutrients (iron, cobalamin, and ascorbic acid) with the incidence of anemia among adolescent girls at Senior High School Makassar.

3. Intake of iron and cobalamin are the most influential variables on the incidence of anemia in adolescent girls at Senior High School, in Makassar, Indonesia.

Suggestions

1. It is recommended an intervention by sectors related to increasing the intake of nutrients affecting anemia such as protein, iron, folic acid, cobalamin, and ascorbic acid, as with high bioavailability in the diet of young women, implementing food diversification, iron supplementation, and increasing knowledge about iron-rich food sources. The program iron tablet supplementation in young women should be a priority program.
2. For the prevention of anemia, it is recommended the continuous evaluation of hemoglobin blood levels in the School Health Unit, counseling about anemia, and correct consumption patterns related to the consumption of food sources.
3. Young women should be advised to take part in counseling activities about health, actively seek information on health and balanced nutritional food from the media and be more aware of the importance of consuming food sources that prevent anemia.

REFERENCES

1. Kemenkes. National Nutrition Day Activity Guide. Jakarta; 2021.
2. Raptauli N. Factors Associated with Anemia Status in Young Women in the City of Depok in 2011 (Secondary Data Analysis of the Anemia Survey of Young Women at the Depok City Health Office in 2011). University of Indonesia, 2015. Available in: <http://lib.ui.ac.id/opac/ui/detail.jsp?id=20293028&lokasi=lokal>
3. Nadiyah, Dewanti LP, Mulyani Ey, Jus'at I. Nutritional Anemia: Limitations and Consequences of Indonesian Intervention Policy Restricted to Iron and Folic Acid. *Asia Pac J Clin Nutr.* 2020;29:55-73.
4. Bull Fc, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 Guidelines on Physical Activity and Sedentary Behaviour. *Br J Sports Med.* 2020;54(24):1451-1462.
5. Briawan D. Anemia is a nutritional problem in female adolescents. Jakarta: Egc; 2013.

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6. Makan P. Literature Review: Relationship of Diet with Anemia Incidence in Young Women. *J Holistics and Health Sciences*. 2021;3(2).
7. Kurniasih E, Kuswari M, Nuzrina R. Connection Intake of Macro Nutrients (Protein, Fat, Carbohydrates) and Substances Micronutrients (Iron, Folic Acid, Vitamin B12) with Levels Hemoglobin of Female Futsal Athletes, University of Education Indonesia Bandung. *J Gizi Dan Kesehatan Manusia (J Nutrition and Human Health)*. 2022;2(1):
8. Dahlan Ms. *Statistics for Medicine and Health*. Jakarta: Salemba Medika; 2016.
9. Supariasa. *Nutritional Status Assessment*. Jakarta: Egcc; 2002.
10. Gerber GF. Iron Deficiency Anemia (Anemia of Chronic Blood Loss; Chlorosis). *MSD Manual Professional Version*. 2023. Available in: <https://www.msmanuals.com/professional/hematology-and-oncology/anemias-caused-by-deficient-erythropoiesis/iron-deficiency-anemia>
11. Restuti AN, Susindra Y. The Relationship Between Nutritional Intake and Nutritional Status and the Incident of Anemia in Adolescent Women. *Innovation Scientific J*. 2017;16(3).
12. Geoffrey. *Dietary Supplements and Funcional Foods*. Uk: Blackwell; 2006.
13. Ayunita Triananda. Relationship between iron, protein and vitamin C intake with the incidence of anemia in young women at SMA Negeri 7 Bengkulu City in 2022 [Thesis]. Bengkulu Ministry of Health Polytechnic; 2022.
14. Sinta Novita S, Rostika F. The Effect of Giving Sardine Fish Crackers on Hemoglobin Levels of Young Girls at the Dempo Darul Muttaqien Islamic Boarding School (PPDDM) Pagaram City. Sriwijaya University [Thesis]. 2021.
15. Rahfiludin Mz, Arso SP, Joko T, Asna Af, Murwani R, Hidayanti L. Plant-Based Diet and Iron Deficiency Anemia in Sundanese Adolescent Girls at Islamic Boarding Schools In Indonesia. *J Nutr Metab*. 2021;2021:1-7.
16. Almaratus Sholicha C, Muniroh L. Correlation Between Intake of Iron, Protein, Vitamin C And Menstruation Pattern with Haemoglobin Concentration Among Adolescent Girls In Senior High School I Manyar Gresik. *Media Gizi Indonesia*. 2019;14(2):147-153.
17. Azizah Di. Intake of Iron, Folic Acid, and Vitamin C in Young Women in the Jatinangor Area. *J Vocational Health*. 2020;4(4):169.
18. Ayuningtyas IN, Arif Tsany AFA, Candra A, Dieny FF. Analysis of Heme and Non-Heme Iron Intake, Vitamin B12 and Folate as Well As Iron Enhancer and Inhibitor Intake Based on Anemia Status in Santriwati. *J Nutrition College*. 2022;11(2):171-181.
19. Suraidah Nasution, Ida Nurhayati, Ade Indah Dwicahya. Determinant Factors Associated with the Incidence of Anemia in Adolescent Girls at Lubukpakam Middle School. *Jurnal Ilmiah Panmed*. 2020;15(1):140-145.
20. Nugroho MR, Sartika RAD. Intake of Vitamin B12 Against Megaloblastic Anemia in Vegetarians at the Meitriya Khirti Temple in Palembang. *J Community Health*. 2018;4(2):40-45.

Differentiated diagnostic and surgical algorithm for isolated and combined Chiari malformation Type I

Diagnóstico diferencial y algoritmo quirúrgico para malformación de Chiari Tipo I aislada y combinada

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SUMMARY

Introduction: Arnold-Chiari malformation (ACM) type I is a craniovertebral junction pathology with ectopy of the cerebellar tonsils through the great occipital foramen with compression of the brain stem and upper cervical spinal cord. Until now, there have been more than 20 types of surgical interventions for the Arnold-Chiari malformation type. **Objective:** The main purpose of this research is the decompression of craniovertebral stem structures and occipital foramen, and the search for effective methods to repair cerebrospinal fluid (CSF) circulation. **Methods:** The complex examination and surgical treatment at the Neurosurgery Department No. 1 of the National Hospital of the Ministry of Health of the Kyrgyz Republic (Bishkek, Kyrgyzstan) passed 201 patients (aged 16-74)

with symptomatic ACM I from 2008 to 2020. **Results:** Regression of preoperative clinical symptomatology was detected in 117 cases (58%), significant reduction of hypertension and vestibulo-ataxic disturbances in 76 cases (38%), and stabilization of the process with preservation of focal damages in 8 cases (4%). In 10 (5%) cases, there was syringomyelia progression, for which syringosubarachnoid shunting was carried out in the second stage. In the presence of a tight filum terminale syndrome detected in 4 (2%) patients, the first step was excision of the filum terminale followed by regression of clinical manifestations. The most effective results of surgical interventions were obtained when the pathogenetic approach was followed, in particular, the cerebrospinal fluid flow repair during craniocervical decompression; a regression of both the underlying disease and concomitant pathologies was achieved.

Keywords: Cerebrospinal fluid, syringomyelia, hydrocephalus, craniocervical decompression, craniovertebral junction.

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RESUMEN

Introducción: La malformación de Arnold-Chiari tipo I es una patología de la unión craneovertebral con ectopía de las amígdalas cerebelosas a través del gran agujero occipital con compresión del tronco encefálico y la médula espinal cervical superior. Hasta el momento, existen más de 20 tipos de intervenciones quirúrgicas en malformaciones tipo Arnold-Chiari. **Objetivo:** El objetivo principal de esta investigación es la descompresión de las estructuras del tallo

craneovertebral y el agujero occipital, y la búsqueda de métodos efectivos para reparar la circulación del líquido cefalorraquídeo (LCR). Métodos: El examen complejo y el tratamiento quirúrgico en el Departamento de Neurocirugía No. 1 del Hospital Nacional del Ministerio de Salud de la República Kirguisa (Bishkek, Kirguistán) pasaron 201 pacientes (de 16 a 74 años) con ACM I sintomático de 2008 a 2020. Resultados: Se detectó regresión de la sintomatología clínica preoperatoria en 117 casos (58 %), reducción significativa de la hipertensión y alteraciones vestibuloatáxicas en 76 casos (38 %), estabilización del proceso con preservación de daños focales en 8 casos (4 %). En 10 (5 %) casos hubo progresión de la siringomielia, por lo que se realizó derivación siringosubaracnoidea en la segunda etapa. Ante la presencia de un síndrome de filum terminale apretado detectado en 4 (2 %) pacientes, el primer paso fue la escisión del filum terminale seguido de la regresión de las manifestaciones clínicas. Los resultados más efectivos de las intervenciones quirúrgicas se obtuvieron cuando se siguió el enfoque patogénico, en particular, la reparación del flujo de líquido cefalorraquídeo durante la descompresión craneocervical; se logró una regresión tanto de la enfermedad de base como de las patologías concomitantes.

Palabras clave: Líquido cefalorraquídeo, siringomielia, hidrocefalia, descompresión craneocervical, Unión craneovertebral.

INTRODUCTION

Arnold-Chiari malformation (ACM) type I stands as a distinctive and intricate craniovertebral junction (CVJ) pathology that engenders a significant impact on neurological health (1). This malformation manifests through the displacement of the cerebellar tonsils, vital components of the brain responsible for balance and coordination, downward through the great occipital foramen (2). As researchers continue to delve into the nuances of ACM type I, insights into the underlying pathophysiology and the dynamic relationship between the brain, spinal cord, and surrounding structures are continually being refined, paving the way for improved diagnostic techniques, treatment strategies, and ultimately, enhanced patient outcomes (3,4).

The history of the study of ACM morphology and its corresponding symptomatology is well

known (5,6). Meanwhile, this malformation aetiology and pathogenesis remain controversial; however, all discussions are based on the disembryogenetic theory (7,8). Neuroimaging advanced techniques have dramatically increased the number of patients with this pathology in neurosurgical institutions. Pre- and postoperative brain magnetic-resonance (MRI) capabilities using different modules with the assessment of cerebrospinal fluid (CSF) circulation and hemodynamics have significantly expanded the range of surgical interventions in ACM (9).

The foundation for ACM development is rooted in disturbances during fetal cerebellar formation. Genetic factors play a pivotal role in embryogenesis, particularly genes associated with paraxial mesoderm differentiation, such as *GDF7*, *GDF3*, *ALDH1A2*, *FLT1*, and *CDX1* (10). The inadequate development of the occipital bone derived from the paraxial mesoderm leads to the improper formation of the small posterior cranial fossa, contributing to ACM. However, the precise genetic underpinnings remain to be fully elucidated, likely involving multiple gene mutations working in a complex interplay (11). Embryonic asphyxia and respiratory infections further contribute as triggers for malformation. The pathophysiology involves several mechanisms, including elevated intracranial pressure, ventricular fluid accumulation, skull constriction and hindbrain herniation, spinal canal pressure reduction, spinal cord compression, and abnormal atlantoaxial joint mobility, often linked to connective tissue anomalies.

Surgical interventions for ACM I primarily aim to decompress craniovertebral structures and restore CSF circulation. The decompression of the great occipital foramen, often combined with duraplasty, is a common approach to reestablish cerebrospinal fluid flow through the foramen magnum (12). Although the first decompression surgery dates back to 1930 by Dutch surgeon Graafthdijk (1), the diverse morphological variations in the CVJ region result in a polymorphic array of clinical manifestations, especially in conjunction with conditions like syringomyelia, hydrocephalus, and fixed terminal filum (13). Consequently, a standardized algorithm for surgical intervention methods in ACM I remains elusive. Despite the proposal of over 20 surgical

approaches, a consensus is lacking regarding the optimal timing, sequencing, and evaluation criteria for multistage interventions (14).

This paper aims to identify and establish the most effective set of criteria for choosing appropriate diagnostic and treatment methods. The primary objectives of this study revolve around overcoming key challenges to achieve its overarching purpose. These objectives encompass the comprehensive collection and analysis of patient data, both in isolated cases of ACM I and when coexisting with other anomalies. Additionally, the study assessed patients' conditions before surgical interventions, monitor their statuses following these procedures, and meaningfully interpret the outcomes.

MATERIALS AND METHODS

The results of the complex examination and surgical treatment of 201 patients with symptomatic ACM I treated at the Neurosurgery Department No. 1 of the National Hospital of the Ministry of Health of the Kyrgyz Republic (Bishkek, Kyrgyzstan) from 2008 to 2020, aged 16-74 years were analysed (Figure 1).

All patients had magnetic resonance (MR) imaging of the brain and CVJ, sometimes to the lumbosacral region, to eliminate syringomyelia and tethering syndrome associated with ACM I. The degree of cerebellar ectopia into the subarachnoid space of the spinal cord was

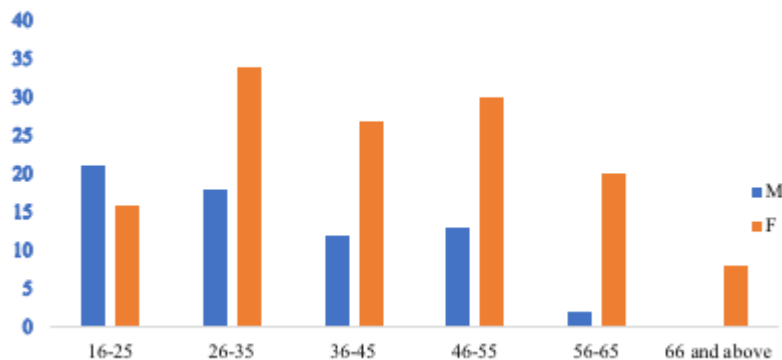


Figure 1. Distribution by gender and age of patients with symptomatic ACM I.

determined by the Chamberlain line (the line connecting the edge of the hard palate and opisthion) and the eligibility criteria for patients was a descent of more than 5 mm. In the last 3 years, phase-contrast cardiac synchronized MR trials to study CSF circulation (studied in 20 patients) and MR angiography were performed. To clarify bone changes, the patients underwent computed tomography with topometry.

All patients in this group took the examination algorithm (Figure 2).

Upon completion of the algorithm for examination of patients with ACM I, a detailed diagnosis of ACM I was made, which determined the tactics of surgical treatment of the patient. Excel spreadsheets were used to process the data. The work was performed in compliance with all ethical standards and under conditions of non-disclosure. Before the start, the patients were informed about the goals of the work, its plan, and the manipulations foreseen for the performance. All methods have not been introduced for the first time but were used earlier in other institutions.

DIFFERENTIATED DIAGNOSTIC AND SURGICAL ALGORITHM

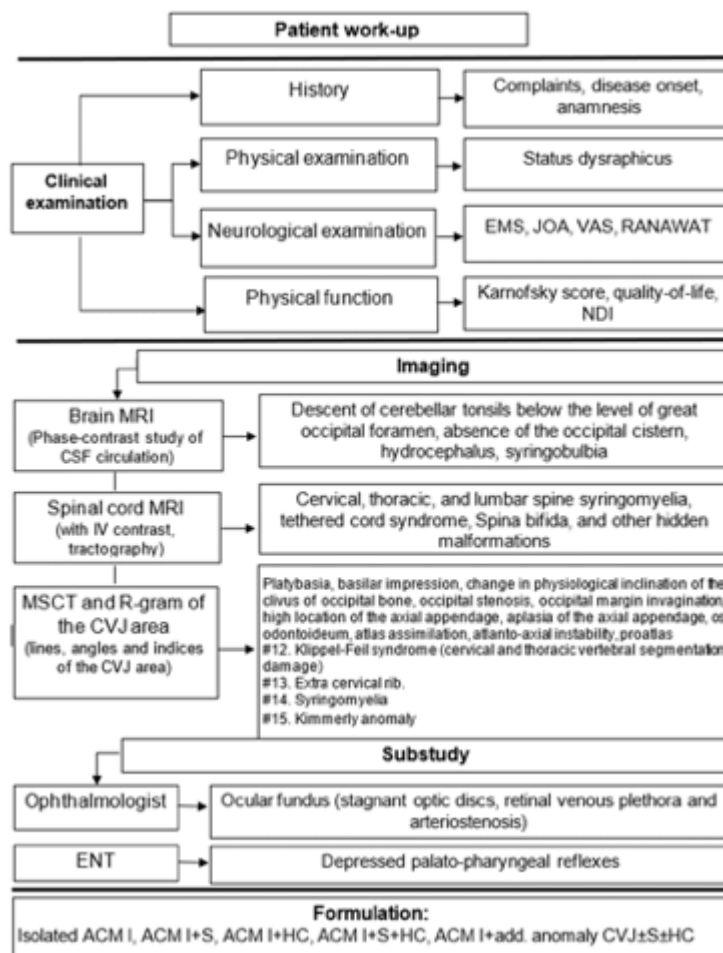


Figure 2. Algorithm of complex examination of a patient with ACM type I

Note: HC – hydrocephalus, S – syringomyelia). ACM I – Arnold-Chiari I type, S – syringomyelia, HC – hydrocephalus, CVJ – Cranio-vertebral junction.

RESULTS

During the objective examination, in more than half of the patients – 113 (56 %), different signs of dysraphic status were found: kyphoscoliosis, gothic palate, different position of auricles and shoulder blades, short neck, keeled and funnel chest, flatfoot, facial asymmetry. Comorbid bone structure anomalies of the craniovertebral area were found in this group of patients (Table 1).

Status dysraphicus and common comorbid bone anomaly in the craniovertebral region are

Table 1

The incidence of associated ACM I craniovertebral junction anomalies

Anomaly	Quantity	%
Bone anomaly of the cranio-vertebral region		
Platybasia (flattening of the skull base)	18	8.9
Basilar impression	3	1.5
Elevation of the odontoid process	1	0.5
Kimmerly anomaly	8	4

quite common in the ACM I group. No correlation was found between the cerebellar tonsil ectopia below the Chamberlain line on brain sagittal MR imaging and the above-mentioned changes. In almost all patients, the disease manifested with pain in the cervico-occipital region, intensifying with coughing, with progression, accompanied by nausea and vomiting. Then vestibulo-attachment disorders with obnubilations associated with

congestive changes on the ocular fundus joined. As the disease progressed, bulbar disorders with dysarthria, dysphagia, and dysphonia were defined. Extreme manifestations of motor disorders were di-tetraparesis with sensory impairment, more often dissociated. The highly variable clinical symptoms in the patients were summarized in Table 2.

Table 2
ACM I clinical manifestations in a group of patients. Distinguished syndromically by symptoms

Syndromes	Manifestations
Hypertension syndrome – 193 (96%)	Pain in the cervico-occipital region, intensifying with coughing, diffuse bursting headaches, nausea, vomiting; photo and noise phobia at the headache maximum
Vestibulo-ataxic (cerebellar) – 169 (84%)	Dizziness, shaky walk
Focal syndromes:	
1) Movement abnormalities – 48 (24%)	Paresis, changes in reflexes.
2) Sensory abnormalities – 32 (16%)	Impaired sensibility.
3) Pelvic abnormalities – 12 (6%)	Disorder of diuresis and defecation,
4) Bulbar abnormalities – 16 (8%)	Dysarthria, dysphagia, dysphonia.

The dependence of ACM I clinical manifestations on cerebellar tonsil ectopia

through the great occipital foramen is shown in Figure 3.

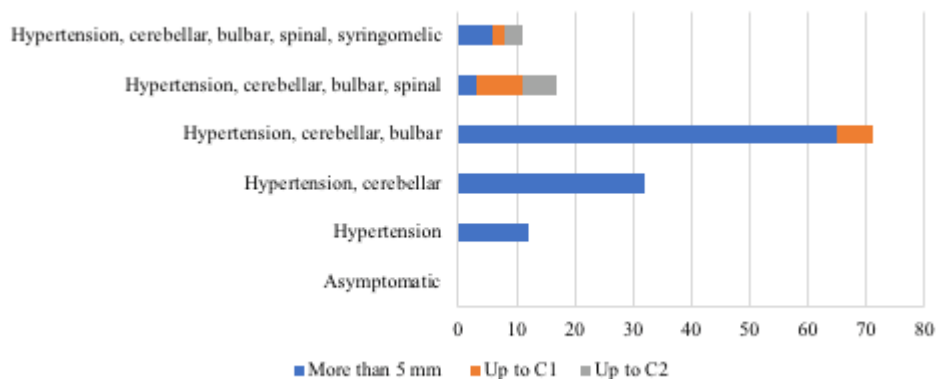


Figure 3. ACM I clinical manifestations depend on the degree of cerebellar amygdala prolapse below the level of the great occipital foramen.

All surgeries were performed in the Concorde-type supine position, with conservative resection of the posterior margin of the greater occipital foramen (3×3 cm) and laminectomy of the C1 vertebra, or otherwise craniocervical decompression (CCD) without duroplasty. The scope of surgical intervention in the clinic has undergone a certain development with experience. Initial CCD without duroplasty is performed extremely rarely, the area of decompression of the occipital bone is markedly

reduced. The optimal size is considered to be 3×3 cm, to prevent prolapse of the cerebellar tissue into the CVJ area and prevent craniocervical instability. It should be noted that isolated CCD without duroplasty often leads to dynamic changes directly in the subarachnoid space up to the elimination of the cerebellar tonsils' ectopy with their spontaneous "return" to the vacated cisterna cerebellomodularis. However, the above-described scope of surgical intervention was often insufficient (Figure 4).

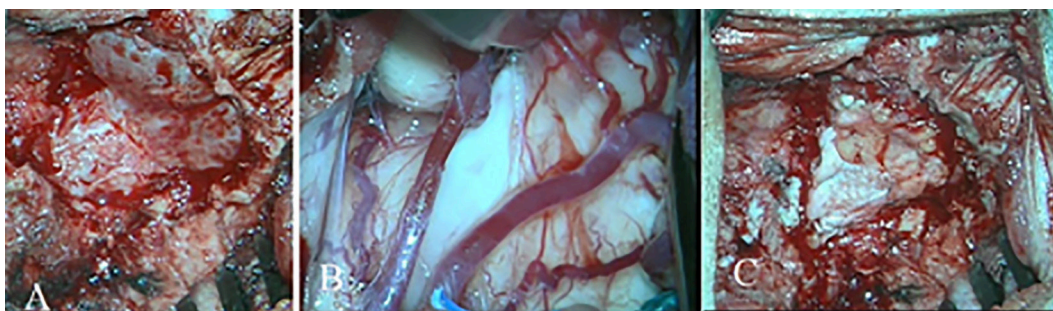


Figure 4. The main stages of surgery.

Note: A – Bone decompression with conservative resection of the occipital bone and C1 vertebral arch. B – Revision of the posterior cranial fossa with the main anatomical structures' visualization, adhesiolysis, and repair of CSF flow; C – Dura mater plastic repair by autograft from the fasciae latae.

After the duramater incision, the arachnoid membrane was examined. In the absence of visible changes in the arachnoid membrane and visualization of the structures involved, the surgery was completed by dura mater plasty, in 70 cases (35 %). Thus, the further scope of surgical intervention changes accordingly. In the case of severe adhesions, the arachnoid meninges were dissected and meningoradiculomyelolysis was performed throughout with the repair of CSF flow. Magendie's foramen was inspected for patency in 109 cases (54 %). If there was a strangulation sulcus on the descended cerebellar tonsils below the C1 vertebral arch, their subpial resection with enlargement of Magendie's foramen was performed. Then the surgery was also completed with dura mater plasty of the fasciae latae. The edges of the dissected arachnoid meninges were sutured to the dura mater to prevent scarring and adhesion. Most often, the duramater was sutured after plasty to tighten it to the surrounding bone structures to prevent adhesions and early formation of the cisterna cerebellomodularis.

No stents in Magendie's foramen or artificial sheaths were used. Relatively small accesses, up to 6-7 cm in length, and careful layer-by-layer suturing of muscles and subcutaneous fat made it possible to achieve adequate sealing and prevent liquorrhea. On the day following the intervention, a lumbar puncture was performed to sanitize the cerebrospinal fluid (CSF).

Afterward, the patients had control MRI examinations in 3-6 months. In the presence of superior cervical syringomyelia with severe neurological symptoms, the above surgery was supplemented with syringostomy at one time. Follow-up studies were conducted from 6 months to 12 years. According to the obtained data, complete regression of preoperative clinical symptomatology was detected in 117 cases (58 %), significant reduction of hypertension and vestibulo-ataxic disturbances in 76 cases (38 %), stabilization of the process with preservation of focal disturbances in 8 cases (4 %). There was no postoperative mortality (Figure 5).

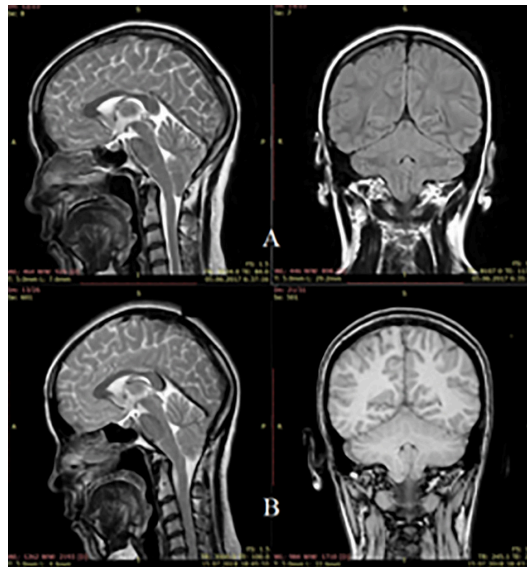


Figure 5. Brain MRI (T1-2 mode in the sagittal and frontal planes) of a patient with isolated Arnold-Chiari malformation type I before and after CCD with revision of the posterior cranial fossa and duroplasty.
 Note: A – The descent of the cerebellar tonsils below the level of the foramen magnum by 11 mm; B – Formation of the occipital cistern, liquor flow restored.

When ACM I was combined with spinal cord syringomyelia, 80 cases (40 %), assumed to be the first stage of CVJ surgery, it resulted in a

spontaneous reduction of syringomyelia severity, and the second stage of surgery, syringostomy obviated in 9 (4.5 %) patients (Figure 6).

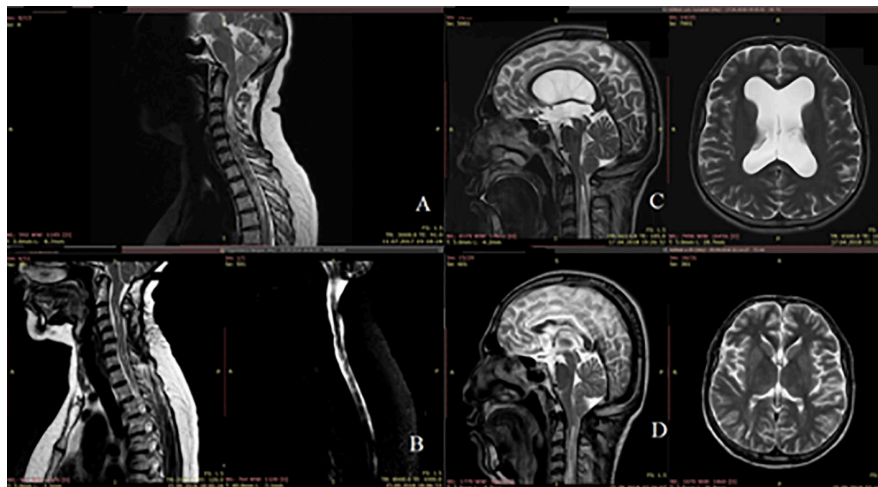


Figure 6. Brain and cervical spine MRI, T2 mode.
 Note: A – Expansion of the central canal of the spinal cord and descent of the tonsils of the cerebellum by 8 mm before surgery; B – the result of syringomyelic cyst regression after craniocervical decompression, the result after 6 months; C – Total expansion of the ventricles of the brain due to a block at the level of the foramen of Mogendie before surgery; D – positive dynamics in the form of syringomyelic cyst reduction after ventriculo-peritoneal shunting with concomitant hydrocephalus, the result after 3 months.

A total of 59 (29.4 %) patients had reduced syringomyelia in ACM I+S. In 10 cases (5 %), progression of syringomyelia with increasing motor, sensory, and pelvic disorders was noted in the control MRI study from 1 to 3 months, for which syringo-subarachnoid shunting was performed as the second stage, provided there was no block at the Majandi level (based on the phase-contrast MRI study). In these patients, regression of syringomyelitic cysts with the repair of neurological functions was noted in all of them at 3 months of follow-up.

The next associated ACM I pathology was hydrocephalus in 10 cases (5 %), which spontaneously regressed in half of the patients. Five patients underwent VP shunting (Figure 6), and all patients achieved hydrocephalus regression. In the presence of a tight filum terminale syndrome detected in 4 patients (2 %), the first step was excision of the filum terminale followed by regression of clinical manifestations. A number of patients had complications such as lycvoria in 3 cases (1.5 %), and in 2 patients (1 %) secondary bacterial meningitis developed in the early postoperative period. These complications were eliminated during an inpatient period.

Overall, the impact of comorbidities such as hypertension, diabetes mellitus, and other chronic diseases on the course of Arnold-Chiari malformation type 1 (ACM I) and treatment outcomes represents a significant area of research. Chronic conditions like hypertension and diabetes can impact overall health and potentially complicate treatment and recovery processes. Hypertension, for instance, may exacerbate symptoms related to cerebrovascular function and increase the risk of complications during surgery. Diabetes can affect wound healing, immune responses, and overall recovery after surgical interventions. Moreover, these comorbidities might influence the response to surgical treatments, as well as the overall effectiveness of decompression and symptom alleviation.

Also, it is important to note that thorough rehabilitation after surgical interventions for Arnold-Chiari malformation type I (ACM I) is essential to enhance the effectiveness of long-term treatment results. Postoperative recovery entails physical therapy to improve mobility, muscle strength, and posture, addressing discomfort

and muscle atrophy. Neurological rehabilitation targets deficits in coordination, sensation, and muscle function, aiding neuromuscular re-education and functional independence. Pain management techniques alleviate immediate discomfort while contributing to long-term pain reduction. Addressing potential cerebrospinal fluid-related complications and hydrocephalus management through education and close monitoring is integral. Additionally, psychological support and coping strategies enhance patients' psychosocial well-being, collectively ensuring that rehabilitation plays a pivotal role in minimizing complications, promoting recovery, and elevating the overall quality of life for ACM I patients.

DISCUSSION

Despite a better understanding of the pathogenetic mechanisms, significant improvement in diagnostic methods, a large number of clinical studies performed, and accumulated experience, the management of patients with Chiari malformation type I remains unresolved. The main works carried out in different countries recognize the inexpediency of surgical treatment in asymptomatic ACM I (15). Patients with brainstem and cranial nerve dysfunction, as well as hydro syringomyelia associated with ACM I, require surgical treatment (16). The wide range of surgical interventions in ACM I demonstrates the versatility of morphological changes accompanying this pathology. The previously prevailing CCD with duroplasty still is the basic surgical approach, which is applicable in most patients with ACM I and is performed by most neurosurgeons (17,18). The findings of these papers agree with the findings of this article regarding the importance of surgical intervention in specific cases of CM1. However, the author's study focuses on comorbid craniovertebral anomalies and details postoperative outcomes, while the second study recognizes the global consensus on surgical strategies and the popularity of MCC.

Preoperative detailing of morphological changes in ACM I determines the basic strategy in planning surgery and the tactics of intervention are determined directly during surgery (19). The

changes detected during surgery in the subdural and subarachnoid spaces of the CVJ determine its final volume. Many authors suggest not to dissect the arachnoid membrane if there are no obstacles at the level of Magendie's foramen, being sure of good CSF permeability for the prevention of subsequent postoperative adhesions (20). Most authors recommend duroplasty to form a cisterna cerebellomedullaris with artificial sheaths, which, in their opinion, simplifies the surgery and is a reliable way to prevent scarring and adhesions. For this purpose, duroplasty with autotissue from the fasciae latae was applied, fixing its dome to the periosteum of the occipital bone (21). Previous studies and the current study agree on the symptoms of Chiari malformation type 1, such as hypertension, movement disorders, and cranial nerve damage, with the severity of symptoms correlating with cerebellar amygdala prolapse. However, the papers differ in the description of postoperative outcomes, treatment of complications, and surgical techniques.

The latter measure with a proper microsurgical technique without bleeding allows satisfactory clinical results. In addition, the use of autologous tissue reduces the risk of liquorrhea due to better edge sealing during suturing and early healing. The use of a proper microsurgical technique indicates that the surgery is being performed with high magnification and precision using specialized instruments. Microsurgery allows the surgeon to work on delicate structures with minimal tissue damage, reducing the risk of bleeding. This is crucial in surgeries involving sensitive areas like the brain or spinal cord. The choice of this technique is also justified by the fact that it leads to satisfactory clinical outcomes. This means that the technique has proven to be effective in achieving the desired results for patients.

The connection between ACM I and syringomyelia is well-known. However, the treatment strategy for syringomyelia in these patients also remains controversial (22). Many neurosurgeons prefer a pathogenetic approach, suggesting that the repair of CSF flow eliminates CSF dynamic abnormalities in the CVJ and leads to syringomyelia regression. This principle causes the disappearance or reduction of syringomyelia up to 90 % (23). In the absence of results from

the first stage of intervention and the rapid progression of syringomyelia, many authors recommend syringo-subarachnoid shunting. The results obtained in the present study confirm the feasibility of this algorithm (24). However, there is also the opposite tactic of patient management, when syringostomy and even syringo-peritoneal shunting is the first-line therapy in the case of extensive and large syringomyelic cavities. This may be considered a less rational strategy, and it could be used only in exceptional cases of the "avalanche" phenomenon of spinal and bulbar disorders (25). All the sources, including the author's work, underline the complex challenges in managing ACM I patients and highlight ongoing debates within the medical community regarding optimal treatment pathways.

The work of Liang et al., also proved the effectiveness of surgical correction with the inclusion of duroplasty in the case of Arnold-Chiari type I malformation (26). During surgery, compression of the tonsils, cerebellar hemisphere, and bone tissue was detected in most patients. Decompression of the large occipital foramen and craniocervical department was performed in parallel with the removal of the atlanto-occipital membrane. At the same time, patients underwent a resection of the arachnoid membrane of the cerebellar-medullary fissure. Afterward, an artificial dura mater implant was installed. The last two manipulations were introduced to expand the posterior fossa without resection of the cerebellar tonsils and shunting. The operation was performed for 21 patients with subsequent monitoring of their condition for 6-36 months after the intervention. In 15 cases, syringomyelia was recorded, but in all these cases there was a significant relief of the symptom. Among the complications, osteocompression of the cerebellar hemisphere was observed in 12 patients; in 18 cases – the appearance of a thickened tissue ring, which was fixed between the cerebellar hemisphere and the arachnoid membrane. No fatalities have been recorded. Thus, artificial duroplasty in this case became an alternative to shunting. Comparatively, both studies underscore the complexity of ACM I and the diverse symptomatology associated with the condition. They highlight the importance of tailored surgical approaches to address various manifestations.

Marković et al. described a case of atypical Arnold-Chiari type I malformation without syringomyelia (27). The patient suffered from movement coordination disorder for 6 years. During the last 7 months, the gait has worsened and mild quadriplegia has been added to the symptomatology with a dominant mobility disorder of the lower limbs. The damage to the cranial nerves has been diagnosed immediately before the operation. During the surgical intervention, resection of the posterior arch of the first cervical vertebra and C2 laminectomy, microsurgical displacement of the tonsils, and an artificial dura mater implant were performed. The result of the intervention was a significant improvement in the patient's condition. In children, only 15 % of Arnold-Chiari type I malformation manifests itself as symptoms. In such cases, surgical intervention is recommended for dysfunction of cranial nerves and nerves of the brain stem, loss of sensitivity, syringomyelia, and occipital pain, provided with radiological detection of malformation. Targeted surgical intervention, as in the case of adult patients, also includes decompression by removing the occipital bone, the posterior margin of the foramen magnum, and a part of the posterior arch of C1. In specific cases, it is possible to remove part of the cervical vertebrae, and cerebellar tonsils, and use Dural plastic surgery. Usually, the operation is completed within 2-3 hours. The rare complications after surgery are represented by spasms of the neck muscles, which are eliminated by muscle relaxants; development of infection, and liquorrhea (28-30). Although these studies focus on ACM I and surgical interventions, they differ in patient populations, symptom correlations, outcomes, and focus. Together, these studies make valuable contributions to understanding the complexities and nuances of treating ACM I given the different patient profiles and manifestations.

While surgical resection remains the primary treatment for solid tumor malignancies, it is well established that surgery alone is often inadequate for achieving long-term cures. In cancers such as breast, colon, and lung, relapse rates remain high even after apparently complete surgical removal of the primary tumor (31,32). The high risk of recurrence is attributable to micrometastases and residual

localized disease not eliminated by surgery. Therefore, careful post-surgical monitoring and consideration of adjuvant therapies are critical for preventing progression. Administration of systemic chemotherapy or radiation as adjuvant therapy plays a key role in eradicating microscopic residual disease and improving outcomes. Additionally, there is increasing recognition that lifestyle factors including diet, physical activity, smoking cessation, and stress reduction can favorably impact cancer recurrence risks (33-35). Such lifestyle changes may act by inhibiting microscopic tumor growth, reducing inflammation, and improving overall health.

Detecting relapse at the earliest possible point is also crucial, as a disease that is caught early is more likely to be responsive to salvage therapy. Intensive radiographic and clinical follow-up in the post-surgical setting allows prompt identification of progression while therapeutic options are still viable. Though surveillance protocols vary by cancer type, regular cross-sectional imaging and biomarker testing generally facilitate the earliest possible diagnosis of recurrent disease. Management of surgically-treated malignancies does not end with the operation itself. Only through diligent long-term monitoring, selective administration of adjuvant therapy, promotion of lifestyle changes, and a multidisciplinary commitment can the risk of relapse be minimized.

Surgical intervention in ACM is associated with a wide range of intraoperative and postoperative complications. Adherence to anatomical access with cutting along the white line of the muscular complex of the cervico-occipital area, delicate periosteal dissection of the CVJ bone structures with careful haemostasis, and the same delicate suturing thereafter allow for avoiding traditional postoperative complications (36,37). A microsurgical technique with subdural and subarachnoid "dry" space is a condition for the prevention of vascular and neural damage. Postoperative development of liquorrhea is the most common complication in these patients, often associated with inadequate sealing of the dura mater (38). Careful closure of the dura mater is important to prevent postoperative liquorrhea.

The research gap addressed by this study involves a comprehensive understanding of the

diagnostic and treatment processes for patients with Arnold-Chiari malformation type 1 (ACM I) and associated conditions. While previous studies have examined symptoms and surgical outcomes, this study contributes by highlighting the prevalence of comorbid abnormalities in craniovertebral bone morphology, particularly platybasia, which was common among patients.

CONCLUSIONS

In the diagnostic process, patients with Chiari malformation type 1 were found to have comorbid abnormalities in the morphology of the bones of the craniovertebral region, among which platybasia was the most common, but they were not associated with the degree of ectopy of the cerebellar tonsils. The hypertensive syndrome was found in 96 % of patients, motility disorders in 48 %, and cranial nerve damage in 8 %. These symptoms were closely correlated with the degree of ectopy and were most clearly expressed in patients with prolapse of more than 5 mm. 201 patients underwent surgery. If syringomyelia was detected, the operation was supplemented with syringostomy, which made it possible to eliminate the symptom of syringomyelia in 5 % of patients, however, in 29 % of cases after I+S, relapse was observed. As a result of the operation, preoperative symptoms completely disappeared in 58 % of patients; in 38 % there was an alleviation of vestibulo-atactic abnormalities and hypertension syndrome; stabilization of the process with preservation of focal damages was noted in 4 % of cases. Patients with progressive postoperative syringomyelia and hydrocephalus (5 %) underwent shunting, as a result of which the symptoms subsided after 3 months. In 2 % of cases after surgeon treatment, a tight filum terminale syndrome has been developed, which was eliminated by excision of the filum terminale.

Enhancing care for Arnold-Chiari malformation type 1 involves leveraging high-resolution MRI and computational modelling for accurate diagnosis, alongside tailored surgical strategies based on herniation severity and associated conditions. Intraoperative tools like ultrasound and neurological monitoring aid precise decompression. Optimization of surgical techniques such as suboccipital craniectomy and

duraplasty, and exploration of adjuvant therapies like CSF shunting, contribute to improved outcomes. Standardized metrics, follow-up procedures, and data analysis through patient registries further refine treatment approaches.

The significance of this study lies in its potential to revolutionize the approach to diagnosing and treating patients with ACM I, ultimately improving their quality of life and healthcare outcomes. The key limitations of this study on surgical treatment for Arnold-Chiari malformation type 1 include the retrospective observational design without a control group, modest sample size from a single center, lack of long-term postoperative follow-up, incomplete evaluation of factors underlying clinical outcomes, limited use of advanced imaging modalities for surgical planning, no assessment of adjuvant therapies or quality of life impact, and no analysis of costs versus benefits. The main future research priorities for improving surgical management of Arnold-Chiari malformation should focus on prospective multicenter randomized controlled trials incorporating long-term follow-up, advanced diagnostic imaging, analysis of prognostic factors, cost-effectiveness, quality of life impacts, adjuvant therapies, and basic science models to better define optimal treatment protocols for restoration of normal anatomy and physiology.

REFERENCES

1. Fric R, Eide PK. Chiari type 1 – A malformation or a syndrome? A critical review. *Acta Neurochir (Wien)*. 2020;162(7):1513-1525.
2. Chu W, Chen X, Xue X. Treatment of symptomatic Chiari I malformation by “all-factors-surgery”: A report of 194 cases. *Eur Spine J*. 2021;30:1615-1622.
3. Gallo P, Copley PC, McAllister S, Kaliaperumal C. The impact of neurosurgical technique on the short- and long-term outcomes of adult patients with Chiari I malformation. *Clin Neurol Neurosurg*. 2021;200:106380.
4. Nash J, Cheng JS, Meyer GA, Remler BF. Chiari type I malformation: Overview of diagnosis and treatment. *Wisconsin Medical J*. 2002;101(8):35-40.
5. Schijman E. History, anatomic forms, and pathogenesis of Chiari I malformations. *Child’s Nervous System*. 2004;20(5):323-328.

6. Strahle J, Muraszko KM, Kapurch J, Bapuraj JR, Garton HJL, Maher CO. Natural history of Chiari malformation Type I following decision for conservative treatment: Clinical article. *J Neurosurg.* 2011;8(2):214-221.
7. Joseph N, Rajderkar D, Baker D, Prabhakaran S. Arnold-Chiari malformation: An uncommon etiology for a brief resolved, unexplained event in an infant. *J Clin Sleep Med.* 2020;16(11):1983-1984.
8. Nishikawa M, Sakamoto H, Hakuba A, Nakanishi N, Inoue Y. Pathogenesis of Chiari malformation: A morphometric study of the posterior cranial fossa. *J Neurosurg.* 1997;86(1):40-47.
9. Sakushima K, Tsuboi S, Yabe I, Hida K, Terae S, Uehara R. Nationwide survey on the epidemiology of syringomyelia in Japan. *J Neurological Sciences.* 2012;313(1-2):147-152.
10. Urbizu A, Garrett ME, Soldano K, Drechsel O, Loth D, Marcé-Grau A, et al. Rare functional genetic variants in *COL7A1*, *COL6A5*, *COL1A2* and *COL5A2* frequently occur in Chiari Malformation Type 1. *PLoS One.* 2021;16(5):e0251289.
11. Barpujari A, Kiley A, Ross JA, Veznedaroglu E. A systematic review of non-opioid pain management in Chiari Malformation (Type 1) patients: Current evidence and novel therapeutic opportunities. *J Clin Med.* 2023;12(9):3064.
12. Rosenblum JS, Pomeranic JJ, Heiss JD. Chiari Malformation (update on diagnosis and treatment). *Neurol Clin.* 2022;40(2):297-307.
13. Labula R, Talla Nwotchouang BS, Inrahimy A, Allen PA, Oshinski JN, Klinge P, et al. A new hypothesis for the pathophysiology of symptomatic adult Chiari malformation Type I. *Med Hypotheses.* 2022;158:110740.
14. Alluhaybi AA, Abdulqader SB, Alanazi T, Altuhayni K, Albanyan A. Chiari I malformation with neurogenic hypertension after suboccipital decompression. *Child's Nervous System.* 2021;37(2):659-663.
15. Zhang Y, Zhang N, Qiu H, Zhou J, Li P, Ren M. An efficacy analysis of posterior fossa decompression techniques in the treatment of Chiari malformation with associated syringomyelia. *J Clin Neuroscience.* 2011;18(10):1346-1349.
16. Valentini L, Visintini S, Saletti V, Chiapparini L, Estienne M, Solero, CL. Treatment for Chiari I malformation (CIM): Analysis of a pediatric surgical series. *Neurological Sciences.* 2011;3:321-324.
17. Yundt KD, Park TS, Tantuwaya VS, Kaufman BA. Posterior fossa decompression without duraplasty in infants and young children for treatment of Chiari malformation and achondroplasia. *Pediatric Neurosurg.* 1996;25(5):221-226.
18. Sindou M, Chávez-Machuca J, Hashish H. Cranio-cervical decompression for Chiari type I-malformation, adding extreme lateral Foramen Magnum opening and expansile duroplasty with arachnoid preservation. Technique and long-term functional results in 44 consecutive adult cases – Comparison with literature data. *Acta Neurochirurgica.* 2022;144(10):1005-1019.
19. Sindou M, Gimbert E. Decompression for Chiari type I-malformation (with or without syringomyelia) by extreme lateral foramen magnum opening and expansile duraplasty with arachnoid preservation: Comparison with other technical modalities (literature review). *Advances and Technical Standards in Neurosurgery.* 2009;34:85-110.
20. Zhang ZQ, Chen YQ, Chen YA, Wu X, Wang YB, Li XG. Chiari I malformation associated with syringomyelia: A retrospective study of 316 surgically treated patients. *Spinal Cord.* 2007;46(5):358-363.
21. Vega A, Quintana F, Berciano J. Basichondrocranium anomalies in adult Chiari type I malformation: A morphometric study. *J Neurological Sciences.* 1990;99(2-3):137-145.
22. Eule JM, Erickson MA, O'Brien MF, Handler M. Chiari I malformation associated with syringomyelia and scoliosis: A twenty-year review of surgical and nonsurgical treatment in a pediatric population. *Spine.* 2022;27(13):1451-1455.
23. Aghakhani N, Parker F, David P, Morar S. Long-term follow-up of Chiari-related syringomyelia in adults. *Neurosurgery.* 2009;64(2):308-315.
24. Weprin BE, Iskandar BJ, Hedlund GL, Grabb PA, Oakes WJ. The resolution of syringohydromyelia without hindbrain herniation after posterior fossa decompression. *J Neurosurg.* 1998;89(2):212-216.
25. Zérach M. Syringomyelia in children. *Neurochirurgie.* 1999;45(1):37-57.
26. Liang CJ, Dong QJ, Xing YH, Shan M, Wen LX, Qiang ZY. Posterior fossa decompression combined with resection of the cerebellomedullary fissure membrane and expansile duraplasty: A radical and rational surgical treatment for Arnold-Chiari type I malformation. *Cell Biochemistry and Biophysics.* 2014;70(3):1817-1821.
27. Marković M, Berisavac I, Bojović V, Kostić B, Dulejić V. Surgical treatment of Arnold-Chiari malformation type I in an adult patient. *Vojnosanitetski Pregled.* 2008;65(8):648-652.
28. Albert GW. Chiari malformation in children. *Pediatric Clinics of North America.* 2021;68(4):783-792.
29. Tursynova A, Omarov B, Sakhipov A, Tukenova N. Brain Stroke Lesion Segmentation Using Computed Tomography Images based on Modified U-Net Model

- with ResNet Blocks. *International J Online and Biomedical Engineering*. 2022;18(13):97-112.
30. Belenichev I, Burlaka B, Bukhtiyarova N, Aliyeva O, Makyeyeva L, Bak P. The effect of intranasal administration of an IL-1b antagonist (rail) on the state of the nitroxydergic system of the brain during modeling of acute cerebrovascular accident. *Azerbaijan Pharmaceut Pharmacoth JI*. 2022;22(1):78-85.
 31. Slivkina N, Abduldayeva A, Tardjibayeva S, Doszhanova G, Kuanyshbayeva G. The health of the population, according to prenosological diagnostics. *Georgian Medical News*. 2020;(303):188-193.
 32. Nuradilova D, Kaliyeva L, Vaitkiene D, Kalimoldayeva S, Issenova S. Urogenital mixed infections in reproductive aged women with pelvic inflammatory disease. *Georgian Medical News*. 2021;(312):114-118.
 33. Sagandykova NS, Fakhradiyev IR, Sajjala SR, Taukeleva SA, Shemetova DE, Saliev TM, et al. Patient-specific CFD simulation of aerodynamics for nasal pathology: A combined computational and experimental study. *Computer Methods in Biomechanics and Biomedical Engineering: Imaging and Visualization*. 2021;9(5):470-479.
 34. Nazarchuk O, Dmyrtriiev D, Babina Y, Faustova M, Burkot V. Research of the activity of local anesthetics and antiseptics regarding clinical isolates of *Acinetobacter baumannii* as pathogens of postoperative infectious complications. *Acta Biomedica*. 2022;93(1):e2022003.
 35. Latka K, Kolodziej W, Pawlak K, Sobolewski T, Rajska R, Chowanec J, et al. Fully Endoscopic Spine Separation Surgery in Metastatic Disease—Case Series, Technical Notes, and Preliminary Findings. *Medicina (Lithuania)*. 2023;59(5):993.
 36. Sakaguchi T, Tanaka M, Sake N, Latka K, Fujiwara Y, Arataki S, et al. The Most Significant Factor Affecting Gait and Postural Balance in Patients' Activities of Daily Living Following Corrective Surgery for Deformity of the Adult Spine. *Medicina (Lithuania)*. 2022;58(8):1118.
 37. Navruzov SN, Polatova DS, Geldieva MS, Nurieva EI. Possibilities of study of the main cytokines of the immune system in patients with osteogenic sarcoma. *Voprosy Onkologii*. 2013;59(5):599-602.
 38. Sahalevych AI, Sergiychuk RV, Ozhohin VV, Khrapchuk AYU, Dubovyi YO, Frolov OS. The Modified Procedure of Totally Tubeless PNL. *International J Biol Biomed Engineer*. 2022;16:82-89.

Effect of Resilience, Well-Being, Happiness, and Social Support on the Levels of Perceived Negative Emotions of Colombian People During the COVID-19 pandemic

Efectos de la Resiliencia, el Bienestar, la Felicidad y el Apoyo Social Sobre el Nivel de Percepción de Emociones Negativas de Personas Colombianas Durante la Pandemia por COVID-19

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SUMMARY

The research established the relationships between resilient coping, subjective well-being, subjective happiness, and social support on anxiety levels, depression, and perceived stress among Colombians during the COVID-19 pandemic in the department of Córdoba, Colombia. Participants were 997 elderly people of both genders with literacy skills and without

the presence of cognitive impairment. The Brief Resilient Coping Scale (BRCS), the Happiness Scale (SHS), the Subjective Wellness Scale (SWLS), the Duke-UNC 12 social support scale, the PHQ-4 scale (anxiety-depression), and the Perceived Stress Scale (PSS-14) were used as measuring instruments. We worked with a nonexperimental cross-sectional design and a correlative scope. The results of the binary logistic regression model indicate, on the one hand, that resilience and coping, together with social support, were inversely and significantly related to anxiety and depression, and on the other, that at the level of

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sociodemographic variables, being a woman with lower levels of education and a low sociodemographic stratum was related to higher levels of anxiety. Subjective happiness and subjective well-being were not significantly related to anxiety and depression, nor was there an association with age, area of residence, health system, or occupation.

Keywords: *Resilient coping, subjective happiness, subjective well-being, social support, anxiety, stress, and depression.*

RESUMEN

La investigación consistió en establecer relaciones entre el afrontamiento resiliente, el bienestar subjetivo, la felicidad subjetiva y apoyo social sobre niveles de ansiedad, depresión y estrés percibido de personas colombianas durante la pandemia por COVID-19 de una población residente en el departamento de Córdoba, Colombia. Los participantes fueron 997 personas de mayores edades de ambos géneros, con capacidades de lectoescritura, sin presencia de deterioro cognitivo. Como instrumentos de medición se utilizaron, la escala de afrontamiento resiliente (BRCS), la escala de la Felicidad (SHS), la escala de bienestar subjetivo (SWLS), la escala Duke UNC 12 de apoyo social, la escala PHQ-4 (ansiedad- depresión) y la Escala de Estrés percibido (PSS-14). Se trabajó con un diseño no experimental de corte transversal y un alcance correlacional. Los resultados del modelo de regresión logística binaria indican por un lado que la resiliencia y el afrontamiento, junto con el apoyo social, se relacionaron inversa y significativamente con la ansiedad y la depresión y por otro que a nivel de variables sociodemográficas ser mujer con menores niveles de educación y de estrato sociodemográfico bajo se relacionaron con mayores niveles de ansiedad. La felicidad y el bienestar subjetivos no se relacionaron significativamente con la ansiedad y la depresión como tampoco se registró una asociación con la edad, zona de residencia, sistema de salud y ocupación.

Palabras clave: *Afrontamiento resiliente, felicidad subjetiva, bienestar subjetivo, apoyo social, ansiedad, estrés y depresión.*

INTRODUCTION

In December 2019, the World Health Organization (WHO) identified a new coronavirus, first reported in Wuhan (China), as a cause of pneumonia. Later, the International Committee

on Virus Taxonomy named the new virus “severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2). WHO designated the disease it caused as “COVID-19” (coronavirus disease 2019). On January 31, 2020, WHO issued a Global Health Emergency (1).

The COVID-19 pandemic was first reported in Colombia on March 6, 2020, and the first confirmed case in the country was that of a 19-year-old woman. On March 20, 2020, a total of 19 days of quarantine were declared in the country to prevent the spread of the virus. Later, there were extensions of the quarantine until August 31 of that year. On March 26, 2023, Colombia had 6 361 810 people confirmed by a coronavirus, 813 active cases, and 142 665 deaths (2-3). Specifically in the Colombian Department of Córdoba, there have been some 122 677 cases and 3 990 deaths in the same period (2). Worldwide, by March 2023, there was an estimated 676 609 million cases and more than 6 881 915 million deaths, according to the independent count of Johns Hopkins University, which monitors the situation of the coronavirus (4).

The presence of this unknown pandemic-type disease such as the Coronavirus and the subsequent isolation quarantine periods of a large part of the world population for long periods has produced an increase in the sources of negative emotions such as anxiety, depression, and stress in the general population (5-10).

Increased levels of negative emotions can affect people’s mental and physical health and trigger various problems, including chronic fatigue, affective symptoms (low mood and anxiety), cognitive dysfunctions, and sleep disturbances, along with somatic manifestations such as autonomic symptoms, muscle pain, muscle tension, headache, general flu-like discomfort, gastrointestinal symptoms (GI), breathing difficulty, persistent cough, and chest pain (11-17).

All this can lead to a deterioration of their well-being and quality of life, which leads to inadequate control of their disturbances and, therefore, the appearance of episodes of negative emotions (11,18,19).

The literature has consistently shown an inverse relationship between psychological resilience and distress, especially in the case

of stressful life events, defining it as the ability of people to maintain health and psychological well-being in a dynamic and challenging environment (20). Evidence-based research has been conclusive in stating that resilience is a protective variable of physical and mental health in times of strong levels of negative emotions (21-24).

On the other hand, in recent years, several studies have been developed where the relevance of subjective well-being has been investigated since it is the set of strategies that allow people to acquire a state of well-being with themselves and with others (25). Subjective well-being is conceptualized as evaluation and judgment and involves two fundamental dimensions, which are positive and negative affective and cognitive vital satisfaction (26,27). Numerous studies have found how subjective well-being has been affected in its different dimensions by the coronavirus pandemic (27).

In this regard, Dhiengra and Dhiengra (28) developed research to find out the mediating effect of subjective happiness in the relationship between perceived stress and the psychological well-being of 231 health workers who perform COVID-19 hospital functions. The results show that there is a significant effect of perceived stress on psychological well-being, with a mediating role for subjective happiness. Perceived stress diminishes subjective happiness, which in turn affects the psychological well-being of doctors and health professionals. The higher the level of subjective happiness, the lower the impact or delayed impact of perceived stress on psychological well-being.

Similarly, some studies refer to the role of social support in the coronavirus pandemic. Higher ratings of perceived family social support have been reported to be associated with lower levels of depression and insomnia (29,30). In addition, low levels of social support have been associated during the pandemic among university students with high levels of anxiety, depression, and stress (31). On the other hand, it has been observed that health workers with higher levels of social support are more likely to show higher levels of health.

Finally, negative emotions such as stress, anxiety, and depression have played a fundamental

role in the pandemic since its inception in China at the end of the year 2019. The mysterious origin of the disease that to date has not been clarified yet, the initial hesitation of WHO to declare it a pandemic, the quarantine that left millions of people unprepared, the panic associated with millions of infected and hundreds of thousands of dead, and the role of social networks about vaccination, among others, were the causes of a negative news epidemic. In this regard, systematic reviews and meta-analyses have identified a high prevalence of moderate depression, anxiety, and Post-Traumatic Stress Disorder (PTSD) among health workers during the COVID-19 pandemic, which was the first to face it (32).

On the other hand, studies at a more advanced stage of the pandemic with the general population found that psychological distress, including depression, anxiety, worry, perceived stress, and loneliness, was associated with an increased risk of prolonged COVID-19. To determine the effects of psychological distress before COVID-19 infection on the development of long-term COVID-19, researchers from the nutrition department of Harvard University enrolled more than 54 000 people in April 2020. At the beginning of the study, researchers asked participants about their psychological distress. Over the next year, more than 3 000 participants contracted COVID-19, and researchers asked participants about their COVID-19 symptoms and the duration of symptoms. After analyzing the responses and comparing those who developed prolonged COVID-19 with those who did not, it was determined that pre-infection distress from COVID-19, including depression, anxiety, worry, perceived stress, and loneliness, was associated with an increased risk of prolonged COVID-19 between 32 % and 46 %. These types of psychological distress were also associated with a 15-51 percent higher risk of impairment of daily life due to long-term COVID-19 (33).

However, starting from the broad idea that social and psychological factors are risk factors associated with COVID-19 infection and considering the impact of the coronavirus pandemic in the department of Córdoba and the lack of more empirical studies in Colombia in the field of positive constructs protective of the threat of the presence of negative emotions, it was intended in this study to analyze and compare the

relationship between resilient coping, happiness, subjective well-being, and social support on anxiety, depression, and stress perceived in Colombian people in the department of Córdoba during the coronavirus epidemic.

MATERIALS AND METHODS

Design

This is quantitative, nonexperimental, cross-sectional research of correlative scope with a model of data collection type survey (34).

Population and sample

The population of the department of Córdoba was 1 075 participants, of whom 77 did not accept informed consent or did not meet the inclusion criteria. (a) be of legal age; (b) have or have had COVID-19; and/or (c) have cared for a patient with COVID-19. There were 998 participants: 306 men, 691 women, and one participant identified as another.

Instruments

The Life Satisfaction Scale (SWLS) by Diener et al. (35) is a short five-element Likert 7-point rating instrument, from 1 as “strongly disagree” to 7 as “strongly agree”, with scores between 5 and 35, that assesses the general satisfaction that the individual has with his life, understanding that a higher score reflects greater satisfaction. For this research, the Colombian version was used with its respective scale (36).

The Brief Resilient Coping Scale (BRCS) (37) is another short, one-dimensional, four-item measure that is easy to apply and interpret. BRCS assesses the ability of individuals to cope with stress adaptively. It is a short, four-element instrument. The items score on a Likert scale from 1 (not describing me at all) to 5 (describing me very well), where the scores range between 4 and 20. The Colombian version of Trejos et al. (38) was used for this research.

Subjective Happiness Scale (39): It is a global measure of subjective happiness that evaluates a molar category of well-being as a global psychological phenomenon, considering the definition of happiness from the perspective of the respondent. It consists of four items with a Likert response that respond using a Likert scale with seven possible response alternatives ranging from not very happy to very happy (item 1), from less happy to happier (item 2), or from almost nothing to very much (items 3 and 4). The correction is made by summing up the scores obtained and dividing the total number of items. The Chilean version of Vera et al. (40) was used for this research.

The Patient Health Questionnaire 4, or PHQ-4, is the result of merging the ultrashort questionnaire for the evaluation of depression. PHQ-2 had 2 items, and the ultrashort questionnaire of 2 items known as GAD-2 obtained a very short questionnaire of 4 items to evaluate two factors with excellent values of validity and reliability (41). The questionnaire has been validated and standardized in several places, such as the United States, Germany, some parts of Asia, and some African countries (42-45). In the Colombian case, PHQ-4 has also been validated and standardized, and the model of two factors that were independent of age and gender was confirmed using confirmatory factor analysis. Likewise, the questionnaire obtained a high degree of reliability in both factors. This study also obtained normative data for both genders and different age groups (46).

The Perceived Stress Scale (PSS) used the Spanish version of the EEP-14 validated with adults in Spain (47). This scale measures the perception of psychological stress—the extent to which everyday situations are perceived as stressful. The scale includes a series of direct consultations that explore the level of stress experienced during the last month. The subparagraphs are easily understood. The scale provides five response options: ‘never’, ‘rarely’, ‘from time to time’, ‘many times’, and ‘always’, which are classified from zero to four. Questionnaire Duke-UNC 11 evaluates two dimensions of social support with a Cronbach alpha reliability level of 0.93 (48). The dimensions are confidential support, which

refers to the possibility of communicating, and emotional support, which deals with the possibility of having manifestations of love and affection. In the Colombian case, it was found that the questionnaire has construct validity and internal consistency (49).

Procedure

The proposal was discussed and approved by the Research Committee of Sinú University. Then the scales were digitized in a single online format through Google Forms, accompanied by the questionnaire of sociodemographic data and informed consent, which was applied in a single moment and in a virtual way. Participants agreed to respond to the scales after reading the informed consent, explaining the confidential nature of the results.

The study was carried out with the considerations referred to in Article 2 (paragraphs 5, 6, and 8) of Law 1 090 of 2006 on the professional practice of psychologists in Colombia, thus guaranteeing the principles of privacy, anonymity, and full knowledge by the participants. The implementation of this project did not include invasive actions that put at risk the physical, mental, or moral integrity of the participants, consistent with the provisions of Resolution 8430 of the Ministry of Health of Colombia (paragraph 11). The project was approved by the Research Ethics Committee of the Faculty of Health Sciences of Sinú University.

Statistical analysis

First, the database was examined to identify possible transcription errors without finding inconsistencies. Subsequently, the analysis of lost values revealed that there was no loss of information at the level of variables, cases, or cells. As a result, no records were deleted and no imputation techniques were used, which allowed the full database to work. The parametric assumptions of multiple linear regression were then evaluated. In this sense, linearity was weighed with residual diagrams against predicted values, while residual normality was studied with the Shapiro-Wilk and Kolmogorov-Smirnov tests as well as with the Q-Q graph. The homogeneity

of variances was inspected with the modified Levene test, while the heteroscedasticity was evaluated with the standardized Breusch-Pagan test. Residual autocorrelation was revised with the Durbin-Watson statistic, while multicollinearity was discarded using variance inflation factors. The existence of atypical data or points of influence was corroborated with standardized residuals, Mahalanobis distances, and Cook distances (50,51).

The previous phase exposed the violation of several assumptions. Linearity was not satisfied in the regression models proposed for anxiety and depression, and the premise of homoscedasticity could not be corroborated either. Likewise, the model built for perceived stress exhibited residuals that significantly departed from normal. Therefore, binary logistic regression was used, establishing the dichotomy of dependent variables from the cut-off points of each instrument. To avoid further loss of information and given that logistic regression supports any type of regressor, psychological constructs were included as continuous variables, whereas sociodemographic conditions were incorporated as nominal or ordinal aspects. Thus, three regression models were built for anxiety, depression, and perceived stress. For each, the main regressors were resilience and coping, subjective well-being, subjective happiness, and social support. The covariates introduced were gender, age, area of residence, health system, occupation, educational level, and socioeconomic stratum.

Logistic regression assumptions were also verified. In this sense, the Box-Tidwell test was used to verify that the relationship between the logarithm of the dependent variables and the continuous independent variables was linear. On this occasion, no significant deviations were found that would invalidate this assumption. Likewise, the inflation factors of the variance were close to the unit, so multicollinearity was discarded. Neither a high fraction of atypical data nor points of influence were found (50,51). As for the description of the results, the categorical variables were presented in the form of counts and percentages. Likewise, continuous variables were characterized using measures such as the minimum, 5th percentile, lower quartile, median, upper quartile, 95th percentile, maximum, range, interquartile range, average, fashion, variance,

standard deviation, coefficient of variation, standard error, and confidence interval. The data processing and analysis were done with the IBM SPSS statistical package version 27 for 64-bit Windows. The significance of the results was established for levels lower than 0.05.

RESULTS

Sociodemographic characteristics of the participants

The sociodemographic aspects of the participants are presented in Table 1. It is shown that most of the people were women; they were aged between 18 and 25 years, lived in urban areas, had health systems through Health Providing Entities (EPS), were students, had a university degree, were pursuing a professional career, or were in the first socioeconomic stratum.

Psychological constructs are used as independent variables

The description of the psychological constructs used as independent variables is shown in Table 2. Resilient coping will be used as an example in this section. In this sense, the scores ranged from 4 to 20 points, with lower and upper quartiles of 14 and 18 points, respectively. The range was 16, while the interquartile range was 4. The median was 16, revealing that 50 % of participants showed levels of resilience and coping equal to or lower than this value. The average was located at 15.68, with a fashion of 16 and a standard deviation of 3.02 points, implying a coefficient of variation of 19.25 %. Based on the interval estimate, it can be believed with a 95 % confidence level that the resilience coping scores of this Colombian population range from 15.50 to 15.87. The description of the rest of the psychological constructs is omitted to gain conciseness and practicality. An inspection of Table 2 will allow a similar characterization of subjective well-being, subjective happiness, and social support

Table 1

Sociodemographic characteristics of the participants

Feature	Rank	Recount	Rec. accu.	Percentage	Perc. Accu.
Gender	Women	691	691	69.31	69.31
	Men	306	997	30.69	100.00
Age	From 18 to 25 years	728	728	72.95	72.95
	From 26 to 40 years	168	896	16.83	89.78
	From 41 years forward	102	998	10.22	100.00
Residential area	Urban	874	874	87.58	87.58
	Countryside	124	998	12.42	100.00
Health System	Sisbén ^a	199	199	19.94	19.94
	EPS ^b	711	910	71.24	91.18
	Prepaid or particular	88	998	8.82	100.00
Occupation	Employee ^c	300	300	30.06	30.06
	Student	663	963	66.43	96.49
	Unemployed	23	986	2.30	98.79
	Retired	12	998	1.21	100.00
Education	baccalaureate	353	353	35.37	35.37
	Technical or Technology	162	515	16.23	51.60
	Professional career	483	998	48.40	100.00
Social Class	Stratum 1	570	570	57.11	57.11
	Stratum 2	295	865	29.56	86.67
	Stratum 3 or upper	133	998	13.33	100.00

^aSystem of identification of potential beneficiaries of social programs, ^bEPS: health-promoting entity. ^cThis category includes employees, self-employed workers, domestic workers, and working students.

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Table 2
Description of the psychological constructs used as independent variables

Statistical	Resilient Coping	Subjective Happiness	Subjective Well-being	Social Support
Minimum	4	4	5	11
Percentile 5	11	13	16	26
Under Quartile	14	17	22	36
Median	16	20	26	43
Upper Quartile	18	22	30	50
Percentile 95	20	27	35	55
Maximum	20	28	35	55
Rank	16	24	30	44
Interquartile Rank	4	5	8	14
Median	15.68	19.77	25.73	42.17
Mode	16	20	30	55
Variance	9.12	16.73	34.34	86.12
Standard Deviation	3.02	4.09	5.86	9.28
Coefficient of variation (%)	19.25	20.70	22.76	22.01
Standard Error	0.10	0.13	0.19	0.29
Lower Confidence Limit 95 %	15.50	19.52	25.37	41.59
Upper confidence limit 95 %	15.87	20.02	26.10	42.75

Psychological constructs are used as dependent variables

The characterization of anxiety, depression, and perceived stress is indicated in Table 3. On this occasion, stress will be used as an example for the description of the results. Thus, scores ranging from 1 to 56 were observed, involving a range of 55 points. Also, the lower and upper quartiles were 30 and 39 points, which generated an interquartile range of 9 points. On the other hand, the average score amounted to 34.62, with a fashion of 34 and a standard deviation of 7.64 points, assuming a coefficient of variation of 22.07 %. The median was 34 points, meaning that 50 % of the people who participated in the research showed perceived stress with values lower than or equal to this amount. The confidence interval suggests that the stress scores perceived by people in this population are between 34.14 and 35.09 points, an assertion that can be made with a safety margin of 95 %. The description of the findings linked to anxiety and depression can be obtained in the same way by a thorough review of Table 3.

Relationship between anxiety, psychological constructs, and socio-demographic characteristics

This section presents the results of the binary logistic regression model to explain the relationship between anxiety and the psychological constructs that functioned as major independent variables, while also considering the effect of sociodemographic covariates. As can be seen in Table 4, resilient coping, along with social support, is inversely and significantly related to anxiety. Note that higher scores of resilient coping involve lower values in this construct. The probability ratio (OR) indicates that, if the other factors remain constant, the unit increase in resilience and coping decreases the probability of being classified as anxious by 10 % (OR = 0.90, p= 0.001, 95 % BCI: 0.84-0.96). Social support also exhibited a negative and significant association but of a lesser magnitude. In this case, point increases imply a 3 % reduction in the probability of being classified as a person with anxiety if the other terms remain unchanged (OR = 0.97, p= 0.001, BCI 95 %: 0.95-0.98).

Table 3
Description of the psychological constructs used as independent variables

Statistical	Anxiety	Depression	Perceived Stress
Minimum	0	0	1
Percentile 5	0	0	22
Under Quartile	2	1	30
Median	3	3	34
Upper Quartile	4	4	39
Percentile 95	6	6	47
Maximum	6	6	56
Rank	6	6	55
Interquartile Rank	2	3	9
Median	3.29	2.65	34.62
Mode	4	4	34
Variance	2.62	2.96	58.37
Standard Deviation	1.62	1.72	7.64
Coefficient of variation (%)	49.27	65.00	22.07
Standard Error	0.05	0.05	0.24
Lower Confidence Limit 95 %	3.19	2.54	34.14
Upper confidence limit 95 %	3.39	2.76	35.09

In terms of socio-demographic characteristics, women were more likely than men to have high scores on the anxiety scale. Specifically, female participants had a 44 % higher probability of being classified as persons with anxiety than men, provided that the other coefficients of the model remain unchanged (OR = 1.44, p = 0.019, BCI 95 %: 1.06–1.96). A similar result was found at the educational level. Note that people with a high school degree had a 47 % higher probability than their university peers of being identified with anxiety under the premise of not modifying the other factors (OR = 1.47, p = 0.021, BCI 95 %: 1.06-2.05). The socioeconomic stratum was also significantly linked to anxiety. On this occasion, individuals in stratum 1 were 49 % less likely to reflect anxiety than those in stratum 3 or higher if the other elements of the model remained constant (OR = 0.51; p = 0.006; BCI 95 %: 0.31-0.82). Subjective happiness and subjective well-being were not significantly related to anxiety. There was also no association with age, area of residence, health system, or occupation. Table 4 sets out in detail the results of this phase and makes it possible to supplement the interpretation provided in this section.

Relationship between depression, psychological constructs, and socio-demographic characteristics

The findings of this stage are shown in Table 5. Note that both resilience coping, subjective well-being, and social support were inversely and significantly associated with depression, also showing similar values in terms of the magnitude of that relationship. Specifically, it was found that unit increases in resilient coping cause a 9 % decrease in the probability of generating high depression scores, provided the other coefficients of the model remain fixed (OR = 0.91, p = 0.001, 95 % BCI: 0.86-0.96). Concerning subjective well-being, it was evidenced that increases of a point in this construct would imply a 6 % reduction in the probability of being classified as someone with depression, assuming that no other term of the model is modified (OR = 0.94, p < 0.001, 95 % BCI: 0.90-0.97).

Similarly, one-off growth in social support values was associated with a 4 % percentage decrease in the probability of generating high depression scores, provided no other coefficient is altered in the logistic regression equation

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Table 4

Relationship between anxiety, psychological constructs, and socio-demographic characteristics

Model coefficients	Coef. beta no Stand.	Standard Error	Odds ratio (OR)	Valor-p of OR	ICB 95 % by OR
Intercept	4.99	0.91	146.68	<0.001	Does not apply
Resilient Coping	-0.11	0.03	0.90	0.001	[0.84, 0.96]
Subjective Happiness	-0.03	0.03	0.97	0.241	[0.92, 1.02]
Subjective Well-being	-0.03	0.02	0.97	0.167	[0.94, 1.01]
Social Support	-0.04	0.01	0.97	<0.001	[0.95, 0.98]
Women (between men)	0.37	0.16	1.44	0.019	[1.06, 1.96]
From 18 to 25 years (between 41 years forward)	0.33	0.31	1.39	0.290	[0.76, 2.54]
From 26 to 40 years (between 41 years forward)	-0.01	0.30	0.99	0.966	[0.55, 1.77]
Urban area (between Countryside area)	-0.14	0.23	0.87	0.540	[0.56, 1.36]
Sisbén (between prepaid or particular)	0.12	0.29	1.12	0.690	[0.63, 2.01]
EPS (between prepaid or particular)	0.16	0.26	1.18	0.520	[0.71, 1.95]
Employee (between Retired)	0.12	0.67	1.12	0.861	[0.30, 4.21]
Student (between Retired)	0.17	0.71	1.19	0.805	[0.30, 4.78]
Unemployed (between Retired)	-0.49	0.82	0.61	0.547	[0.12, 3.05]
Baccalaureate (between Professional career)	0.39	0.17	1.47	0.021	[1.06, 2.05]
Technical (between Professional career)	0.24	0.21	1.27	0.268	[0.83, 1.92]
Stratum 1 (between Stratum 3 or upper)	-0.68	0.25	0.51	0.006	[0.31, 0.82]
Stratum 2 (between Stratum 3 or upper)	-0.37	0.26	0.69	0.150	[0.42, 1.14]

(OR = 0.96, p= 0.001, 95 % BCI: 0.94-0.98). However, of the sociodemographic aspects, only the educational level showed a significant association with depression. Thus, individuals who achieved high school or lower studies had a 46 % higher probability of reflecting depression than those who reached university levels, under the assumption that the other factors remained constant (OR = 1.46, p=0.015, BCI 95 %: 1.08–1.99). There was no evidence of a relationship between subjective happiness and depression, nor was there evidence of an association between this construct and gender, age, area of residence, health system, occupation, or socioeconomic stratum. Table 5 provides a review of these results.

Relationship between perceived stress, psychological constructs, and socio-demographic characteristics

Table 6 provides the relationship between perceived stress, psychological constructs, and sociodemographic characteristics of participants. Unlike what was observed in anxiety and depression, no statistically significant association was found between the level of stress experienced

by these people and variables such as resilient coping, subjective happiness, subjective well-being, and social support. Note in Table 6 that no probability ratio (OR) was significantly different from the unit.

On the contrary, several social and economic aspects showed an important relationship with stress. In terms of gender, it could be evidenced that women had a 44 % higher probability than men of generating high scores in this variable, provided that the other terms of the model remain fixed (OR = 1.44, p=0.020, BCI 95 %: 1.06–1.95). Also, those who have a health system based on EPS demonstrated a 40 % lower probability of manifesting stress than those who must resort to a prepaid or particular medicine, assuming that the other coefficients of the regression equation are not modified (OR = 0.60, p = 0.035, BCI 95 %: 0.37-0.96). The economic stratum was also significantly linked to stress. In this case, those in the first stratum showed a 53 % lower probability of experiencing this emotion than people in the middle or high strata, if the other factors remain unchanged (OR = 0.47, p<0.001, 95 % BCI: 0.31-0.71). Similarly, participants at the second socioeconomic level reflected a 40 %

Table 5
Relationship between depression, psychological constructs, and socio-demographic characteristics

Model coefficients	Coef. beta no Stand.	Standard Error	Odds ratio (OR)	Value-p of OR	ICB 95 % by OR
Intercept	5.00	0.88	148.43	<0.001	No aplica
Resilient Coping	-0.10	0.03	0.91	0.001	[0.86, 0.96]
Subjective Happiness	0.01	0.02	1.01	0.563	[0.97, 1.06]
Subjective Well-being	-0.07	0.02	0.94	<0.001	[0.90, 0.97]
Social Support	-0.04	0.01	0.96	<0.001	[0.94, 0.98]
Women (between men)	0.04	0.15	1.04	0.814	[0.77, 1.40]
From 18 to 25 years (between 41 years forward)	0.23	0.30	1.26	0.447	[0.70, 2.28]
From 26 to 40 years (between 41 years forward)	-0.04	0.30	0.96	0.887	[0.53, 1.73]
Urban area (between Countryside area)	-0.37	0.21	0.69	0.081	[0.45, 1.05]
Sisbén (between prepaid or particular)	-0.01	0.29	0.99	0.985	[0.56, 1.76]
EPS (between prepaid or particular)	-0.03	0.25	0.97	0.895	[0.59, 1.59]
Employee (between Retired)	-0.29	0.68	0.75	0.664	[0.20, 2.81]
Student (between Retired)	0.05	0.71	1.06	0.940	[0.26, 4.23]
Unemployed (between Retired)	-0.22	0.83	0.80	0.788	[0.16, 4.07]
Baccalaureate (between Professional career)	0.38	0.16	1.46	0.015	[1.08, 1.99]
Technical (between Professional career)	0.20	0.21	1.22	0.338	[0.81, 1.84]
Stratum 1 (between Stratum 3 or upper)	-0.21	0.22	0.81	0.354	[0.53, 1.26]
Stratum 2(between Stratum 3 or upper)	-0.03	0.23	0.97	0.893	[0.62, 1.53]

lower probability of generating high perceived stress scores than those at stratum 3 or higher, under the premise that no other coefficient of

the regression equation is altered (OR = 0.60, p = 0.023, 95 % BCI: 0.39-0.93).

Table 6
Relationship between perceived stress, psychological constructs, and socio-demographic characteristics

Model coefficients	Coef. beta no Stand.	Standard Error	Odds ratio (OR)	Value-p of OR	ICB 95 % By OR
Intercept	-2.74	0.79	0.06	0.001	[0.00, 0.00]
Resilient Coping	0.05	0.03	1.05	0.121	[0.99, 1.11]
Subjective Happiness	0.00	0.02	1.00	0.893	[0.96, 1.05]
Subjective Well-being	0.00	0.02	1.00	0.974	[0.96, 1.04]
Social Support	0.01	0.01	1.01	0.160	[0.99, 1.03]
Women (between men)	0.36	0.16	1.44	0.020	[1.06, 1.95]
From 18 to 25 years (between 41 years forward)	0.51	0.31	1.67	0.097	[0.91, 3.04]
From 26 to 40 years (between 41 years forward)	0.17	0.31	1.18	0.579	[0.65, 2.15]
Urban area (between Countryside area)	-0.02	0.21	0.98	0.916	[0.64, 1.49]
Intercept	-0.01	0.28	0.99	0.957	[0.57, 1.70]
EPS (between prepaid or particular)	-0.51	0.24	0.60	0.035	[0.37, 0.96]
Employee (between Retired) ^a	0.87	0.51	2.39	0.088	[0.88, 6.53]
Student (between Retired) ^a	0.92	0.53	2.51	0.080	[0.90, 7.02]
Baccalaureate (between Professional career)	0.29	0.16	1.34	0.063	[0.98, 1.82]
Technical (between Professional career)	0.03	0.21	1.03	0.880	[0.68, 1.57]
Stratum 1 (between Stratum 3 or upper)	-0.76	0.21	0.47	<0.001	[0.31, 0.71]
Stratum 2(between Stratum 3 or upper)	-0.51	0.22	0.60	0.023	[0.39, 0.93]

^aIn this analysis, it was necessary to group the unemployed and pensioners into one category to avoid problems in the estimation process due to the low count observed.

DISCUSSION

This study involved 997 inhabitants of 30 municipalities of the department of Cordoba on the Colombian Atlantic coast, mostly female, of a range of ages between 18 and 41 years, with bachelor's and university studies mostly among low socioeconomic strata. It should be noted that most of the instruments used had validation in the Colombian context and had high alpha Cronbach indices. In terms of the results achieved in the study, the levels of resilient coping had an average of 15.68, close to the criteria of high resilient frontiers of Sinclair and Walston (37), conceptualizing resilient coping behavior as a tendency to effectively use cognitive assessment skills in a flexible, active problem-solving approach, despite stressful circumstances. People who support these four items would be expected to be more goal-oriented, believe in their ability to cope with adverse situations, and often succeed in selected challenges (38). Limonero et al. (52) have observed in young people that those with high scores in the BRCS had higher levels of emotional regulation and better levels of vital satisfaction. On the other hand, concerning those found on the Happiness scale, their scores are close to the average scores of the validation in Spanish in Chile by Vera et al. (40), where, from the perspective of the respondent, it is assumed that even when there are various reasons to be happy, most people have their own idea of what it is to be happy, and when they are happy or not, they can report it.

On the subjective welfare scale, the average scores were 25.73, which implies from the criteria of Diener (26) in the USA, Vazquez et al. (53) in Spain, and Vinaccia et al. (36) in Colombia that our sample has good satisfaction with life. In general terms, satisfaction with life is the personal perception of well-being or happiness, that is, the valuation of life based on one's own goals, expectations, or interests mediated by the cultural context. Concerning the total scale of social support at Duke University, our sample reached an average level of 42.17. The test measures social support in both its confidential and affective dimensions. Social support is an essential factor in the well-being of individuals, associated with health, and generates a significant

factor in the well-being of individuals, associated with health (54).

On the results for negative emotions, we found insignificant levels of anxiety and depression with respective averages of 3.29 and 2.65, which is considered a population at medium risk (43). In relation to this, the average score was 34.62. The concept of perceived stress comes from the transactional theory of stress, which defines it as a particular relationship between the individual and his environment when the latter is assessed by the subject as threatening or overflowing with his resources and capable of endangering his welfare (55).

However, resilient coping, along with social support, were inversely and significantly related to anxiety. Labrague and Santos (20), with a sample of 325 health personnel, found that anxiety related to the COVID-19 pandemic is frequent in health personnel, which can affect their well-being and work performance. They found the influence of resilience and social support in reducing anxiety from COVID-19.

In addition, women were more likely than men to have high scores on the anxiety scale. Specifically, female participants had a 44 % higher chance of being classified as anxious than men. The socioeconomic stratum was also significantly linked to anxiety. On this occasion, individuals in stratum 1 were 49 % less likely to reflect anxiety than those in stratum 3 or higher.

These results are like those found in Mexico according to the COVID-19 follow-up survey on the welfare of Mexican households (ENCOVID-19), corresponding to the year 2020, when women and people of low socioeconomic level were those who presented severe symptoms of anxiety (ENCOVID, 2021). We found an association between sociodemographic factors such as sex, age, and economic income and depressive symptoms, stress level, and anxiety at the time of COVID-19 results like those found in different parts of Latin America (56,57).

Finally, subjective happiness and subjective well-being were not significantly related to anxiety and depression, nor was there an association with age, area of residence, health system, or occupation. These results are different from the research carried out in the US

by Serrao et al. (58) using data collected from 1366 older adults residing in a western US state, where they found that higher levels of anxiety and depressive symptoms were related to lower levels of happiness. Consistently, mental health symptoms have been associated with lower levels of happiness and life satisfaction, even among older adults (59,60). These differences may be due to the differences in the age range of this research.

This study has some limitations. First, although we captured anxiety and depression using a short-established measure, these self-reported mental health symptoms did not specifically capture “pandemic stress”. Stress caused by the pandemic itself should be further explored, as the COVID-19 pandemic continues to affect many vulnerable populations. Secondly, the exploratory cross-sectional nature of the study prevented the search for better explanations for the causal relationships found. Future research could assess a more complex and complete picture of positive and negative variables among adults around impactful events and explore the challenges experienced by adults who contracted COVID-19 or cared for relatives with COVID-19.

In conclusion, despite the challenges that people have experienced because of the COVID-19 pandemic, some may have experienced positive benefits and even resilience during this time, thus providing a glimmer of hope in what has been a difficult time for most of the world. In particular, the results of this study show that some adults with anxiety and self-declared depressive symptoms demonstrated high levels of resilience and social support. The results of this study suggest that resilience can occur in vulnerable populations, such as those suffering from anxiety and depressive symptoms and those in difficult times of life. With greater knowledge and perspective, adults may experience less distress and more hope in coping with future natural disasters such as the coronavirus. It also shows that positive dimensions are protective factors against anxiety and depression, so including strengthening these factors in individual and community interventions can become a protective factor against anxiety and depression.

REFERENCES

1. Liu YC, Kuo RL, Shih SR. COVID-19. The first documented coronavirus pandemic in history. *Biomed J.* 2020;43(4):328-333.
2. Instituto Nacional de Salud. Instructivo para la vigilancia en salud pública intensificada de infección respiratoria aguda asociada al nuevo coronavirus 2019 (COVID-19). 2023.
3. Johns Hopkins University. COVID-19 dashboard. The Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). 2023. Coronavirus Resource Center. Disponible en: <https://coronavirus.jhu.edu/map.html>.
4. Aydin A, Aktuğ C, Koçan S, Erkaya R, Yasak K, Cengiz B, et al. Determining the coronavirus awareness of the Turkish society and the anxiety stress levels. *Curr Psychol.* 2023;42(3):2558-2564.
5. Altıntaş M, Korkut S. Investigation of coronavirus anxiety, health anxiety, and anxiety symptom levels in vertigo patients during COVID-19 pandemic. *Braz J Otorhinolaryngolog.* 2023;89(2):313-320.
6. Aslan I, Çınar O. Predictors and prevalence of stress, anxiety, depression, and PTSD among university students during the second wave of the COVID-19 pandemic in Turkey. *Front Psychol.* 2023;10(13):1087528.
7. Zhu C, Zhang T, Li Q, Chen X, Wang K. Depression and Anxiety During the COVID-19 Pandemic: Epidemiology, Mechanism, and Treatment. *Neurosci Bull.* 2023; 39(4): 675-684.
8. Khushboo A, Siddiqi NJ, Sharma. Pathophysiology of SARS-CoV2 Mediated Depression, Therapeutics, and Consequences: A Comprehensive Narrative. *Mini-Rev Med Chem.* 2023;23(2):217-229.
9. Niu Y, Liu Y, Ren S. Investigation on anxiety and depression of different populations in the area with low incidence of New Coronavirus pneumonia and analysis of related factors. *Pak J Med Sci.* 2023;39(2):380-384.
10. Anastasio F, Barbuto S, Scarnecchia E, Cosma P, Fugagnoli A, Rossi G, et al. Medium-term impact of COVID-19 on pulmonary function, functional capacity, and quality of life. *Eur Respir J.* 2021;16,58(3):2004015.
11. Bogucki ZA, Giniewicz K. Difference in the occurrence and intensification symptoms of stomatognathic system between women and men in medical staff working with patients infected with COVID-19. *Adv Clin Exp Med.* 2022;31(4):457-464.
12. El Khouly RM, Elsabagh HM, Moawad AAR, Afifi S, Abo El Hawa MA. Functional and mental

- health affection (depression, anxiety, stress) among Egyptian rheumatic disease patients during COVID-19 pandemic. *Eur Rev Med Pharmacol Sci*. 2022;26(12):4477-4485.
13. I-Hakeim HK, Al-Rubaye HT, Almulla AF, Al-Hadrawi DS, Maes M. Chronic Fatigue, Depression and Anxiety Symptoms in Long COVID Are Strongly Predicted by Neuroimmune and Neuro-Oxidative Pathways Which Are Caused by the Inflammation during Acute Infection. *J Clin Med*. 2023;12(2):511.
 14. Law EF, Zhou C, Seung F, Perry F, Palermo TM. Longitudinal study of early adaptation to the coronavirus disease pandemic among youth with chronic pain and their parents: Effects of direct exposures and economic stress. *Pain*. 2021;162(7):2132-2144.
 15. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: A systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet*. 2020;7(7):611-627.
 16. Zhan YX, Zhao SY, Yuan J, Liu H, Liu YF, Gui LL, et al. Prevalence and Influencing Factors on Fatigue of First-line Nurses Combating with COVID-19 in China: A Descriptive Cross-Sectional Study. *Curr Med Sci*. 2020;40(4):625-635.
 17. Buselli R, Corsi M, Baldanzi S, Chiumiento M, Del Lupo E, Dell'Oste V, et al. Professional Quality of Life and Mental Health Outcomes among Health Care Workers Exposed to SARS-CoV-2 (COVID-19). *Int J Environ Res Public Health*. 2020; 26(17): 6180.
 18. Sayin Kasar K, Karaman E. Life in lockdown: Social isolation, loneliness and quality of life in the elderly during the COVID-19 pandemic: A scoping review. *Geriatr Nurs*. 2021;42(5):1222-1229.
 19. Zautra AJ, Hall JS, Murray KE. Resilience: A new integrative approach to health and mental health research. *Health Psychol*. 2008;27(1):41-64.
 20. Labrague LJ, De Los Santos JAA. COVID-19 anxiety among front-line nurses: Predictive role of organizational support, personal resilience and social support. *J Nurs Manag*. 2020;28(7):1653-1661.
 21. Prime H, Wade M, Browne DT. Risk and resilience in family well-being during the COVID-19 pandemic. *Am Psychol*. 2020;75(5):631-643.
 22. Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al. Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. *Int J Environ Res Public Health*. 2020;17(5):1729.
 23. Wu DD, Mitchell J, Lambert JH. Global systemic risk and resilience for novel coronavirus in post-pandemic era. *Risk Anal*. 2022;42(1):1-4.
 24. Barragán-Giraldo DF, Anzola-Pardo G, Guerrero-Lucero MA. Subjective Well-Being in Healthcare Professionals in Colombia: On the Constitution of Subjectivity and the Ethics of Care in Times of the COVID-19 Pandemic. *Front Psychol*. 2021;12:773173.
 25. Diener E. Subjective well-being: the science of happiness and a proposal for a national index. *Am Psychol*. 2000;55:34-43.
 26. Diener E, Lucas RE, Oishi S. Subjective well-being: the science of happiness and life satisfaction in Handbook of positive psychology. In: Snyder CR, Lopez SJ, editors. England: Oxford University Press; p.463-473.
 27. Sieverding M, Krafft C, Selwaness I, Nassif AA. Impacts of the COVID-19 pandemic on subjective wellbeing in the Middle East and North Africa: A gender analysis. *PLoS One*. 2023;18(5): e0286405.
 28. Dhiengra V, Dhiengra M. Effect of perceived stress on psychological well-being of health care workers during COVID-19: Mediating role of subjective happiness. *EJMCM*. 2020;7(2):3683-3701.
 29. Grey I, Arora T, Thomas J, Saneh A, Tohme P, Abi-Habib R. The role of perceived social support on depression and sleep during the COVID-19 pandemic. *Psychiatry Res*. 2020;293:113452.
 30. Guo K, Zhang X, Bai S, Minhat HS, Nazan AINM, Feng J, et al. Assessing social support impact on depression, anxiety, and stress among undergraduate students in Shaanxi province during the COVID-19 pandemic of China. *PLoS One*. 2021;16(7): e0253891.
 31. Hou T, Zhang T, Cai W, Song X, Chen A, Deng G, et al. Social support and mental health among health care workers during Coronavirus Disease 2019 outbreak: A moderated mediation model. *PLoS One*. 2020;15(5):e0233831.
 32. Li Y, Scherer N, Felix L, Kuper H. Prevalence of depression, anxiety and post-traumatic stress disorder in health care workers during the COVID-19 pandemic: A systematic review and meta-analysis. *PLoS One*. 2021;16(3): e0246454.
 33. Wang S, Quan L, Chavarro JE, et al. Associations of Depression, Anxiety, Worry, Perceived Stress, and Loneliness Prior to Infection with Risk of Post-COVID-19 Conditions. *JAMA Psychiatry*. 2022;79(11).
 34. Hernández Sampieri R, Fernández Collado C, Baptista Lucio P. Metodología de la investigación. 6th edition. México D.F.: McGraw-Hill; 2014.
 35. Diener E, Emmons RA, Larsen RJ, Griffin S. The Satisfaction with Life. Scale. *J Per Assess*. 1985;49:71-75.
 36. Vinaccia Alpi E, Parada N, Quiceno JM, Riveros Munévar F, Vera Maldonado LA. Escala de satisfacción con la vida (SWLS): análisis de validez, confiabilidad

- y baremos para estudiantes universitarios de Bogotá. *Psicogente*. 2019;22(42):1-20.
37. Sinclair VG, Wallston KA. The development and psychometric evaluation of the Brief Resilient Coping Scale. *Assessment*. 2004;11:94-101.
 38. Trejos-Herrera AM, Vinaccia S, Bahamón M, Alarcón Y, Rodríguez M, Gaviria G. Validación de las propiedades psicométricas de la escala breve de estrategias resilientes BRCS en adultos colombianos. *Interdisciplinaria*. 2023;39(2):479-496.
 39. Lyubomirsky S, Lepper HS. A measure of subjective happiness: Preliminary reliability and construct validation. *Soc Ind Res*. 1999;46:137-155.
 40. Vera-Villaruel P, Celis-Atenas K, Córdova-Rubio N. Evaluación de la Felicidad: Análisis Psicométrico de la Escala de Felicidad Subjetiva en Población Chilena. *Ter psic*. 2011;29(1):127-133.
 41. Kroenke K, Spitzer RL, Williams JBW, Lowe B. An Ultra-Brief Screening Scale for Anxiety and Depression: The PHQ-4. *Psychosomatics*. 2009;50:613-621.
 42. Löwe B, Wahl I, Rose M, Spitzer C, Glaesmer H, Wingenfeld K, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord*. 2009;122(2010):86-95.
 43. Mendoza NB, Frondoza CE, Dizon JIWT, Buenconsejo JU. The factor structure and measurement invariance of the PHQ-4 and the prevalence of depression and anxiety in a Southeast Asian context amid the COVID-19 pandemic. *Curr Psychol*. 2022;
 44. Lenz AS, Li C. Evidence for measurement invariance and psychometric reliability for scores on the PHQ-4 from a rural and predominately Hispanic community. *Rev Cubana Enfer*. 2022;55(1):17-29.
 45. Materu J, Kuringe E, Nyato D, Galishi A, Mwanamsangu A, Katebalila M, et al. The psychometric properties of PHQ-4 anxiety and depression screening scale among out-of-school adolescent girls and young women in Tanzania: A cross-sectional study. *BMC Psychiatry*. 2020;20:321.
 46. Kocalevent RD, Finck C, Jimenez-Leal W, Sautier L, Hinz A. Standardization of the Colombian version of the PHQ-4 in the general population. *BMC Psychiatry*. 2014;14:205.
 47. Remor E, Carroble JA. Versión Española de la Escala de Estrés Percibido (PSS-14): Estudio psicométrico en una muestra VIH+ [Spanish version of the Perceived Stress Scale (PSS-14): Psychometric study in a HIV+ sample]. *Ansiedad y Estrés*. 2021;7(2-3):195-201.
 48. Velasco-Durantez V, Jimenez-Fonseca P, Carla M, Abreu M, Ghanem I, González M, et al. Resilience, social support, and anxious preoccupation in patients with advanced cancer during COVID-19 pandemic. *Cancer Invest*. 2022;40(6):474-482.
 49. Alvarado BE, Zunzunegui MV, Delisle H. Validación de escalas de seguridad alimentaria y de apoyo social en una población afro-colombiana: aplicación en el estudio de prevalencia del estado nutricional en niños de 6 a 18 meses. *Cad. Saúde Pública*. 2005;21(3):724-736.
 50. Montgomery DC, Peck EA, Vining GG. *Introduction to Linear Regression Analysis*. 2021: John Wiley & Sons.
 51. Pardoe I. *Applied Regression Modeling*. 2020: John Wiley & Sons.
 52. Limonero JT, Tomás-Sábado J, Fernández-Castro J, Gómez-Romero MJ, Aradilla-Herrero A. Estrategias de afrontamiento resilientes y regulación emocional: Predictores de satisfacción vital. [Resilient coping strategies and emotion regulation: Predictors of life satisfaction]. *Behav Psychol*. 2012;20:183-196.
 53. Vázquez C, Duque A, Hervás G. Satisfaction with life scale in a representative sample of Spanish adults: Validation and normative data. *Span J Psychol*. 2013;16E:82.
 54. Londoño NE, Rogers H, Castilla JF, Posada S, Ochoa N, Jaramillo MA, et al. Validación en Colombia del cuestionario MOS de apoyo social. *Inter J Psychol Res*. 2012;5(1):142-150.
 55. Lazarus RS, Folkman S. *Stress, appraisal, and coping*. 1994. New York: Springer.
 56. Nicolini H. Depresión y ansiedad en los tiempos de la pandemia de COVID-19. *Cirugía y Cirujanos*. 2020;88(5):542-547.
 57. Trujillo-Hernández PE, Gómez-Melasio DA, Lara-Reyes BJ, Medina-Fernández IA, Hernández-Martínez EK. Asociación entre características sociodemográficas, síntomas depresivos, estrés y ansiedad en tiempos de la COVID-19. *Enfermería Global*. 2021;20(64):1-25.
 58. Serrao Hill MMY, Hauck N, Yorgason JB, Bown C, Tankersley K. An exploration of happiness, anxiety symptoms, and depressive symptoms among older adults during the coronavirus pandemic. *Front Psychol*. 2023;14:1117177.
 59. Fakouri C, Lyon B. Perceived health and life satisfaction among older adults: The effects of worry and personal variables. *J Gerontol Nurs*. 2005;31:17-24.
 60. Luchesi BM, de Oliveira NA, de Moraes D, de Paula Pessoa RM, Pavarini SCI, Chagas MHN. Factors associated with happiness in the elderly persons living in the community. *Arch. Gerontol Geriatr*. 2018;74:83-87.

Effect of Silicone Rubber/Polyvinyl Alcohol /Zirconium Oxide Compound on Mesenchymal Stromal Cells

Efecto del Compuesto de Caucho De Silicona / Alcohol Polivinílico / Óxido de Circonio Sobre las Células Estromales Mesenquimales

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SUMMARY

Objective: This study aimed to conduct a cytotoxicity test in determining the viability and proliferation profile for novel material of silicone rubber/polyvinyl alcohol (PVA) with or without Zirconium oxide on mesenchymal stromal cell culture. **Methods:** An in vitro study was carried out on adipose-derived mesenchymal stromal cell culture. Samples were divided into five groups: control, silicone rubber/polyvinyl alcohol (PVA) without Zirconium oxide, silicone rubber/polyvinyl alcohol (PVA) with Zirconium oxide 1 %, 3 %, and 5 %. Each group contained 2×10^5 seeded MSCs/well stained with MTT for its viability. For proliferation, MTT staining was performed on days 1, 3, and 5 to assess the trend of the percentage of the living cell.

Statistical analysis was conducted using ANOVA, or the Kruskal-Wallis test with a CI of 95 %. **Results:** After exposure to silicone rubber/PVA+ZrO₂ material, the viability of mesenchymal stromal cells was significantly lower in Silicone rubber/PVA+ZrO₂ 3 % ($p < 0.05$), compared to Silicone rubber/PVA+ZrO₂ 5 % ($90,998 \pm 3,970$ vs. $107,762 \pm 7,892$). The percentage of living cells from mesenchymal stromal cell cultures after exposure to silicone rubber/PVA+ZrO₂ day-1 was not statistically significant, but silicone rubber/PVA had the maximum percentage (102.47 %). In contrast to day 1, the results of the ANOVA test on days -3 and -5 revealed a significant difference between the 5 groups ($p < 0.001$). Similarly, the Tukey-Kramer post-hoc test on the group yielded comparable results. Decreased across all groups were observed on day 5 of observation with 3 % ZrO₂ group being the lowest. **Conclusion:** Silicone rubber/polyvinyl alcohol (PVA) compound with or without Zirconium oxide

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(ZrO₂) exposure did not show a toxic effect on mesenchymal stroma cell culture. Further, in vivo studies are needed to confirm our findings.

Keywords: *Silicone rubber, Polyvinyl alcohol (PVA), Zirconium oxide (ZrO₂), Cytotoxicity, MTT assay.*

RESUMEN

Objetivo: *Este estudio tuvo como objetivo realizar una prueba de citotoxicidad para determinar la viabilidad y el perfil de proliferación de un nuevo material de caucho de silicona/alcohol polivinílico (PVA) con o sin óxido de circonio en cultivos de células estromales mesenquimales. Métodos:* *Se realizó un estudio in vitro en cultivo de células estromales mesenquimales derivadas del tejido adiposo. Las muestras se dividieron en cinco grupos: control, caucho de silicona/alcohol polivinílico (PVA) sin óxido de circonio, caucho de silicona/alcohol polivinílico (PVA) con óxido de circonio al 1 %, 3 % y 5 %. Cada grupo contenía 2x10⁵ MSC sembradas/pocillo teñido con MTT para determinar su viabilidad. Para la proliferación, se realizó tinción con MTT los días 1, 3 y 5 para evaluar la tendencia del porcentaje de células vivas. El análisis estadístico se realizó mediante ANOVA, la prueba de Kruskal-Wallis con IC del 95 %. Resultados:* *Después de la exposición al material de caucho de silicona/PVA+ZrO₂, la viabilidad de las células estromales mesenquimales fue significativamente menor en caucho de silicona/PVA+ZrO₂ 3 % (p < 0,05), en comparación con caucho de silicona/PVA+ZrO₂ 5 % (90,998 ± 3.970 frente a 107.762 ± 7.892). El porcentaje de células vivas procedentes de cultivos de células estromales mesenquimales después de la exposición al caucho de silicona/PVA+ZrO₂ día-1 no fue estadísticamente significativo, pero el caucho de silicona/PVA tuvo el porcentaje máximo (102,47 %). A diferencia del día 1, los resultados de la prueba de comparación ANOVA de los días -3 y -5 revelaron una diferencia significativa entre los 5 grupos (p < 0,001). De manera similar, la prueba post hoc de Tukey-Kramer en el grupo arrojó resultados comparables. Se observó una disminución en todos los grupos el día 5 de observación, siendo el grupo con 3 % de ZrO₂ el más bajo. Conclusión:* *El compuesto de caucho de silicona/alcohol polivinílico (PVA) con o sin exposición a óxido de circonio (ZrO₂) no mostró un efecto tóxico en el cultivo de células del estroma mesenquimatoso. Se necesitan más estudios in vivo para confirmar nuestros hallazgos.*

Palabras clave: *Caucho de silicona, alcohol polivinílico (PVA), óxido de circonio (ZrO₂), citotoxicidad, ensayo MTT.*

INTRODUCTION

Lumbar disc herniation (LDH) is an early and rather common sign of degeneration in the lumbar spine (1). Lumbar disc herniation results from several changes in the intervertebral disc including reduced water retention in the nucleus pulposus, increased type 1 collagen ratio in the nucleus pulposus and inner annulus fibrosus, destruction of collagen and extracellular material, and an upregulated activity of degrading systems such as matrix metalloproteinase expression, apoptosis, and inflammatory pathways. Ultimately, resulting in a local increase in inflammatory chemokines and mechanical compression applied by the protruding nucleus pulposus on the exiting nerve (1). The prevalence of LDH is estimated to be around 12 %, with a reported incidence of 2 % to 3 % (2). Patients with classical signs of motor deficit, cauda equina syndrome, and persistent pain will not benefit from conservative treatment and will require surgery to decompress the nerve involved (3). Numerous studies have compared conservative versus surgical treatment in lumbar disc herniation, observing faster pain relief and recovery in the early surgery groups, however, similar outcomes in the mid- and long-term were discovered (4,5). This phenomenon might be explained by the occurrence of substantial disc height reduction following discectomy which is proportional to the amount of nucleus removed (6). Disc height changes can have both local and global consequences. Reduced disc height and volume increase the stress on the remaining nucleus pulposus (NP), which can lead to a decrease in cell matrix synthesis and an increase in cell necrosis and apoptosis. Reduced disc height also causes major alterations in the spine's overall mechanical stability, which may lead to further spinal segment degeneration (7).

Several treatment options are currently available for LDH which focus on pain management, extruded disc tissue excision, and intervertebral disc (IVD) replacement or spinal fusion (8). The purpose of nucleus pulposus augmentation following disc removal is to prevent disc height decline and the associated biomechanical and biochemical changes (7). Clinical translation of implanted biomaterials cannot occur without evidence of durability, or

the ability to maintain physical support across millions of cycles of loading, as well as the generation of no or limited wear debris that could elicit a systemic immune response (9). Injectable biomaterials that can replace the disc nucleus pulposus after microdiscectomy have been developed. The novel injectable biomaterial was comprised of 40% PVA and 60% silicone rubber and the biomechanical compression test results revealed that the stress (MPa) and strain (%) values of the biomaterial resemble human nucleus pulposus properties (10,11). Although several NP augmentation biomaterials have been developed, only several have progressed beyond clinical trials to market approval (11,12).

Materials used in medical devices, particularly those in which the device contacts or is temporarily inserted or permanently implanted in the body, must meet basic biocompatibility requirements, generally defined by the American Society for Testing and Materials (ASTM) F-748 and the International Standards Organization (ISO) 10993 standards, to be nontoxic, non-thrombogenic, noncarcinogenic, nonantigenic, and nonmutagenic (13). The cytotoxicity test is one of the biological evaluation and screening techniques that uses tissue cells *in vitro* to observe how medical devices affect cell growth, reproduction, and morphology (14). Because it is simple, fast, has a high sensitivity, and can rescue animals from poisoning, cytotoxicity is recommended as a pilot project test and an important signal for toxicity evaluation of medical devices (15). To examine the safety of our novel biomaterial of silicone rubber/polyvinyl alcohol with additional Zirconium oxide (ZrO_2) compound usage against surrounding intervertebral disc (IVD) cells, this study aimed to conduct an *in vitro* cytotoxicity test against viability and proliferation on Mesenchymal Stromal Cells (MSCs) culture.

MATERIAL AND METHODS

Preparation of Silicone Rubber, PVA Material, and Zirconium oxide (ZrO_2)

PVA crosslinked with glutaraldehyde (GA) is obtained by mixing 20% wt. PVA in distilled water. This solution is added with H_2SO_4 (aq)

solution at as much as 10% wt. to initiate crosslinking between PVA and GA. Room-temperature-vulcanizing (RTV) silicone rubber, RTV 585, was prepared with a variety of 5% catalysts. Silicone rubber RTV 585 was mixed with 40PVA60SR (40% PVA and 60% silicone rubber) and additional compositions of Zirconium oxide (ZrO_2) 1%, 3%, and 5% (10,11).

Radio opacity was assessed by the addition of ZrO_2 and was qualitatively assessed under conventional X-ray. The material was then soaked in culture medium for 24 hours of which 100 μ L of the treated medium was placed into the well that had been seeded with mesenchymal stromal cells followed by an incubation period for 1 day, 3 days, and 5 days for each treatment groups.

Preparation of Mesenchymal Stromal Cells (MSCs) culture and MTT staining

Adipose-derived MSCs were taken from the CO_2 incubator in 80% confluence for harvesting. Then, harvest the cells until they become single cells and homogenize them in the culture medium. Placed the cells into 3 pieces of 96 well culture plates with a concentration of 2×10^5 /well for evaluation on day 1, day 3, and day 5, then 2 rows of well were left on each plate for blanks. The cells were incubated in a 96-well plate by placing them into the incubator CO_2 for 24 hours until the cells adhered perfectly.

Cytotoxicity test: viability and proliferation

The evaluation of cytotoxicity was performed on two cytotoxicity parameters, cell viability and cell proliferation. The study material was introduced using intervention on four treatment groups which consisted of silicone rubber/PVA alone and silicone rubber/PVA+ ZrO_2 1%, 3%, and 5% as separate groups. The groups were comprised of control (n=6), silicon rubber/PVA (n=6), silicon rubber/PVA+ ZrO_2 1% (n=6), 3% (n=6), and 5% (n=6). Cell culture viability was estimated with a colorimetric assay using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) staining (Sigma-Aldrich Corp., St. Louis, MO, USA) on day-1 (24h). This assay measures the reduction of yellow MTT to an

insoluble blue formazan product by mitochondrial succinate dehydrogenase, and the amount of formazan produced is directly proportional to the number of livings, not dead cells, present during MTT exposure. Proliferations were evaluated with a colorimetric assay using subsequent MTT techniques on the first (24h), third (72h), and fifth days (120h) for the proliferation test.

In total 25 μL /well of 5 mg/mL MTT was used before the third incubation for 4h. The medium was discarded following the third incubation. *Dimethyl sulfoxide* (DMSO) 200 μL /well was added. MSCs absorbance was determined with the use of an ELISA reader (Multi Reader Promega GM35000) at 595 nm wavelength. The percentage of viable cells and IC_{50} value were calculated using linear regression of log concentration. All the samples were also evaluated under a microscope to assess the cell distribution using a Cell Culture Microscope (Olympus CKX53FL-DP27) with 100x magnification.

Statistical analysis

The results of data collection were presented as mean \pm standard deviation (SD), median minimum-maximum, and percentage (%). Statistical analysis was performed using the IBM SPSS Statistics software version 23.0 for Mac (IBM Corp., Armonk, NY, USA). Data distributions were calculated using the Saphiro-Wilk test, while data variance was calculated

using Levene's test. ANOVA test followed by Tukey-Kramer test a post-hoc statistical test used to determine whether the means of two sets of data are statistically different from each other. This test is based on the studentized range distribution. Kruskal-Walli's test, a nonparametric method, was used to test whether samples originated from the same distribution. A p-value of 0.05 was considered a significant difference between the means, and correlation was determined within 95 % CI with $p < 0.05$.

RESULTS

The radio-opacity of a mixture of Silicon Rubber/PVA+ ZrO_2 (1 %, 3 %, and 5 %) was qualitatively evaluated using conventional X-ray. The result showed that the addition of ZrO_2 produces a radiopacity which corresponded to an increase in ZrO_2 concentrations (Figure 1).

Viability of MSCs exposed with Novel compound

MSCs data evaluation showed normal data distribution ($p=0.896$) and homogeneous data ($p=0.056$). The mean percentage (%) of living cells is 100 ± 8.843 for the control group, 93.867 ± 12.283 for the Silicone rubber/PVA group, 97.605 ± 6.524 for the Silicone rubber/PVA+1 % ZrO_2 group, 90.998 ± 3.970 for the Silicone rubber/PVA+ group ZrO_2 3 %, and 107.762 ± 7.892 for the Silicon rubber/PVA+ ZrO_2 5 % group. A



Figure 1. Conventional X-ray image of the composite material Silicon Rubber/PVA + ZrO_2 [1 % (11-12E/D), 3 % (1-2E/D), and 5 % (21-22E/D)].

EFFECT OF SILICONE RUBBER/POLYVINYL ALCOHOL /ZIRCONIUM OXIDE COMPOUND

significant difference ($p < 0.05$) was observed between the Silicon rubber/PVA+ZrO₂ 3 %

group when compared with the Silicon rubber/PVA+ZrO₂ 5 % group (Table 1).

Table 1
ANOVA test for MSCs viability following exposure to the treated culture medium

Group	Viable cell (%) Mean	SD	p
Control	100	8.843	
Silicone rubber/PVA	93.867	12.283	
Silicone rubber/PVA+ZrO ₂ 1%	97.605	6.524	0.02
Silicone rubber/PVA+ZrO ₂ 3%	90.998	3.970	
Silicone rubber/PVA+ZrO ₂ 5%	107.762	7.892	

Proliferation of MSCs

On days 3 and 5, the live cell counts with MTT staining in each well (n=30) were read by colorimetric assay. Cell confluences in all groups

were captured under the microscope and are shown in Figures 2 and 3. ANOVA test showed a significant difference ($p < 0.01$) between groups for each day. The mean percentage value can be seen in Table 2.

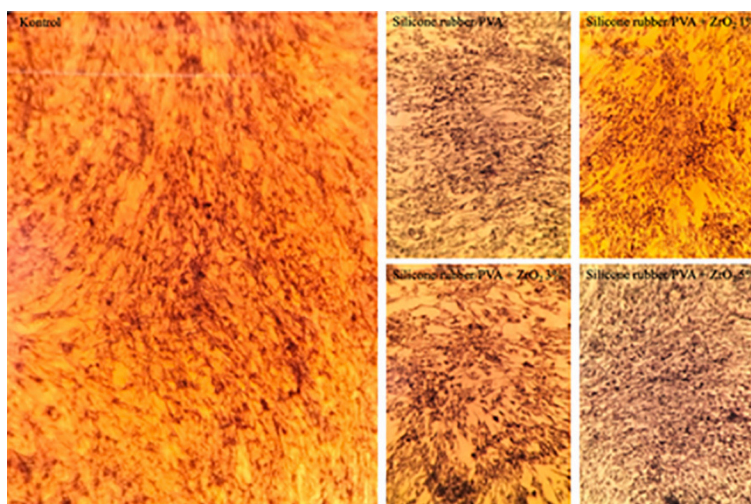


Figure 2. Mesenchymal Stromal cell culture for examination on day 3 with MTT staining for the five groups: control, silicone rubber/PVA, silicone rubber/PVA+ZrO₂ 1 %, 3 %, and 5 %. (Olympus Microscope CKX53FL-DP27, 100x magnification).

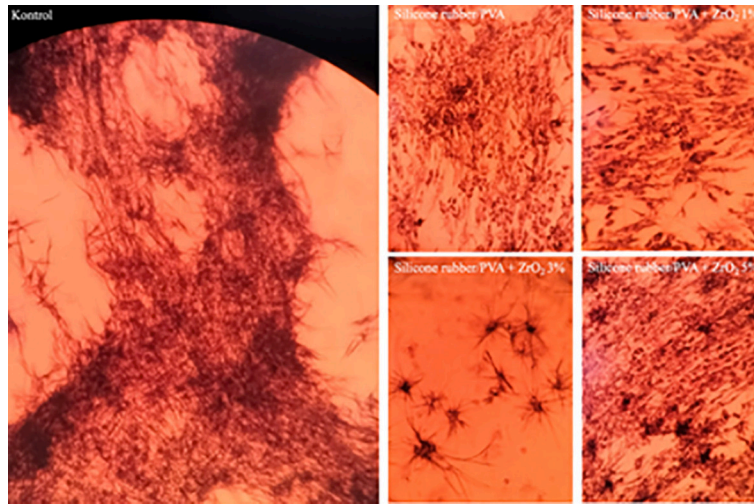


Figure 3. Mesenchymal Stromal Cells culture for examination on day 5 with MTT staining for the five groups: control, silicone rubber/PVA, silicone rubber/PVA+ZrO₂ 1 %, 3 %, and 5 %. (Olympus Microscope CKX53FL-DP27, 100x magnification).

Table 2
ANOVA Test for Day 3 and 5 observations of MSCs following treated culture medium

Group	Viable cell (%)			
		Mean	SD	p
Day 3	Control	100	5.761	
	Silicone rubber/PVA	76.430	9.051	< 0.001
	Silicon rubber/PVA+ZrO ₂ 1 %	72.173	2.761	
	Silicon rubber/PVA+ZrO ₂ 3 %	66.693	6.933	
	Silicon rubber/PVA+ZrO ₂ 5 %	92.762	5.705	
Day 5	Control	100	20.437	
	Silicone rubber/PVA	57.945	16.408	< 0.001
	Silicon rubber/PVA+ZrO ₂ 1 %	58.077	7.941	
	Silicon rubber/PVA+ZrO ₂ 3 %	10.345	4.799	
	Silicon rubber/PVA+ZrO ₂ 5 %	86.688	7.254	

We further analysed for significant differences between each observation's days (1,3,5) using the Mann-Whitney test, which revealed a statistically significant difference in the percentage of living cells between the groups treated. Day 1 and 3 comparison of silicone rubber/PVA, silicone rubber/PVA+ZrO₂ 1 %, and silicone rubber/PVA+ZrO₂ 3 % showed a significant difference (p<0.05), whereas day 1 and 5 comparison showed statistically significant difference (p<

0.05) between the percentage of living cells observed in the groups treated with silicone rubber/PVA, silicone rubber/PVA+ZrO₂ 1 %, and silicone rubber/PVA+ZrO₂ 3 %. We also found statistically significant differences (p< 0.05) between the percentage of viable cells when comparing days 3 and 5 in the treatment group between 1 % silicone rubber/PVA+ZrO₂ and 3 % silicone rubber/PVA+ZrO₂. Figure 4 illustrates

the trend of the average percentage of living cells in each treatment group for five days. The percentage decreased, which is generally stable.

From day 3 to day 5, the Rubber / PVA + ZrO₂ 3 % group showed a significant decrease.

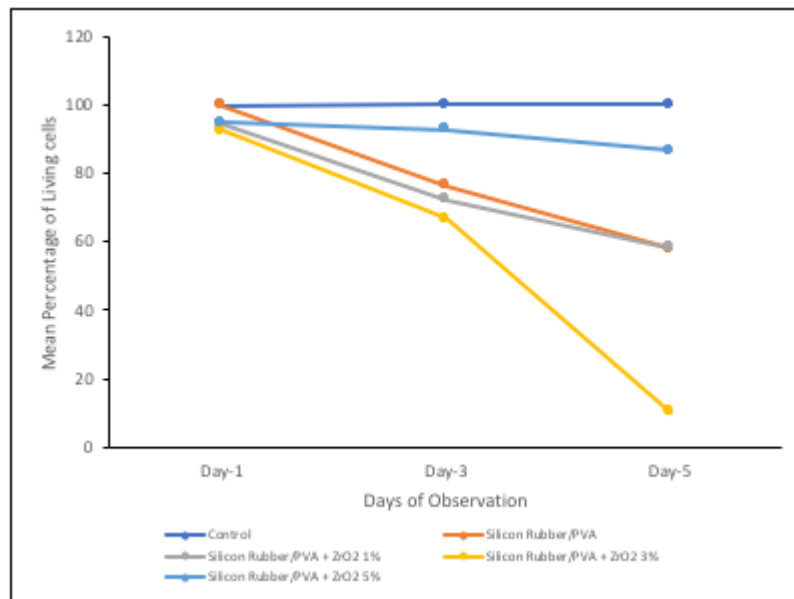


Figure 4. Percentage of surviving cells in the treatment group.

DISCUSSION

American Standards and Test Methods (ASTM) International developed the first standards for testing cytotoxicity in the early 1980s. This standard has then been adapted by various countries and by the International Organization for Standardization (ISO), where cytotoxicity testing is specifically addressed in ISO 10993-5 (14). Types of cytotoxicity tests are stated in ISO 10993-5: Extract, direct contact, and indirect contact tests (including agar overlay assay and filter diffusion). In general, the extracted test is suitable for detecting the toxicity of soluble substances of medical devices and is usually consistent with the results of animal toxicity tests (10,13,15). Applications for silicones extend to extracorporeal devices, catheters, drains, shunts, various long-term implants, orthopaedic implants, and aesthetic implants (16). An ideal NP implant should

have the same biomechanical properties and bioavailability as human NP (17,18). A composite of silicon rubber and polyvinyl alcohol (PVA) is a promising material for artificial disc replacement (15,19-22).

Cytotoxicity is one of the many parameters of compatibility and should be one of the principal parameters assessed in biocompatibility testing (23). Cytotoxicity can be evaluated by various tests, including the Cytotoxicity elution test (MEM elution), MTT assay, Agar overlay assay, and other means. Among these tests, the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay is considered the gold standard for *in vitro* cytotoxicity testing (24). The direct contact assay is the most sensitive for testing the cytotoxicity of medical devices; the medical devices can be measured even with weak cytotoxicity. It does however have a prerequisite that the sample should cover only 10 % of the culture dish surface. Therefore, the dimension

of the test subject might not allow direct testing in this study. Furthermore, direct testing is dependent on the contact regime affected by the material density and adherence to cell culture. A certain material with a higher density might potentially crush the cells, while a less dense material might float in the medium. Adherent synthetic material might cause rupture of the underlying cell during removal and might cause a falsely perceived reduction in cell count. Extract testing through a conditioned medium is thought to have an advantage in this study, providing a uniform concentration exposure to the cell culture. This concentration is reflective of the constituents released from the initial contact, as opposed to the direct method, where the maximal concentration is achieved only at the end of the treatment period, normally 24 h (14). This standard recommends Phosphate Buffer saline (PBS) as a buffer solution which is isotonic and non-toxic and aims to maintain cell osmolarity and not interfere with tissue viability (25). MTT undergoes enzymatic reduction to purple formazan in metabolically active cells. Assay is then done by comparing cell exposure to a substance and measuring the decrease in optical density. Studies also compare optical density at different times to determine exposure duration. According to previous studies, a cell viability decrease of over 50 % indicates positive cytotoxicity (26,27). The biocompatibility standards conform regarding material–tissue contact duration, which is differentiated into three time periods: (i) <24 h, intra-operative contact, (ii) 24 h to 30 days, defined as short-term implantation, and (iii) >30 days, which is called permanent or chronic implantation (28). This study uses MSCs *in vitro*, as stroma cells exist in embryos and adult cells with multiple differentiation stages (29). MSCs are easy to isolate, culture, and manipulate in *ex vivo* culture. The cell populations could represent different points of a hierarchy or a continuum of differentiation, for example, the intervertebral disc tissue (30). Preliminary assessment of the material *in vitro* can already provide insight into the applicability of the biomaterial *in vivo* (31). Determining *in vivo* cytotoxicity is found to be more expensive and needs a longer duration of observation, therefore *in vitro* experiments are chosen in the study. The study found that the Silicon rubber/PVA group had the maximum viability, with a median percentage of living cells

of 102.47. The Silicon rubber/PVA+ZrO₂ 3 % group had the lowest viability, with a median percentage of living cells of 89.06 which was in conjunction with the study by Mirzadeh, showing silicone having the highest viability for MSCs (32). Silicone's use as a biomaterial necessitates consideration of its surface properties, including surface charge, water-binding ability, chemistry, topography, electrical conductivity, critical surface tension, morphology, roughness, and rigidity (32). Zirconium, which can generate reactive oxygen species, affects cytotoxicity (33). Due to its biocompatibility and corrosion resistance, zirconium is still utilized in bioceramics and implants despite the lack of information regarding its toxicity (34). Despite Ye and Shi (35) assertion that the addition of zirconium in a certain proportion increased toxicity, additional research is required to determine the cytotoxicity of the zirconium component.

Biomimetic scaffold is one of the most promising strategies in the field of bone tissue engineering. Zirconium oxide (ZrO₂), as a kind of bioceramic material, has attracted much attention in biomimetic scaffolds due to its excellent biocompatibility, high mechanical strength, and great chemical stability. ZrO₂ is widely used in industry, biomedicine, and dentistry, for example as ceramic dental prostheses, dental implant coatings, and bone restorative materials. A lot of work has been carried out to investigate the characteristics and applications of zirconia-based biomimetic scaffolds. However, few works can provide a systematic comparison and overview of the research progress of zirconia-based biomimetic scaffolds. It was proposed the use of ZrO₂ as the basis for the scaffold and the use of bioactive materials as layers to achieve a combination of mechanical properties and bioactivity (36). However, it was suggested that ZrO₂-NPs have negative impacts on the liver and exhibit potential risks for non-alcoholic fatty liver disease. In this regard, Sun et al. investigated the hepatic biodistribution and toxicological effects of ZrO₂-NPs after intravenous administration (20 mg/kg, bw) *in vivo* and the toxicological mechanism toward hepatocytes *in vitro*. They demonstrated that the liver showed continuous ZrO₂-NP accumulations associated with oxidative stress, increased inflammatory responses, and

functional injury. Meanwhile, the results of the *in vitro* studies demonstrated that ZrO₂-NPs exposure resulted in cytotoxicity in Hepg2 cells in a dose- and time-dependent manner. RNA-sequence from the spleen and brain of mice injected with ZrO₂ nanoparticles showed significant changes in gene expression (37). Alzahrani et al. reported the apoptotic and DNA-damaging effects of Yttria-stabilized ZrO₂-NPs also known as Yttria Zirconia, Yttria Stabilized Zirconium Oxide, on human skin epithelial cells (38). In addition, it was studied the effects of ZrO₂-NPs on early life stages of the zebrafish (*Danio rerio*) to examine such effects on embryonic development in this species. ZrO₂-NPs instigated developmental acute toxicity in these embryos, causing mortality, hatching delay, and malformation. Developmental toxicity of zebrafish embryos caused by zirconium oxide nanoparticles in aquatic environments shows that exposure to zirconium oxide nanoparticles is toxic to embryonic zebrafish (39). However, Yang et al. (40) stated that mice injected with ZrO₂ had remained material in lysosomal vesicles, in the liver and spleen macrophages, without any abnormal ultrastructural changes up to a dose of 500 mg/kg. Our study showed a decrease in the number of living mesenchymal stroma cells, which was found below 50 % in the group with 3 % ZrO₂ levels, suggesting that at concentration used does not present cytotoxic effects.

The present study examined the proliferation of mesenchymal stroma cell cultures exposed to a silicone rubber/PVA mixture on days 1, 3, and 5 using the MTT method (41). In this study, we used a period of 1, 3, and 5 days which is the midterm category for this analytical test, a long-term evaluation is needed to find out more about the effect of silicon rubber/PVA exposure on mesenchymal stroma cell culture after day 5. Another classification regarding the period is mentioned in ISO 10993 by observing the interventions in a certain period. They divided the tests into systemic toxicity (acute toxicity), subacute toxicity, and subchronic toxicity. Acute toxicity is observed within the first 24 hours, while subacute and subchronic toxicity is observed for a period not less than 24 hours and <10 % of the total lifespan of the mesenchymal

stroma cell. The subacute period is chosen in this research to evaluate the progressivity of cytotoxic effects on the short-term implantation period, as mentioned above, within 24 hours to 30 days (34). The IC₅₀ is the concentration of the biomaterial that causes 50 % cell mortality when tested. Consistent with research by Ye and Shi demonstrating zirconium's apoptotic effect, our study showed a decrease in cell proliferation proportional to exposure duration (35). In addition to the concentration of zirconium, exposure duration also impacts proliferation. Silicon, despite its widespread use, is toxic, as demonstrated by Onnekink et al. and Chen et al., who demonstrated that nano silicon carbide had a toxic effect on human mesenchymal stroma cells, but not on cancer cell lines at a concentration of 0.1 mg/mL (42,43). It can be assumed that tissue integration of material is correlated with optimal cell proliferation. The scaffold creates tissue with cells, factors, or a bioreactor. Factors for choosing a scaffold in tissue engineering. A biocompatible scaffold is necessary for cells to attach, function, migrate, and proliferate without an immune response. It should be biodegradable, non-toxic, and easily expelled to support cells in creating their extracellular matrix. The perfect implant scaffold must be site-specific, and strong yet allow cell infiltration. The scaffold for tissue engineering should have a porous structure and high porosity for cell penetration, nutrient diffusion, and waste removal without harming nearby organs or tissues. The pore size is vital for cell-scaffold interaction (44). Since our data are not conclusive, further research is required to determine the optimal concentration and changes in bonding or morphology resulting from the mixture of the experimental constituents and their effects on proliferation.

Study Limitations

The limitations of this study include (1) The immunocytochemical assessment is not directly analysed by evaluating cell morphology; (2) Neither inflammation nor morphology was evaluated; (3) No animal experimental investigations (*in vivo*) were conducted.

CONCLUSION

The cytotoxicity profile of novel silicone rubber/PVA compound with or without Zirconium oxide (ZrO_2) was found as a biomaterial for nucleus pulposus replacement on a mesenchymal stromal cell culture. The mixture of silicone rubber/PVA treated with or without ZrO_2 concentrations of 1, 3, and 5 % did not decrease cell viability in mesenchymal stroma cell cultures. Comparing the four components of the silicone rubber/PVA compound with or without Zirconium oxide (ZrO_2), it was determined that the mixture containing 5 % ZrO_2 had the greatest cell proliferation results. The silicone rubber/PVA compound with or without Zirconium oxide (ZrO_2) was not toxic for up to 5 days of exposure, except the SR/PVA+ ZrO_2 3 %.

Ethical approval

All procedures performed and materials included in the study are by the ethical standards of Dr. Soetomo Hospital, Surabaya, Indonesia (Ethical number 0869/111/2/VIII/2021).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

- Saleem S, Aslam HM, Rehmani MAK, Raees A, Alvi AA, Ashraf J. Lumbar Disc Degenerative Disease: Disc Degeneration Symptoms and Magnetic Resonance Image Findings. *Asian Spine J.* 2013;7(4):322.
- Vialle LR, Vialle EN, Suárez Henao JE, Giraldo G. Lumbar Disc Herniation. *Rev Brasil Ortop (English Edition).* 2010;45(1):17-22.
- Weiner BK, Zibis A. Lumbar discectomy. In: *Operative Techniques in Spine Surgery.* Wolters Kluwer Health Adis (ESP). 2014.p.108-115.
- Jacobs WCH, Van Tulder M, Arts M, Rubinstein SM, Van Middelkoop M, Ostelo R, et al. Surgery versus conservative management of sciatica due to a lumbar herniated disc: A systematic review. *Eur Spine J.* 2011;20(4):513-522.
- Gugliotta M, Da Costa BR, Dabis E, Theiler R, Jüni P, Reichenbach S, et al. Surgical versus conservative treatment for lumbar disc herniation: A prospective cohort study. *BMJ Open.* 2016;6(12):e012938.
- Brinckmann P, Grootenboer H. Change of Disc Height, Radial Disc Bulge, and Intradiscal Pressure from Discectomy An *in Vitro* Investigation on Human Lumbar Discs: *Spine (Phila Pa 1976).* 1991;16(6):641-646.
- Boyd LM, Carter AJ. Injectable biomaterials and vertebral endplate treatment for repair and regeneration of the intervertebral disc. *Eur Spine J.* 2006;15(S3):414-421.
- Gadjradj PS, Arts MP, Van Tulder MW, Rietdijk WJR, Peul WC, Harhangi BS. Management of Symptomatic Lumbar Disk Herniation: An International Perspective. *Spine (Phila Pa 1976).* 2017;42(23):1826-1834.
- Schmitz TC, Salzer E, Crispim JF, Fabra GT, Le Visage C, Pandit A, et al. Characterization of biomaterials intended for use in the nucleus pulposus of degenerated intervertebral discs. *Acta Biomater.* 2020;114:1-15.
- Permana G, Bajamal A, Subagio E, Parenrengi M, Rasyida A, Utomo B. Novel silicone rubber and polyvinyl alcohol (PVA) compound as nucleus pulposus replacement in intervertebral disc herniation surgery. *Turk Neurosurg.* 2022;32(5):779-785.
- Rasyida A, Halimah S, Wijayanti ID, Wicaksono ST, Nurdiansah H, Silaen YMT, et al. A Composite of Hydrogel Alginate/PVA/r-GO for Scaffold Applications with Enhanced Degradation and Biocompatibility Properties. *Polymers (Basel).* 2023;15(3):534.
- Berlemann U, Schwarzenbach O, Diwan A, Kitchel S, Coric D. Nucleoplasty with NuCore® Injectable Nucleus Replacement for Herniated Lumbar Disc: A Multicenter Study With A Minimum Five-Year Follow-Up: Gp147. In: *Spine J Meeting Abstracts.* LWW; 2014.p. 202.
- Helmus MN, Gibbons DF, Cebon D. Biocompatibility: Meeting a Key Functional Requirement of Next-Generation Medical Devices. *Toxicol Pathol.* 2008;36(1):70-80.

14. Bruinink A, Luginbuehl R. Evaluation of Biocompatibility Using *In Vitro* Methods: Interpretation and Limitations. In: Kasper C, Witte F, Pörtner R, editors. Tissue Engineering III: Cell - Surface Interactions for Tissue Culture. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011.p.117-152.
15. Li W, Zhou J, Xu Y. Study of the *in vitro* cytotoxicity testing of medical devices. Biomed Rep. 2015;3(5):617-620.
16. Zare M, Ghomi ER, Venkatraman PD, Ramakrishna S. Silicone-based biomaterials for biomedical applications: Antimicrobial strategies and 3D printing technologies. J Appl Polym Sci. 2021;138(38):50969.
17. Bergknut N, Smolders LA, Koole LH, Voorhout G, Hagman RE, Lagerstedt AS, et al. The performance of a hydrogel nucleus pulposus prosthesis in an ex vivo canine model. Biomaterials. 2010;31(26):6782-6788.
18. Di Martino A, Vaccaro AR, Lee JY, Denaro V, Lim MR. Nucleus Pulposus Replacement: Basic Science and Indications for Clinical Use. Spine (Phila Pa 1976). 2005;30(Supplement):S16-S22.
19. Thomas J, Gomes K, Lowman A, Marcolongo M. The effect of dehydration history on PVA/PVP hydrogels for nucleus pulposus replacement. J Biomed Mater Res. 2004;69B(2):135-140.
20. Luo X, Akram MY, Yuan Y, Nie J, Zhu X. Silicon dioxide/poly(vinyl alcohol) composite hydrogels with high mechanical properties and low swell ability. J Appl Polym Sci. 2019;136(1):46895.
21. Li Q, Huang X, Liu H, Shang S, Song Z, Song J. Properties Enhancement of Room Temperature Vulcanized Silicone Rubber by Rosin Modified Aminopropyltriethoxysilane as a Cross-linking Agent. ACS Sustain Chem Eng. 2017;5(11):10002-10010.
22. Sonker AK, Rathore K, Nagarale RK, Verma V. Crosslinking of Polyvinyl Alcohol (PVA) and Effect of Crosslinker Shape (Aliphatic and Aromatic) Thereof. J Polym Environ. 2018;26(5):1782-1794.
23. ISO ISO. 10993-1: 2009. Biological evaluation of medical devices 1: Evaluation and testing within a risk management process. International Organization for Standardization, Geneva. 2009.
24. Huzum B, Puha B, Necoara RM, Gheorghevi S, Puha G, Filip A, et al. Biocompatibility assessment of biomaterials used in orthopedic devices: An overview. Exp Ther Med. 2021;22(5):1-9.
25. Budi HS, Setyawati MC, Anitasari S, Shen YK, Pebriani I, Ramadan DE. Cell detachment rates and confluence of fibroblast and osteoblast cell culture using different washing solutions. Brazilian J Biol. 2024;84:1-8.
26. Bellagamba BC, Abreu BRR de, Grivicich I, Markarian CF, Chem E, Camassola M, et al. Human mesenchymal stem cells are resistant to cytotoxic and genotoxic effects of cisplatin *in vitro*. Genet Mol Biol. 2016;39(1):129-134.
27. Ghasemi M, Turnbull T, Sebastian S, Kempson I. The MTT Assay: Utility, Limitations, Pitfalls, and Interpretation in Bulk and Single-Cell Analysis. Int J Mol Sci. 2021;22(23):12827.
28. Sampogna G, Guraya SY, Forgione A. Regenerative medicine: Historical roots and potential strategies in modern medicine. J Microsc Ultrastruct. 2015;3(3):101-107.
29. Sampogna G, Guraya SY, Forgione A. Regenerative medicine: Historical roots and potential strategies in modern medicine. J Microsc Ultrastruct. 2015;3(3):101-107.
30. Beyer Nardi N, da Silva Meirelles L. Mesenchymal stem cells: isolation, *in vitro* expansion and characterization. Handb Exp Pharmacol. 2006;(174):249-282.
31. Schmitz TC, Salzer E, Crispim JF, Fabra GT, Le Visage C, Pandit A, et al. Characterization of biomaterials intended for use in the nucleus pulposus of degenerated intervertebral discs. Acta Biomater. 2020;114:1-15.
32. Mirzadeh H, Shokrolahi F, Daliri M. Effect of silicon rubber crosslink density on fibroblast cell behavior *in vitro*. J Biomed Mater Res. 2003;67A(3):727-732.
33. Yu KN, Yoon TJ, Minai-Tehrani A, Kim JE, Park SJ, Jeong MS, et al. Zinc oxide nanoparticle-induced autophagic cell death and mitochondrial damage via reactive oxygen species generation. Toxicology *in Vitro*. 2013;27(4):1187-1195.
34. Ju-Nam Y, Lead JR. Manufactured nanoparticles: An overview of their chemistry, interactions and potential environmental implications. Scienc Total Environm. 2008;400(1-3):396-414.
35. Ye M, Shi B. Zirconia Nanoparticles-Induced Toxic Effects in Osteoblast-Like 3T3-E1 Cells. Nanoscale Res Lett. 2018;13(1):353.
36. Weng W, Wu W, Hou M, Liu T, Wang T, Yang H. Review of zirconia-based biomimetic scaffolds for bone tissue engineering. J Mater Sci. 2021;56(14):8309-8333.
37. Sun T, Ou L, Zhan X, Zhao W, Huang R, Feng X, et al. Toxicity of Zirconia oxide Nanoparticles: Liver Biodistribution and Liver Damages. Research Square. 2020:1-24.
38. Izahrani FM, Katubi KMS, Ali D, Alarifi S. Apoptotic and DNA-damaging effects of yttria-stabilized zirconia nanoparticles on human skin epithelial cells. Int J Nanomedicine. 2019;14:7003-7016.
39. Karthiga P, Ponnanikajamdeen M, Rajendran R S, Gurusamy Annadurai, S Rajeshkumar S. Characterization and toxicology evaluation of zirconium oxide nanoparticles on the embryonic

- development of zebrafish, *Danio rerio*. *Drug Chem Toxicol.* 2019;42(1):104-111.
40. Yang Y, Bao H, Chai Q, Wang Z, Sun Z, Fu C, et al. Toxicity, biodistribution and oxidative damage caused by zirconia nanoparticles after intravenous injection. *Int J Nanomedicine.* 2019;14:5175-5186.
 41. Fotakis G, Timbrell JA. *In vitro* cytotoxicity assays: Comparison of LDH, neutral red, MTT and protein assay in hepatoma cell lines following exposure to cadmium chloride. *Toxicol Lett.* 2006;160(2):171-177.
 42. Onnekink C, Kappel RM, Boelens WC, Puijn GJM. Low molecular weight silicones induce cell death in cultured cells. *Sci Rep.* 2020;10(1):9558.
 43. Chen J. Static compression induces zonal-specific changes in gene expression for extracellular matrix and cytoskeletal proteins in intervertebral disc cells *in vitro*. *Matrix Biology.* 2004;22(7):573-583.
 44. O'Brien FJ. Biomaterials & scaffolds for tissue engineering. *Materials Today.* 2011;14(3):88-95.

Factors that Influence Malnutrition Among Toddlers in Padang, Indonesia after COVID-19

Factores que Influyen en la Desnutrición entre los Niños Pequeños en Padang, Indonesia, Después de la COVID-19

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SUMMARY

Objective: This study aims to determine the factors influencing malnutrition among toddlers in Padang, Indonesia, post-COVID-19. **Method:** This study uses explanatory quantitative methods through a cross-sectional approach. Respondents were all mothers with malnourished children in Padang, totaling 256 people. Variables consist of early breastfeeding; exclusive breastfeeding; complementary feeding; infectious disease; socio-economic; parenting style; and environmental sanitation. All variables were measured through a survey using a questionnaire. **Result:** The bivariate statistical test using the Chi-Square test proved that all factors had a statistically significant p -value <0.05 , meaning all variables significantly affected the incidence of partial malnutrition. Three dominant variables affect malnutrition in children in Padang: history of complementary feeding, socio-economic, and

parenting style. Of the three factors, socio-economic is the factor that has the most influence on malnutrition in children after the COVID-19 pandemic. The $Exp(B)$ value of 0.312 indicates that for every one-unit increase in socioeconomic status, malnutrition will decrease by 31.2%. **Conclusion:** The malnutrition of toddlers in Padang City after COVID-19 is influenced by the history of early initiation of breastfeeding, exclusive breastfeeding, complementary feeding, infectious diseases, environmental sanitation, socioeconomic, and parenting style. The most dominant factor is socio-economic.

Keywords: Malnutrition, toddler, post-COVID-19.

RESUMEN

Objetivo: este estudio tiene como objetivo determinar los factores que influyen en la desnutrición entre los niños pequeños en Padang, Indonesia después de COVID-19. **Método:** Este estudio utiliza métodos cuantitativos explicativos a través de un enfoque transversal. Los encuestados fueron todas madres que tenían niños desnutridos en la ciudad de Padang, con un total de 256 personas. Las variables consisten en: historia de inicio temprano de lactancia materna; historia de lactancia materna exclusiva; historia

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de alimentación complementaria; antecedentes de enfermedades infecciosas; socioeconómico; estilo de crianza; y saneamiento ambiental. Todas las variables medidas a través de una encuesta mediante un cuestionario. Resultado: Los resultados de la prueba estadística bivariada mediante la prueba de Chi-Cuadrado demostraron que todos los factores tenían un valor sig (p) <0,05 por lo que se encontró un efecto significativo en la incidencia de desnutrición parcial. Hay tres variables dominantes que afectan la desnutrición en los niños de la ciudad de Padang, a saber, el historial de alimentación complementaria, socioeconómico y estilo de crianza. De los tres factores, el socioeconómico es el que más influye en la desnutrición infantil tras la pandemia del COVID-19. El valor Exp(B) de 0,312 indica que, por cada aumento de una unidad en el nivel socioeconómico, la incidencia de desnutrición disminuirá en un 31,2%. Conclusión: La desnutrición de los niños pequeños en la ciudad de Padang después de COVID-19 está influenciada por la historia de inicio temprano de la lactancia materna, lactancia materna exclusiva, alimentación complementaria, enfermedades infecciosas, saneamiento ambiental, estilo socioeconómico y de crianza. El factor más dominante es el socioeconómico.

Palabras clave: *Malnutrición, infante, post-COVID-19.*

INTRODUCTION

Malnutrition (undernutrition) is caused by a lack of nutrients, either because of a poor diet or problems absorbing nutrients from food, caused by having a severe or prolonged period of inadequate energy and nutrient intake, this often occurs due to decreased food intake or increased metabolic needs. The COVID-19 pandemic has had a significant economic impact in many countries, including Indonesia. Declining economic activity, unemployment, and declining incomes increase the risk of poverty and economic inequality (1). Therefore, child health, access to nutritious food, health services, and adequate sanitation facilities are challenging to meet ideally. In a difficult economic situation, access to child health services is hampered (2). Decreased household income affects the ability of families to pay for health care costs and limits visits to health facilities so that families cannot detect and treat diseases or health conditions of children early. Economic instability can affect

family access to nutritious food and a balanced diet. Malnourished children have a higher risk of infection, stunted growth, and other health problems (3).

The Indonesian Ministry of Health predicts that the number of cases of malnutrition in toddlers will increase by 15 percent, or the equivalent of 7 million children, after the COVID-19 pandemic. Based on the 2021 Indonesian Nutrition Status Study results, wasting children decreased to 7.1 percent from the previous 7.4 percent in 2019. However, the number of underweight children increased by 17 percent in 2021. This number increased in 2019, reaching 16.3 percent (4). Meanwhile, the prevalence of malnourished toddlers in Padang was 15.40 % in 2018. Several health programs that were delayed and not implemented due to the COVID-19 pandemic are feared to increase the number of malnourished toddlers in the future (5).

A study found that children who experience malnutrition in the first 60 months of life will experience disruption of the neurodevelopmental trajectory (6). Kirolos et al. (2022), in a systematic review of 30 studies on the effect of malnutrition on children's quality of life, indicated that malnutrition affects not only neurodevelopment but also academic achievement, cognitive development, and behavioral problems (7).

Alam et al. assessed the degree of malnutrition risk in Makassar, Indonesia, during the COVID-19 pandemic. They found that less than four prenatal checkups, non-exclusive breastfeeding, and infectious diseases such as acute respiratory infection/diarrhea in low birth weight children in the last three months were risk factors for malnutrition (8). Meanwhile, Loots et al., revealed that the mother's employment status is related to the incidence of malnutrition in children. In effect, they showed no malnourished children from working mothers, few children were found to be malnourished in self-employed mothers, and more malnutrition from non-working mothers (9).

This study aims to identify the factors that influence the incidence of malnutrition in the city of Padang, Indonesia post-COVID-19. The results will allow us to improve our understanding of this issue and help to formulate appropriate public policies. The information

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will give the basis to the government to direct resources and interventions to areas where is needed, such as public health programs, infrastructure improvements, increasing access to health services, and nutrition education for the community.

METHOD

This study uses explanatory quantitative methods through a cross-sectional approach. The data was collected using a survey method using a questionnaire. The research respondents were taken through a total sampling technique, namely all mothers who had malnourished children in Padang with 256 people. Determination of the sample based on data from 23 health centers in Padang. The research was conducted from November 2022 – March 2023.

Data collection used a survey method involving seven independent variables that measured: 1) early initiation of breastfeeding; 2) exclusive breast milk; 3) complementary feeding; 4) infectious diseases; 5) socio-economic; 6) parenting style and 7) environmental sanitation.

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) application with three stages, namely: 1) univariate through the presentation of a frequency distribution to describe each variable; 2) bivariate through the Chi-Square test to analyze the effect of the independent variables on the dependent; 3) multivariate through logistic regression test to examine the overall effect of the independent variables on the dependent simultaneously. The Ethics Committee Dr. MDjamil Padang Hospital approved the research feasibility with number LB.02.02/5.7/481/2022.

RESULT

Most of the mothers were aged 26-35 years (62.9 %), and 68 % had higher education. The majority of respondents were unemployed (86.3 %), so the primary breadwinners were fathers (100 %). In the distribution of the sex of children, boys were 47.3 %, while girls were

52.7 %. Regarding the number of children, most respondents had 1-2 children, with a percentage of 68.8 %. When looking at information about births, a small number of respondents (1.6 %) reported births by traditional birth attendants, while the majority used midwives (58.6 %) or obstetricians (39.8 %).

Table 1
Characteristics of Respondents and Factors that Influence Malnutrition

Variable	Frequency	(%)
Early breastfeeding		
No	162	63.3
Yes	94	36.7
Exclusive breastfeeding		
No	173	67.6
Yes	83	32.4
Complementary feeding		
Less	199	77.7
Good	57	22.3
Infection diseases		
Yes	101	39.5
No	155	60.5
Sanitation		
Not good	143	55.9
Good	113	44.1
Socioeconomic		
Low	195	76.2
High	61	23.8
Parenting style		
Democratic	39	15.2
Otoriter	29	11.3
Permissive	120	46.9
Abandonment	68	26.6

Based on the descriptive survey, we found that most of the respondents (63.3 %) did not initiate early breastfeeding, and 67.6 % of mothers did not give exclusive breastfeeding. Most mothers were less skilled at providing complementary food for breastfeeding, as much as 77.7 %. When looking at the history of infectious diseases, 60.5 % of respondents reported that their child had an infectious disease and was in unhealthy environmental sanitation (55.9 %). For socio-

economic factors, 76.2 % of respondents are in the low category. The main parenting style used by mothers is permissive (46.9 %).

Table 2

Partial effect of each factor on malnutrition

Variable	Sig (p)
Early breastfeeding	0.0001
Exclusive breastfeeding	0.0001
Complementary feeding	0.0001
Infection diseases	0.0001
Sanitation	0.0001
Socioeconomic	0.0001
Parenting style	0.001

The bivariate statistical test using the Chi-Square test proved that all factors had a significant p-value <0.05, affecting the incidence of partial malnutrition.

By removing each variable with a significant p-value > 0.05 at each step, in the regression modeling at step four, it was found three dominant variables that affect malnutrition in children in Padang City: history of complementary feeding, social economics, and parenting. Of the three factors, socio-economic is the factor that has the most influence on malnutrition in children after the COVID-19 pandemic. The Exp(B) value of 0.312 indicates that for every one-unit increase in socioeconomic status, malnutrition will decrease by 31.2 %.

Table 3

The simultaneous effect of all factors on malnutrition

Variable	Step 1		Step 2		Step 3		Step 4	
	Sig (p)	Exp (B)	Sig (p)	Exp (B)	Sig (p)	Exp (B)	Sig (p)	Exp (B)
Early breastfeeding	0.018	0.460	0.002	0.379	0.065	0.765	-	-
Exclusive breastfeeding	0.145	0.604	-	-	-	-	-	-
Complementary feeding	0.042	0.398	0.026	0.270	0.013	0.334	0.007	0.201
Infection diseases	0.088	1.724	-	-	-	-	-	-
Sanitation	0.091	0.568	-	-	-	-	-	-
Socioeconomic	0.001	0.177	0.001	0.476	0.001	0.193	0.000	0.312
Parenting style	0.021	0.468	0.001	0.455	0.001	0.273	0.000	0.305

DISCUSSION

Malnutrition in post-COVID-19 children refers to conditions in which children experience malnutrition, negatively impacting their growth and development after recovering from COVID-19 infection. The COVID-19 pandemic had devastating impacts that risked reversing the slow but gradual progress made in recent years to achieve Sustainable Development Goals. In a context already characterized by a significant increase in the number of people at risk of food insecurity, the pandemic dramatically jeopardized the achievement of many of the objectives of

Agenda 2030, and the number of malnourished people increased with dramatic consequences for the most vulnerable segments of the population such as children, women, and adolescents. In this study, we found that the seven factors significantly influenced the incidence of malnutrition in toddlers.

Early breastfeeding initiation is one of the efforts to provide optimal nutrition to infants early in life. Breast milk contains all the nutrients a baby needs to grow and develop properly. Breast milk contains essential nutrients such as protein, fat, carbohydrates, vitamins, minerals, and antibodies that help protect babies from

infection. Colostrum, the liquid produced by the breasts in the first few days after giving birth, is rich in nutrients and antibodies. Colostrum helps strengthen the baby's immune system and protects it from disease. Early stimulation of the breasts triggers sufficient milk production. Thus, the baby has adequate access to breast milk which is essential for its growth and development. The link between the absence of early initiation of breastfeeding and malnutrition of children under five is evident in this study, as was the previous study by Garti et al. (10), who assess child feeding practices and their association with undernutrition among young children, demonstrated that early initiation of breastfeeding and bottle feeding was associated with acute malnutrition and experiencing feeding challenges were associated with chronic malnutrition. Furthermore, early initiation of breastfeeding within the first hour after birth provides significant benefits in providing early nutrition for the baby. Thus, timely initiation of early breastfeeding is significantly associated with better growth in infants in the form of a better increase in body weight and length at six months (10). Promoting appropriate child-feeding practices can reduce the risk of undernutrition.

In addition to a history of low-quality early breastfeeding, most mothers in this study also had a history of low exclusive breastfeeding. This condition results in the baby not getting the maximum nutrition in breast milk. The baby's digestive tract more easily absorbs the nutritional components in breast milk compared to formula milk. The proper nutritional content in breast milk helps the baby's body utilize nutrients more efficiently, promoting optimal growth and development. In addition, a solid mother-infant bond during the breastfeeding process is a valuable asset besides benefiting from its nutritional content. Research proves that children who grow up in mother-infant solid bonds will have better physical and cognitive development (11).

The pandemic significantly increased the number of children at risk of malnutrition and premature death, due to its direct or indirect consequences such as increased poverty linked to job losses, especially in informal sectors, closure of schools and school canteens, disruption of essential health services and the increase

in various forms of violence and exploitation. Although a year of the COVID-19 pandemic has passed, it still leaves poor quality in serving complementary foods nowadays. Decreased income, changes in daily routine, stress, and worry are all barriers to providing good complementary foods for toddlers. Research in rural areas in China found that poor complementary feeding practices, including malnourished and unbalanced feeding, were associated with a high prevalence of anemia in infants and toddlers (12). Providing complementary food for toddlers is not an easy thing for the community. A study in Myanmar by Mya Kyaw Swa found that out of 1 222 children aged 6-23 months, 20 % of children had obstacles in receiving complementary foods, and 43 % suffered from moderate anemia (13).

The absence of early breastfeeding, exclusive breastfeeding, and poor quality of complementary foods are the causes of infectious diseases in most children under five. Infectious diseases such as diarrhea, pneumonia, and respiratory infections can interfere with the absorption of nutrients in a toddler's body (14), thereby increasing the risk of malnutrition. Roth et al. highlighted the relationship between respiratory infections and nutritional status in children. Respiratory infections can cause decreased appetite, increase energy requirements, and interfere with the absorption of nutrients, which can contribute to the risk of malnutrition in toddlers (15). A study revealed that *Cryptosporidium*, a parasite that infects the human digestive tract, especially the small intestine, is associated with impaired growth in toddlers in sub-Saharan Africa (16). Recurring or prolonged diarrhea can interfere with the absorption of nutrients, including essential nutrients for bone and muscle growth in toddlers, which can impact the risk of malnutrition (17).

Unhealthy environmental sanitation conditions also cause infectious diseases in most toddlers. Prüss-Ustün et al. found an association between inadequate access to clean water, sanitation, and hygiene and the risk of diarrheal disease, respiratory infections, and nutrition-related morbidity in young children in middle and low-income countries (18). Shrestha et al., in a study involving 1 427 respondents in Nepal, found more than 50 % of children were in critical health conditions. The results of this study also emphasize that improving children's

health is highly dependent on appropriate health programs, including meeting optimal nutritional needs, good sanitation management, and reliable health promotion to invite people to understand personal hygiene habits and maintain a clean environment (19).

Socio-economic is the central axis of the cause of maternal and child health problems (20) after the COVID-19 pandemic. This factor is the dominant aspect that influences the incidence of under-five malnutrition in Padang. Decreased income during the pandemic has resulted in economic and infrastructure constraints that hinder access to needed maternal and neonatal care (21). Economic instability also disrupts the food supply, affecting the availability of nutritious food for mothers and babies, which causes the risk of post-pandemic malnutrition. Mothers will experience increased stress and shaken socio-economic conditions that affect the quality of baby care and development (22).

Increased stress can make a mother feel overly tired, overwhelmed, or helpless, which reduces attention and involvement in caring for their children. Mothers who experience decreased mental well-being may be less able to provide adequate time, attention, and interaction with their children. She also has difficulty maintaining a stable daily routine for her children. They may not provide consistent structure regarding sleeping, eating, or other daily activities. This instability can affect the safety and comfort of children, as well as interfere with regular and organized parenting (23).

CONCLUSION

In conclusion, early breastfeeding, exclusive breastfeeding, complementary feeding, infectious diseases, environmental sanitation, socioeconomic status, and parenting style influenced malnutrition among toddlers in Padang City after COVID-19. The most dominant factor is socio-economic.

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REFERENCES

1. Ntambara J, Chu M. The risk to child nutrition during and after COVID-19 pandemic: What to expect and how to respond. *Public Health Nutr.* 2021;24(11):3530-3536.
2. Osendarp S, Akuoku JK, Black RE, Headey D, Ruel M, Scott N, et al. The COVID-19 crisis will exacerbate maternal and child undernutrition and child mortality in low- and middle-income countries. *Nat Food.* 2021;2(7):476-484.
3. Mertens E, Peñalvo JL. The Burden of Malnutrition and Fatal COVID-19: A Global Burden of Disease Analysis. *Frontiers in Nutrition.* 2021;7.
4. BKPK H. Studi Status Gizi Indonesia. Kementrian Kesehatan Republik Indonesia. 2022.
5. Dinkes S. Profil Kesehatan Provinsi Sumatera Barat 2021 [Internet]. 2022. Available from: <https://www.scribd.com/document/605509811/Profil-Kesehatan-Provinsi-Sumatera-Barat-2021>
6. Suryawan A, Jalaludin MY, Poh BK, Sanusi R, Tan VMH, Geurts JM, et al. Malnutrition in early life and its neurodevelopmental and cognitive consequences: a scoping review. *Nutr Res Rev.* 2022;35(1):136-149.
7. Kirolos A, Goyheneix M, Elias MK, Chisala M, Lissauer S, Gladstone M, et al. Neurodevelopmental, cognitive, behavioural and mental health impairments following childhood malnutrition: A systematic review. *BMJ Glob Heal.* 2022;7(7):e009330.
8. Alam AS, Wahiduddin, Ansariadi, Noor NN, Syafar M, Hidayanty H. Determinant of stunting in children aged 12-24 months during the COVID-19 pandemic era in Makassar City. *Gac Med Caracas.* 2023;131(1):31-39.
9. Loots R, Yan B, Vember H. Factors Associated with Malnutrition among Children Aged Six Months to Five Years in a Semi-Rural Area of the Western Cape, South Africa. *Child Care Pract.* 2022;28(4):625-638.
10. Garti H, Bukari M, Wemakor A. Early initiation of breastfeeding, bottle feeding, and experiencing feeding challenges are associated with malnutrition. *Food Sci Nutr.* 2023;11(9):5129-5136.
11. Wallenborn JT, Levine GA, Carreira dos Santos A, Grisi S, Brentani A, Fink G. Breastfeeding, Physical Growth, and Cognitive Development. *Pediatrics.* 2021;147(5):e2020008029.
12. Hipgrave DB, Fu X, Zhou H, Jin Y, Wang X, Chang S, et al. Poor complementary feeding practices and high anaemia prevalence among infants and young children in rural central and western China. *Eur J Clin Nutr.* 2014;68(8):916-924.
13. Mya KS, Kyaw AT, Tun T. Feeding practices and nutritional status of children age 6-23 months in

FACTORS THAT INFLUENCE MALNUTRITION AMONG TODDLERS

- Myanmar: A secondary analysis of the 2015-16 Demographic and Health Survey. *PLoS One*. 2019;14(1):e0209044.
14. Dewi R, Sari P, Programs PS, Education M, Program S, Utama WT, et al. Analysis of Diarrhea, Acute Respiratory Infection (ARI), and Hepatitis with the Nutritional Status of Children in Children in Indonesia (Riskesdas Data 2018). *Res Mil*. 2023;13(2023).
 15. Roth DE, Caulfield LE, Ezzati M, Black RE. Acute lower respiratory infections in childhood: opportunities for reducing the global burden through nutritional interventions. *Bull World Health Organ*. 2008;86(5):356-364.
 16. George CM, Birindwa A, Li S, Williams C, Kuhl J, Thomas E, et al. *Akkermansia muciniphila* Associated with Improved Linear Growth among Young Children, Democratic Republic of the Congo. *Emerg Infect Dis*. 2023;29(1):81-88.
 17. Lan H, Wang H, Chen C, Hu W, Ai C, Chen L, et al. Flavonoids and gastrointestinal health: single molecule for multiple roles. *Crit Rev Food Sci Nutr*. 2023;6:1-19.
 18. Prüss-Ustün A, Wolf J, Bartram J, Clasen T, Cumming O, Freeman MC, et al. Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: An updated analysis with a focus on low- and middle-income countries. *Int J Hyg Environ Health*. 2019;222(5):765-777.
 19. Shrestha A, Six J, Dahal D, Marks S, Meierhofer R. Association of nutrition, water, sanitation and hygiene practices with children's nutritional status, intestinal parasitic infections and diarrhoea in rural Nepal: a cross-sectional study. *BMC Public Health*. 2020;20(1):1241.
 20. Adeyanju O, Tubeuf S, Ensor T. Socio-economic inequalities in access to maternal and child healthcare in Nigeria: Changes over time and decomposition analysis. *Health Policy Plan*. 2017;32(8):1111-1118.
 21. Robertson T, Carter ED, Chou VB, Stegmüller AR, Jackson BD, Tam Y, et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: A modelling study. *Lancet Glob Heal*. 2020;8(7):e901-908.
 22. McCann J, Sinno L, Ramadhan E, Assefa N, Berhane HY, Madzorera I, et al. COVID-19 disruptions of food systems and nutrition services in Ethiopia: Evidence of the impacts and policy responses. *Ann Glob Heal*. 2023;89(1).
 23. Fonseca A, Moreira H, Canavarro MC. Uncovering the links between parenting stress and parenting styles: The role of psychological flexibility within parenting and global psychological flexibility. *J Context Behav Sci*. 2020;18:59-67.

Histological Liver Changes in Experimental Obstructive Cholestasis with Partial Outflow Restoration

Cambios Histológicos Hepáticos en la Colestasis Obstructiva Experimental con Restauración Parcial del Flujo de Salida

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SUMMARY

Objective: This work aimed to establish histological changes in the structure and activity of the liver caused by experimental obstructive cholestasis. **Method:** Several methodological approaches were used such as experimental, biochemical, and comparison were applied. **Results:** It was possible to describe the essence of such a disease as cholestasis and its impact on the liver. At the same time, it was proved that recanalization with incomplete recovery of bile outflow was possible due to the normalization of the total bilirubin (TB) level. Morphological changes in the liver were most pronounced during acute cholangitis. The study examined what processes occur in the body during

the recovery of bile flow, including after the complete blockage of such organs as the liver and bile ducts. Consequently, signs that expressed the abnormality of the liver structure of animals were revealed. At each of the stages of the experiment, specific indicators that determined the condition of the studied internal organs of rats according to the levels that correspond or do not correspond to the norm were established. **Conclusion:** The obtained conclusions are of high value, as they are an important basis for continuing the research on this topic and can also be used in the practical activities of medical workers.

Keywords: Complete obstruction, TB level, bile ducts, recanalization, fibrosis.

RESUMEN

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Objetivo: El trabajo tuvo como objetivo establecer los cambios histológicos en la estructura y actividad del hígado provocados por la colestasis obstructiva

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experimental. Método: Se utilizaron varios enfoques metodológicos, entre ellos el experimental, el bioquímico y el de comparación. Resultados: Fue posible describir la esencia de una enfermedad como la colestasis y su impacto en el hígado. Al mismo tiempo, se demostró que la recanalización con recuperación incompleta del flujo de bilis era posible debido a la normalización del nivel de bilirrubina total (BT). Los cambios morfológicos en el hígado fueron más pronunciados durante el curso de la colangitis aguda. El estudio examinó qué procesos ocurren en el cuerpo durante la recuperación del flujo biliar, incluso después del bloqueo completo de órganos como el hígado y los conductos biliares. En consecuencia, se revelaron signos que expresaban la anormalidad de la estructura del hígado de los animales. En cada una de las etapas del experimento se establecieron indicadores específicos que determinaron el estado de los órganos internos de las ratas estudiadas según los niveles que corresponden o no a la norma. Conclusión: Las conclusiones obtenidas son de alto valor, ya que son una base importante para continuar la investigación de este tema, y también pueden ser utilizadas en las actividades prácticas de los trabajadores médicos.

Palabras clave: *Obstrucción completa, nivel de TB, vías biliares, recanalización, fibrosis.*

INTRODUCTION

Obstruction of the extrahepatic biliary tract is a common complication of benign and malignant diseases of the extrahepatic biliary tract and adjacent organs (1). As a result of the development of obstruction, a number of changes occur in the body, which include the formation of biliary hyperplasia, the appearance of fibrosis, or liver failure. Considerable attention has been paid to this question in scientific doctrine, in particular, it has been actively studied by various specialists. Despite this, in connection with the deterioration of the external conditions of the development and vital activities of society, the question of the effect on the liver of the incomplete recovery of the outflow of bile, which is formed to a greater extent by the natural course of the disease or is achieved by therapeutic procedures, has become especially relevant (2-5). Obstructive cholestasis resulting from benign or malignant disease frequently complicates clinical outcomes through adverse hepatic changes. Partial bile flow restoration, often occurring naturally or following interventions, impacts subsequent liver

pathology in unclear ways. Elucidating these histological alterations is critically important given the high disease burden, yet previous studies have not comprehensively examined the effects of incomplete outflow recovery. Additional research is urgently needed to fully characterize the cellular and tissue changes associated with partial bile drainage restoration after obstruction.

Based on this, the work aimed to study the histological changes of the liver during its experimental obstruction after partial restoration of outflow. For this purpose, it was experimentally induced cholestasis in male rats, establishing indicators of liver pathology, studying the features of reparation, as well as cellular reactions to interference in their activity, describing the process of development of fibrosis and cirrhosis of the liver and establishing the possible complications of cholestasis.

This experimental model of obstructive cholestasis makes it possible to study in depth the pathomorphosis of the liver, features of reparation, cellular reaction, the development of fibrosis and cirrhosis of the liver, and the types of abnormalities that can develop on its basis (6-9). All these indicators play an important role, not only in the process of the liver, as an internal organ, but also in the entire structure of the body. The most common method of experimental modeling of complete and long-term obstruction of the extrahepatic bile ducts is the ligation of the bile duct with its transection (10-13).

At the same time, the impossibility of patency is also characteristic of a ligated bile duct, especially in the initial stages. However, recanalization occurs later with the restoration of bile outflow (14). Special attention should be paid to this aspect in the context of a possible study of the restoration of bile outflow in case of complete obstruction and the effect of this restoration on histological changes of the liver and common bile duct (CBD).

In this regard, Lazcanoiturburu et al. (15) studied the time frame for liver recovery based on the simulation of cholestasis. The researcher also created experimental conditions, because of which they concluded that after two days the regenerative mechanisms of liver tissue were activated. Streltov et al. (16), and Mejidov et al. (17) demonstrated the influence of biliary

tract decompression on the dynamics of lipoperoxidation processes. It was established that on the 7th day after the experiment, lipid peroxidation was at the highest level in terms of pathogenesis and negative impact on the liver, taking into account cholestasis. In turn, Dzyubanovskyi and Gudyma (18), and Hrabchak and Bedeniuk (19) assessed the effect of bile duct decompression on the rate of bile formation in the body after experimental cholestasis. They established that such dynamics are different, depending on the animal whose liver is being studied. Average – two-week indicators, which are characterized by decompression of the common bile duct. Based on the results it was possible to characterize the methodology of conducting experimental cholestasis, as well as to reveal its influence on changes in the liver structure and outflow restoration processes. However, there are some limitations in the studies regarding the process of incomplete recovery of bile outflow after cholestasis, since they may not have addressed this aspect in detail or considered the important variations in histological changes that may result from incomplete restoration of outflow. Also, previous studies did not consider adequately the mechanisms of cellular response and tissue remodeling in the context of partial restoration of bile outflow. Thus, further research is required to obtain a complete and accurate picture of the histological changes occurring in the liver with incomplete recovery of bile outflow. Such research can be of great importance for improving the understanding of the pathological processes that occur in the liver during obstructive cholestasis. This may have practical application in clinical practice to improve the results of treatment of patients with similar diseases.

This research has a significant value as it delves into a lesser-explored aspect of liver health; with obstructive cholestasis being a common complication of various diseases, the study's focus on the effects of incomplete bile outflow restoration on liver histology is particularly relevant. By comprehensively investigating cellular reactions, fibrosis development, and potential complications, the research enhances our understanding of the complexities surrounding liver pathophysiology. This contribution carries the potential to refine treatment approaches, advance the field's knowledge, and ultimately

improve patient outcomes, making it a valuable resource for both researchers and clinicians worldwide.

MATERIALS AND METHODS

The research was organized and conducted based on the Institute of Biology of Karazin Kharkiv National University. In the experiment were used 96 mature male rats, with a body weight of 270-310 g, kept periods of 12 hours of light and dark, with food and tap water *ad libitum*. Two models of cholestasis were used. Surgical procedures were performed in antiseptics conditions; a midline laparotomy was performed under general anesthesia. Complete common bile duct obstruction (CCBDO) was performed by ligation and transection between two sutures (41 animals) (3,13). 39 animals underwent the ligation of the common bile duct without its transaction, which was subsequently accompanied by recanalization and partial bile outflow restoration (PBOR) (11). 10 non-operated and 6 sham-operated animals served as the control.

The animals were removed from the experiment on the 1st, 3rd, 7th, 14th, 21st, 28th, and 35th days of the postoperative (PO) period, the condition of the abdominal organs was assessed, and the diameter of the CBD above the ligature was measured using a caliper and a ruler. The criterion for restoring the passage of bile was its presence in the lumen of the duodenum. The total bilirubin level (TB) in blood serum was determined by a standard biochemical method. Liver samples were stored in a special solution containing formalin (10 %). The Van Gieson method was used for staining histological preparations with hematoxylin and eosin. The degree of fibrosis was assessed (20). Pathological and biochemical examination of the animals that died but were not removed from the experiment was not carried out. The obtained indicators and other numerical data were expressed as mean standard deviation (SD). Student's t-test was used to determine changes between two groups of variables. In the course of working with categorical data, the χ^2 criterion was significant. $P < 0.05$.

HISTOLOGICAL LIVER CHANGES IN EXPERIMENTAL OBSTRUCTIVE CHOLESTASIS

Normalization of the level of bilirubin while preserving the signs of cholestasis in the liver can be caused by several mechanisms related to the regulation of bile secretion, transport of bile, and processing of bilirubin. Some possible mechanisms are Dilatation of the bile ducts; Stimulation of bile secretion; Regulation of bile transport; Reduction of inflammatory processes; Support of liver function and increasing the removal of bilirubin from the blood. These mechanisms can act separately or together, depending on the specific conditions of the disease and the approach to treatment.

The method of comparison in the study involved the comparison of normal indicators with those obtained during the experiment. This tool made it possible to process data that characterized the effect of cholestasis on the liver. In addition, the method of comparison involved the study of such histological changes in different periods, depending on the number of days from which the experiment had passed. It made it possible to compare different states of organisms before and after the formation of experimental conditions.

The work was carried out by the conditions and rules defined in the “European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes” (1986). The study was approved by the Bioethics Commission of the Kharkiv Medical Academy of Postgraduate Education, No. 3266.

RESULTS

12 of 41 animals (29.3%) with CCBDO died during the experiment: up to PO day 7: 3 animals; between the PO days 15 and 21: 2 rats; between the PO day 22 and 28: 5 rats; between the PO day 29 and the PO day 35: 2 animals. Throughout the experiment, the skin, visible mucous membranes, and internal organs at autopsy had icteric discoloration. Moreover, the liver of the animals was enlarged, and the common bile duct above the site of ligation and transection was dilated and contained transparent bile of varying color intensity. The TB blood level significantly exceeded the control group indices, especially on PO day 1 (Figures 1 and 2).

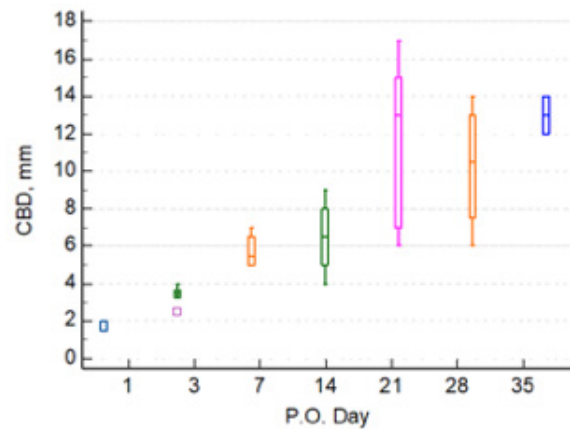


Figure 1. Common bile duct dilatation in CCBDO.

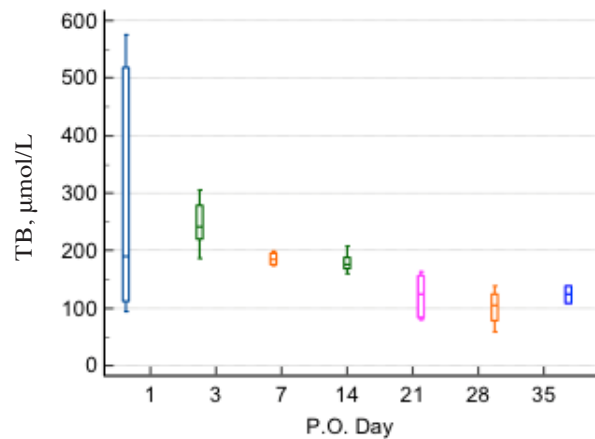


Figure 2. Total bilirubin level in CCBDO. Total bilirubin was expressed in $\mu\text{mol/L}$.

Histological changes of the liver on the PO day 1 are characterized by edema and vascular hyperemia. In addition, they were infiltrated by leukocytes, which provoked an increase in the size and width of the bile ducts. There was no fibrosis. On PO day 3, signs of an acutely developed pathological process remained—edema and hyperemia of vessels with their infiltration by leukocytes. Indicators that show a low level of focal hepatocellular necrosis were obtained. Along with this, there was a proliferation of the bile ducts, moderate infiltration of portal tracts with mononuclear cells, congestion, and vessel

leukocytosis. In one case, fibrosis was absent, in the other 2 cases fibrosis corresponded to grade 1 around the newly formed bile ducts. On PO day 7, the properties of inflammation were less pronounced, including edema, leukocyte infiltration, and hyperemia. Port-portal septa consisting of collagen fibers were established. In addition, such partitions contain new bile ducts. In two cases, the fibrosis corresponded to grade 1, and in another two – to grade 2. On PO day 14, during the expansion of these zones with the phenomena of ductal proliferation, the histoarchitectonics of the liver were rearranged, and functionally active liver parenchyma was observed to shift. In 4 cases, the fibrosis had the grade 4, and 2 animals – grade 5.

On PO day 21, the proliferation processes of cholangiocytes increased. This was expressed in the destruction of the liver lobular structure. As a result, the parenchyma was expressed in the form of islands, which include groups of hepatocytes. The latter lacks a bundle histostructure, because of which they are surrounded by new cholangiocytes. They were characterized by weak fibrosis, which was expressed in the form of a net connected with collagen fibers. Based on the Van-Gieson method for studying connective tissue and fibrous changes in organs in various diseases, it was possible to detect connective tissue fibers on the plane of the partitions. Where these components were distant, the formation of cholangiocytomas of the liver parenchyma occurred. In different cases, the grade of liver fibrosis differed. It was grade 3 three times, grade 4 twice, and only once grade 5 in 1. On PO day 28, mainly due to the progressive proliferation of the bile ducts, hepatocytes, generally, were located in groups and apart from each other, without forming lobules. In all cases, fibrosis corresponded to grade 4. Extreme indicators of the proliferation of salted components were established on PO day 35. Liver fibrosis was grade 4. At the same time, hepatocytes were placed differently, both together (in groups) and singly (without forming lobules).

In the experiment PBOR, 8 animals (20.5%) died: up to the PO day 7 day: 5 animals; no death between the PO day 8 and 15; between the PO day 15 and 21 days: 1 animal; between the PO day 22 and 28: 1 rat; between the PO day 29 and 35: 1 animal. During the first 14 days of the experiment, all the animals had icteric skin,

visible mucous membranes, and internal organs at autopsy. Rat livers were enlarged, CBD above the ligation site was dilated, and it contained clear bile of varying color intensity. However, on PO day 21, despite the CBD dilatation above the ligature (4.5 ± 2 mm), there were no macroscopic signs of obstructive icterus in 2 of 7 cases. In these cases, the TB level was 5.5 ± 1.5 $\mu\text{mol/L}$ and did not significantly differ from the TB level in the control group ($p > 0.05$). TB normal level (3.1 ± 1.5 $\mu\text{mol/L}$) was also observed in 4 of 5 animals on PO day 35. These animals also had dilated CBD (4.1 ± 0.8 mm) (Figure 3).

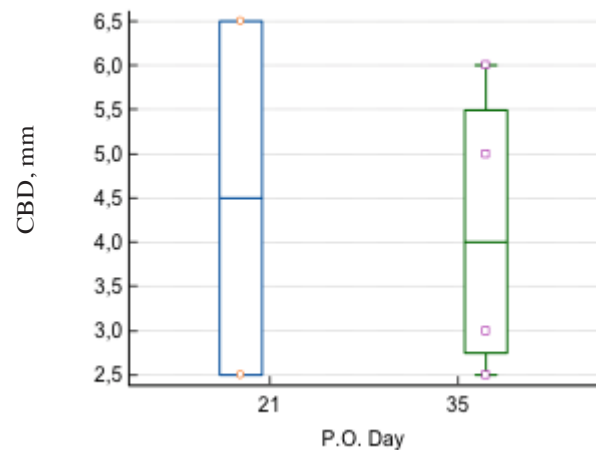


Figure 3. CBD dilatation in PBOR and normal TB level

On the PO days, 7 and 14 animals had bile in the duodenum lumen in 1 of 4, and 2 of 4 cases, respectively. On PO day 21, bile in the duodenum was observed in 4 of 7 animals; on PO day 28 in 2 out of 2 rats; on PO day 35 – in 4 of 5 animals. According to the presence of a normal TB level in several animals on the PO days 21 and 35, it is reasonable to consider the results of the experiment depending on the TB level, which is an important marker of cholestasis. Figures 4 and 5 show the distribution of animals with hyperbilirubinemia depending on the experiment duration, the TB level, and the CBD diameter above the ligature.

HISTOLOGICAL LIVER CHANGES IN EXPERIMENTAL OBSTRUCTIVE CHOLESTASIS

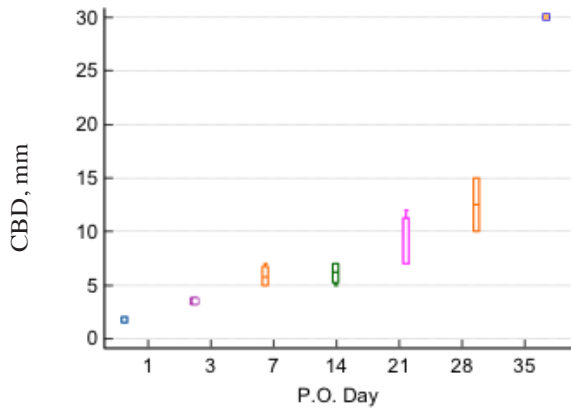


Figure 4. Common bile duct dilatation in PBOR with hyperbilirubinemia.

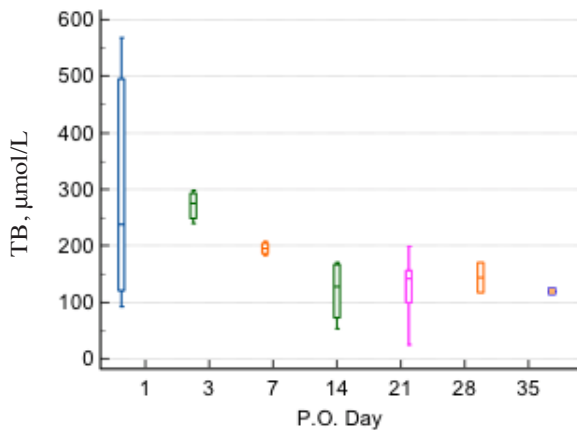


Figure 5. Total bilirubin level in PBOR with hyperbilirubinemia

In the case of ligating the CBD without its transection on the PO days 1-14, the liver histological picture fully corresponded to CCBDO. This also applies to cases in which bile was found in the duodenum lumen. Liver fibrosis was absent on day 1 in all cases. On PO day 3, it occurred in 2 out of 3 cases and corresponded to grade 1. On PO day 7 all 4 cases had fibrosis of grade 2, and on PO day 14: 3 out of 4 cases had grade 4, and one grade 5. Differences in the liver histostructure with PBOR in comparison with CCBDO were found on PO day 21 and

they are associated with the TB level. With an increased level of TB, on PO days 21 and 28, the histological changes in the liver having CCBDO and PBOR were the same and did not depend on the presence of bile in the duodenum. On PO day 21, 4 of 5 cases had liver fibrosis of grades 4, and 1 case grade 5. On PO day 28, only one animal had grade 4 fibrosis. On PO day 35, one animal with PBOR and hyperbilirubinemia in the liver histostructure showed pronounced proliferation of cholangiocytes and oval cells, mainly without glandular lumens. False lobules were found but without significant displacement of the liver parenchyma. In some portal zones, there was scanty mononuclear inflammatory infiltration, and vascular stasis, in the form of a septum and a system of collagen fibers surrounding the newly formed bile ducts, entwining individual cholangiocytes and corresponding to the grade 5. The CBD diameter of this animal was 30 mm, and there was pus bile in its lumen (Figure 6).

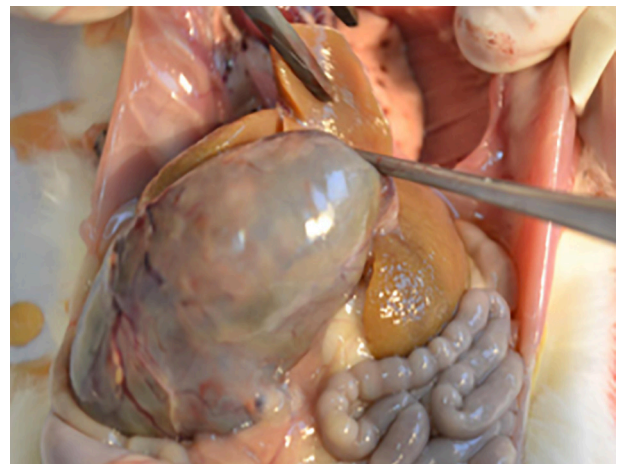


Figure 6. The CBD dilatation of about 30 mm of the animal with PBOR complicated by cholangitis on the PO day 35.

At a normal TB level on PO day 21 (2 animals), the liver histological picture was heterogeneous. In one case, vascular congestion was observed in the liver, a moderate increase in the number of bile ducts due to their proliferation, and a significant expansion of the portal zones due

to predominantly newly formed bile ducts and stromal cells. Grade 2 fibrosis was present in most of the portal zones with rare thin porto-portal septa. In another case, the liver histostructure was close to normal. The bile ducts were slightly dilated, as well as there was a slight mononuclear infiltration with the absence or weak fibrosis of a few portal zones. On the PO day 35 of PBOR, 4 animals with normal TB levels had also variable liver histological pictures. In one case, the liver histostructure was close to normal: a slight expansion of the portal zones due to stromal cells, fibroblasts, cholangiocytes scant infiltration of mononuclear cells (lymphocytes), and vascular congestion. Fibrosis was absent (Figure 7).

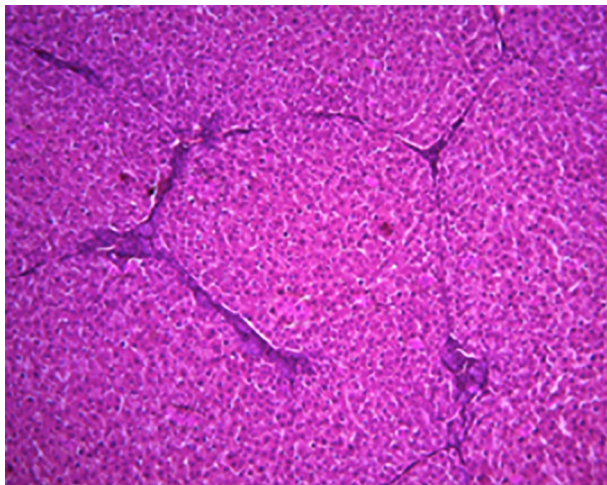


Figure 7. The liver histostructure with PBOR and normal TB level (PO day 35). The lobular structure of the liver is preserved. The portal zones are slightly enlarged and contain the bile ducts. Circular G+E magnifier x100.

The other three cases had enlarged portal zones in the liver due to the stroma, fibroblasts, cholangiocytes, and meager focal infiltration by mononuclear cells and vascular congestion. Fibrosis in one case was grade 1, in another grade 2, and one animal had the grade of fibrosis regarded as 2-3, depending on the field of view of the histological specimen.

DISCUSSION

The study of experimental cholestasis is usually carried out to identify the features of the pathological process development, including the phenomena and substances that initiate further pathological changes in the liver – development of fibrosis and cirrhosis (1,6). The other reasons are evaluating the effectiveness of various medicinal agents in acute and chronic liver pathology (21); studying the natural history of obstructive cholestasis in the aspect of the development of its complications, associated with the hepatobiliary system – cholangitis, liver failure (5,9), or systemic ones (8,12).

There are two main models to study experimental obstructive cholestasis. In one, the bile duct is ligated (22), and in another, the duct is transected between two ligatures (10-13). The difference between these models is that after a simple ligation, over time, leads to recanalization with the restoration of bile outflow (11,14). This phenomenon was first described in 1823. When the ligated bile duct is transected, restoration of bile outflow does not occur and long-term complete obstruction of the CBD remains (3). The main task of the treatment of patients with obstruction of CDB is to restore bile outflow. This encouraged to study experimentally the liver changes in partial obstruction of the CBD, and outflow restoration after complete obstruction (23,24).

To study the bile outflow restoration, models with surgical interventions redo could be used. They include the formation of anastomosis between the dilated bile duct and the intestine or the use of bile drainage (25). The disadvantages of these models are the relative complexity and the need to perform reoperation. To study the liver changes in partial bile outflow restoration after complete obstruction of the CBD, it was decided to use the phenomenon of recanalization of the CBD after its ligation. The obtained results were compared with complete obstruction–ligation and transection of the CBD. Different ways of assessing the restoration of the bile passage in the experiment are used. X-ray confirmation of the passage of contrast media to the duodenum is a reliable one but is associated with the relative complexity of implementation (11,26). The

normalization of TB levels also undoubtedly reflects the fact of bile outflow restoration. However, it does not indicate the exact terms of restoration (14,27). In the current study, the presence of bile in the duodenum as the criterion for restoring the bile passage was used. This assessment may be quite subjective, but it compares favorably with its simplicity. In addition, the histological changes of the liver according to the TB level were compared.

According to the obtained data, the bile passage restoration first was noted on PO day 7 – in 1 of 4 animals. On PO day 14 – in 2 of 4 cases, and at the end of the experiment – on PO day 35 – bile in the duodenal lumen was in 4 of 5 cases. This correlates with another study, according to which the partial restoration of bile outflow in ligation of the CBD of rats occurs on the PO days 7-12 (11). It should be noted that in ligating the CBD at the initial stages of the experiment – up to this term – PO day 7 – almost all cases have complete obstruction. This is confirmed by the histology data of the liver, which are identical in both study groups. Moreover, on PO day 14, when recanalization was recorded in half of the cases, the histological changes of the liver also did not differ from histological changes in the case of complete obstruction (28,29). Histological changes of the liver are characterized by signs of acute inflammation and alteration on the PO days 1 and 3, and subsequently, by progressive proliferation of the bile ducts and the development of liver fibrosis up to grades 4-5, with no significant differences in the degree of fibrosis between the study groups. The blood TB levels up to 14 days also did not differ statistically in both study groups. The absence of significant differences on the PO day 14 (180 ± 7 for CCBDO and 119.5 ± 28 $\mu\text{mol/L}$ for BOPR, $p > 0.05$), probably is associated with the small number of animals – 6 and 4, respectively (28).

Thus, up to 14 days, despite the partial restoration of bile outflow, the morphological picture of the liver and CBD are identical to complete obstruction, despite a tendency for the TB level to decrease. Later, in animals with PBOR and persistence of hyperbilirubinemia, there were no differences in the liver histological picture and the TB value ($p > 0.05$) in comparison with CCBDO. In the liver, there was a proliferation of bile ducts, which predicted the replacement

of hepatocytes, as well as the appearance of fibrosis. As a result, there was a loss of normal histostructure, which included false elements. The degree of fibrosis does not depend on the model. The CBD wall of both groups on the PO days 21 and 28 had subacute inflammation (a type of inflammation that falls between acute and chronic inflammation in terms of its duration and intensity) with decreasing acute inflammation. However, on the PO day 35, the only animal with PBOR and hyperbilirubinemia showed the presence of acute cholangitis. As mentioned before, the normalization of the TB level in animals with PBOR was recorded on the PO days 21 and 35. In these cases, the liver histological picture varied from almost normal to cholestatic changes with grade 3 fibrosis.

With complete bile duct obstruction (CSBDO), already by day 7, liver fibrosis of grades 1-2 is observed. By day 14, fibrosis reaches grades 4-5. Therefore, in CSBDO decompression in the first 7 days is necessary to prevent significant fibrosis. In partial obstruction (PBOR) with hyperbilirubinemia, fibrosis develops similarly to CSBDO, so early decompression is also needed. With PBOR with normal bilirubin, on days 21-35, either no fibrosis or only insignificant grade 1-2 fibrosis is seen. This suggests partial obstruction with preserved biliary function can last up to 3-4 weeks without significant fibrosis. Therefore, the optimal timing of decompression to prevent liver fibrosis is with complete obstruction, within the first 7 days; with partial obstruction with hyperbilirubinemia, also within the first 7 days; and with partial obstruction with normal bilirubin, delayed decompression up to 3-4 weeks is possible (30-32).

Abshagen et al. (33) in their comprehensive study, use a murine model of bile duct ligation to conduct an in-depth study of temporal changes in biochemical, histological, and transcriptional parameters during obstructive cholestasis. Analysis of more than 6 000 data points over time allows us to characterize the different phases of the disease, from early damage to progression. Parameter correlation statistics reveal coordinated responses, relate transcript dynamics to pathological processes, and identify potential biomarkers for disease staging. Careful multilevel profiling provides key insights into the complex pathophysiological processes in

obstructive cholestasis, significantly improving the understanding of this disease. Ultimately, the obtained data lay an important basis for the development of improved diagnostic and therapeutic strategies to overcome the significant clinical burden of cholestatic liver diseases.

Yokoda and Rodriguez (34) demonstrated that comprehensively summarizes current knowledge about the pathogenesis of cholestatic liver diseases. This highlights the central role of cholangiocytes in the response to injury and how sustained inflammatory signaling and genetic/epigenetic dysregulation can contribute to chronic ductular reaction and fibrosis (35-37). The authors detail key mechanisms including bile acid toxicity, mitochondrial dysfunction, immunogenetic factors, and matrix remodeling. They also discuss promising preclinical developments targeting these pathogenic pathways, as well as recent clinical trials of new treatments for specific cholestatic diseases. Overall, their study provides a holistic overview of the complex pathophysiology underlying cholestatic disorders and highlights the need for further research to improve diagnostic and therapeutic strategies.

A recent review by Aller et al. (38) also described three key inflammatory phenotypes that are expressed in the liver interstitium during obstructive cholestasis. They proposed an ischemia/reperfusion phenotype early on mediated by oxidative stress. This is followed by a leukocytic phenotype with activation of liver macrophages and infiltration of immune cells (39). Lastly, an angiogenic phenotype emerges characterized by cholangiocyte proliferation and peribiliary plexus development. Our findings align with this proposed model of successive inflammatory phases in the cholestatic liver interstitium. The ischemia/reperfusion phenotype we observed may explain the edema and oxidative damage in the early stages after bile duct ligation. The later prominence of immune cells and enzymes is consistent with the acquisition of a leukocytic phenotype. Finally, our observation of matrix changes and arterializations agrees with the concept of a late angiogenic phenotype. Further research is needed to fully validate this stepwise model of inflammation in obstructive cholestasis. However, our results lend support to the hypothesis that distinct

inflammatory phenotypes are expressed sequentially during cholestatic liver injury.

CONCLUSIONS

Histological changes occurring in the structure and functions of the liver were determined. The source of such changes is the experimental development of obstructive cholestasis. The essence of the above-mentioned disease and its direct effect on the liver was revealed. The fact that recanalization with incomplete restoration of bile outflow accompanied by normalization of TB was substantiated. As for the structure and activity of the liver, these components were most affected in the case of acute cholangitis.

When ligation of the CBD in rats, its recanalization occurs approximately on the PO day 7-14. By the PO day 35 normalization of the TB level occurs in 4 out of 5 surviving animals ($p < 0.01$). Recanalization with incomplete restoration of bile outflow, which does not lead to normalization of the TB level, is accompanied by histological changes of the liver, the same as in complete cholestasis. An exception is acute cholangitis, in which the morphological changes of the liver are more pronounced.

It is possible to assert the presence of characteristics that indicate the presence of abnormalities in the structure of the liver of male rats, obtained as a result of a comparison at each step of the experiment of the state of the rats' organs and indicators that are the norm.

In purpose to obtain more in-depth knowledge of the processes occurring in the liver and bile ducts in the restoration of the bile outflow after its complete obstruction, further research is needed, including using the morphometric method.

Comparative assessment of the effectiveness of various methods of surgical decompression could provide useful data. Morphometric studies to obtain quantitative data on histological changes would reduce subjectivity. Therefore, this direction requires further study taking into account the above limitations and optimization of the methodology to obtain more thorough data.

It is also necessary to pay attention to the limitations of this study and directions for

further research. A small number of animals in the experimental groups reduces the statistical significance of the results. The lack of a control group of intact animals for comparison of histological changes is another limitation. The subjectivity of assessing the presence of bile in the duodenum as a criterion for restoring bile flow is also a limitation. The effect of sex and age of animals on the results was not studied. To increase statistical significance, the number of animals in experimental groups should be increased. Adding a control group of intact animals would improve the study. More objective methods of assessment of recovery of bile flow should be used.

REFERENCES

1. Marques TG, Chaib E, Da Fonseca JH, Lourenco ACR, Silva FD, Ribeiro MAF, et al. Review of experimental models for inducing hepatic cirrhosis by bile duct ligation and carbon tetrachloride injection. *Acta Cirurgica Brasileira*. 2012;27(8):589-594.
2. Mamontov IN, Tamm TI, Ivakhno IV, Panasenka VA, Padalko VI. Morphological hepatic changes in experimental partial obstruction of the common biliary duct. *Klinich Khirurg*. 2017;12:59-63.
3. De Aro Braz MJ, Corbi LE, Tannuri ACA, Coelho MCM, Goncalves JO, Serafini S, et al. Analysis of the reversibility of biliary cirrhosis in young rats submitted to biliary obstruction. *J Pediatric Surg*. 2018;53(7):1408-1413.
4. Luo WW, Zhou XL, Wang QQ, Shao YJ, Li ZM, Zhao DK, et al. The application of Compont gel in chronic obstructive jaundice rat model. *Acta Cirurgica Brasileira*. 2019;34(5).
5. Arias I, Alter H, Boyer J, Cohen D, Shafritz D, Thorgeirsson SS, et al. *The Liver: Biology and Pathobiology*. Wiley-Blackwell. 1152.
6. Mills S. *Histology for Pathologists*. LWW. 2019;1344.
7. Oruc MT, Ozmen MM, Han U. A new technique for inducing and releasing obstructive jaundice in rats. *Eur Surg Research*. 2009;43(4):354-359.
8. Corbi LE, Tannuri ACA, De Aro Braz MJ, Paes VR, Sbragia L, Figueira RL, et al. Does biliodigestive anastomosis have any effect on the reversal of hepatopulmonary syndrome in a biliary cirrhosis experimental model? *Dig Dis Sci*. 2019;64(11):3192-3202.
9. Mamontov IN, Tamm TI, Ivakhno IV, Panasenka VA, Padalko VI, Zulfugarov II. The impact of partial obstruction of common biliary duct without hyperbilirubinemia on the liver. *Klinich Khirurg*. 2019a;86(8):67-71.
10. Mamontov IN, Tamm TI, Ivakhno IV, Panasenka VA, Padalko VI, Zulfugarov II. Morphological signs of hepatic function decompensation with experimental complete obstruction of the extrahepatic bile ducts. *Mir Med Biol*. 2019b;1(67):162-166.
11. Wright JE, Braitwaite JL. The effects of ligation of the common bile duct in the rat. *J Anatomy*. 1964;98(2):227-233.
12. Yang Y, Chen B, Chen Y, Zu B, Yi B, Lu K. A comparison of two common bile duct ligation methods to establish hepatopulmonary syndrome animal models. *Lab Anim*. 2015;49(1):71-79.
13. Jia R, Yang F, Yan P, Ma L, Yang L, Li L. Paricalcitol inhibits oxidative stress-induced cell senescence of the bile duct epithelium dependent on modulating Sirt1 pathway in cholestatic mice. *Free Radical Biol Med*. 2021;169:158-168.
14. Dorndorf F, Fahrner R, Ardelt M, Patsenker E, Stickel F, Dahmen U, et al. Induction of chronic cholestasis without liver cirrhosis – Creation of an animal model. *World J of Gastroenterol*. 2017;23(23):4191-4199.
15. Lazcanoiturburu N, García-Sáez J, González-Corrales C, Roncero C, Sanz J, Martín-Rodríguez C, et al. Lack of EGFR catalytic activity in hepatocytes improves liver regeneration following DDC-induced cholestatic injury by promoting a pro-restorative inflammatory response. *J Pathology*. 2022;258(3):312-324.
16. Streltsov L, Gudumac V, Rojnovanu G. The effect of bile decompression on pro- and antioxidant markers in the complications of gallstones associated with cholestatic jaundice. *Med-Surg J*. 2022;126(3):378-387.
17. Mejidov RT, Magomedova S, Mamedova EP, Abdullaeva AZ, Nasibova UA. Pathological syndromes of the biliary tract decompression. *J Clinic Practice*. 2021;12(3):21-29.
18. Dzyubanovskyi OI, Gudyma AA. The influence of bile extract decompression on the dynamics of bile formation and bile excretion after experimental cholestasis of different durations. *Klinich Khirurg*. 2017;10:66-69.
19. Hrabchak SO, Bedeniuk AD. Peculiarities of compensatory processes of the duodenum in obstructive cholestasis in combination with biliary tract decompression and enterosorption. *Hospital Surg*. 2021;1:38-43.
20. Feldman M, Friedman LS, Brandt LG. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*. Elsevier. 2020:2488.

21. Van Golen RF, Olthof PB, Lionarons DA, Reiniers MJ, Alles LK, Zu Z, et al. FXR agonist obeticholic acid induces liver growth but exacerbates biliary injury in rats with obstructive cholestasis. *Scientific Reports*. 2018;8.
22. Roncalli M, Park YN, Tommaso LD. Histopathological classification of hepatocellular carcinoma. *Digest Liver Dis*. 2010;42(3):228-234.
23. Burt AD, Ferrell LD, Hübscher SG. *Pathology of the Liver*. Elsevier. 2018.
24. Azmaiparashvili E, Bebiashvili I, Karumidze N, Tsomaia K, Kordzaia D. Ductular reaction at the early and late stages of biliary obstruction: Is the mechanism the same? *Georg Med News*. 2019;286:100-106.
25. Trautwein C, Friedman SL, Schuppan D, Pinzani M. Hepatic fibrosis: Concept to treatment. *J Hepatol*. 2015;62(1):15-24.
26. Hajiyeva NN. Clinical presentations of pain syndrome depending on the grade of CNS lesions at newborns. *Azer Med J*. 2008;(3):50-52.
27. Hryshchenko VA, Tomchuk VA, Lytvynenko OM, Chernyshenko VO, Gryshchuk VI, Platonova TM. An estimate of protein synthesis in liver under induced hepatitis. *Ukrain Biokhim Zhur*. 2011;83(1):63-68.
28. Trauner M, Meier PJ, Boyer JL. Molecular pathogenesis of cholestasis. *N Engl J Med*. 1998;339(17):1217-1227.
29. Gryshchenko VA, Lytvynenko ON. Peculiarities of the bilious acid spectrum of bile and duodenal content in mice at medicamentous hepatitis and use of correction therapy. *Ukraine Biokhim Zhur*. 2007;79(4):97-101.
30. Gryshchenko V, Danchenko O, Musiychuk V. Modification of modeling method of toxic dystrophy of liver in rats. *Modern Development Paths of Agricultural Production: Trends Innovate*. 2019:689-697.
31. Kozłowski P, Parfieniuk-Kowerda A, Tarasik A, Januszkiewicz M, Czauż-Andrzejuk A, Łapiński TW, et al. Occurrence and clinical characteristics of hepatocellular carcinoma in the north-eastern Poland. *Przeład Epidemiolog*. 2017;71(3):405-415.
32. Mel'nychuk DO, Hryshchenko VA, Vesel'skyi SP. Indicators of exchange of bile pigments under the action of ecopathogenic factors on the organism and correction with liposomes. *Ukraine Biokhim Zhur*. 2014;86(3):125-132.
33. Abshagen K, König M, Hoppe A, Müller I, Ebert M, Weng H, et al. Pathobiochemical signatures of cholestatic liver disease in bile duct ligated mice. *BMC Systems Biology*. 2015;9:83.
34. Yokoda RT, Rodriguez EA. Review: Pathogenesis of cholestatic liver diseases. *World J Hepatol*. 2020;12(8):423-435.
35. Zharmakhanova G, Syrlybayeva L, Kononets V, Nurbaulina E, Baikadamova L. Molecular-genetic aspects of methylmalonic aciduria development (review). *Georg Med News*. 2021;(313):118-124.
36. Arapbaevna KZ, Ardak A, Abzhanovna, AG, Bahitkerevna DA, Uringalievna BA, Izbasarovna KE, et al. Modern diagnostic approaches for early detection of antiphospholipid syndrome. *Arch Venez Farmacol Therapeut*. 2021;40(2):178-186.
37. Doszhanova GN, Abduldayeva AA. Hygienic assessment of nutrition status of the population of the gerontological group. *Gigiena Sanitar*. 2017;96(11):1084-1087.
38. Aller MA, Arias J-L, García-Domínguez J, Arias J-I, Durán M, Arias J. Experimental obstructive cholestasis: The wound-like inflammatory liver response. *Fibrogenesis Tissue Repair*. 2008;1:6.
39. Datsko VA, Fedoniuk LY, Ivankiv YI, Kurylo KI, Volska AS, Malanchuk SL, et al. Experimental cirrhosis: Liver morphology and function. *Wiad Lek*. 2020;73(5):947-952.

Imaging and Pathological Features and Recurrence Causes of Cystic Meningioma

Imágenes y Características Patológicas y Causas de Recurrencia del Meningioma Quístico

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SUMMARY

Objective: This study aims to establish preoperative imaging features, establish how they are correlating with post-operative pathological features, and discover the causes of recurrence. **Results:** Data on imaging procedures in the preoperative period, records of surgical operations, and reports from pathology conclusions were collected. Among 623 patients who were undergoing neurosurgery resection of intracranial meningioma, 24 cases of cystic meningioma were identified, corresponding to a world incidence of 3.8%. The hemispheric convexity was the most frequent place of localization. The apparent diffusional coefficient was significantly lower in grade 2 and grade 3 tumors if compared to grade 1. Full resection of the cystic component was possible in 18/24 cases. Partial resection in 3/24 cases. In 2/24 cases, it was not possible to make total or partial resection, but multiple biopsies were performed from the cystic walls. **Conclusion:** Conclusion of the pathology examination

of cells found neoplastic findings within the cyst's wall in 66.6%. All patients were followed up for 24 months. Some of them were followed up for a long-term period. The long-term period was an average of 49 months (range 36-96 months). Cases of recurrences that needed surgery were not observed.

Keywords: Tumor, MRI, neurosurgery, histopathology, radiology.

RESUMEN

Objetivo: El objetivo de este estudio es establecer las características de las imágenes preoperatorias, establecer cómo se correlacionan con las características patológicas postoperatorias y descubrir las causas de la recurrencia. **Resultados:** Se recogieron datos de procedimientos de imagen en el período preoperatorio, registro de operaciones quirúrgicas e informes de conclusión de patología. Entre 623 pacientes que fueron sometidos a resección neuroquirúrgica de meningioma intracraneal, se identificaron 24 casos de meningioma quístico, lo que corresponde a una incidencia mundial del 3.8%. La convexidad hemisférica fue el lugar de localización más frecuente. El coeficiente de difusión aparente fue significativamente menor en los tumores de grado 2 y grado 3 en comparación con el grado 1. La resección completa del componente quístico fue posible en 18/24 casos. Resección parcial en 3/24 casos. En 2/24 casos no fue posible realizar una resección total o parcial, pero se realizaron múltiples biopsias de las paredes quísticas. **Conclusión:** Al concluir el examen anatomopatológico de las células se encontró hallazgo neoplásico dentro de la pared de los quistes en el 66.6%. Todos los pacientes fueron

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seguidos durante 24 meses. Algunos de ellos fueron seguidos durante un período prolongado. El período a largo plazo fue un promedio de 49 meses (rango 36-96 meses). No se observaron casos de recurrencias que necesitaran cirugía.

Palabras clave: *Tumor, resonancia magnética, neurocirugía, histopatología, radiología.*

INTRODUCTION

In the structure of all central nervous system tumors, meningioma is the most common case. The last research showed that 37.6 % of all central nervous system tumors consist of meningiomas and benign are about 50 % of them (1). Meningioma grows from the meningeal layers of the brain and spinal cord. Cystic meningioma represents the same meningioma that arises from the meningeal layer, but it has intra-tumoral or peritumoral cysts. It is quite a rare type of meningioma and comprises about 5.5 % of all meningiomas (2). The problem of cystic meningioma is the complexity of its differential diagnosis with other intra-axial glial or metastatic tumors. In fact, the clear understanding that results of the imaging show cystic meningioma has crucial decisions on tactics of surgical treatment. Usually, meningioma is diagnosed through its imaging features like well-circumscribed form, extra-axial localizations, adjacent to the dura and marked, homogeneously enhancing after intravenous contrast injection on computed tomography (CT) and magnetic resonance imaging (MRI) (3). The vast majority of meningiomas consist of solid, high cellular structures with good vascular supply, but in some cases, meningiomas may consist of (partly or most of its structure) cysts, which make their differentiation from other diagnosis and their definition with further management very difficult.

Most meningiomas' histological profiles are benign, but some of them can have malignant profiles. Salami et al. (4) to the World Health Organization (WHO) classification considered that cystic meningiomas have the same histological image as solid tumors. Preoperative diagnosis is challenging, and usually, the final diagnosis is established only after the histology of the tumor specimen. Zhao et al. (5) reported a case

of valuable imaging evidence for the localizations and classifications of cystic meningiomas. The definition of cystic meningioma is associated with meningiomas macroscopical cysts. These macroscopical cysts can be described as intra-tumoral degenerative cysts, reactive intraparenchymal cysts, or peritumoral arachnoid cysts (6,7).

Researchers have no consensus about the nature of these cysts. Buerki et al. (1) consider that peritumoral cysts can originate from loculated widened subarachnoid spaces, surrounding edema, demyelination, or hemorrhage. Yamada et al. (8) think that intra-tumoral cysts can form as the result of active production of secret from tumor cells.

The gold standard for symptomatic meningioma management is surgery, even for cystic meningiomas and usually under general anesthesia. However, a few years ago, in the journal "Interdisciplinary Neurosurgery" Okunlola et al. (9) published an article about awake craniotomy and considered that it has its advantages to avoid future language or movement deficits. Because radiological appearance is mostly unusual—a tactic of surgery is based on the possibility of distinguishing cysts with gliomas, hemangiopericytomas, metastatic brain tumors as well as other focal cystic lesions of the brain.

Besides the complications in establishing the diagnosis, there are other questions still unsolved including the origins of associated cysts which are debated, the ideal surgical extent of resection weighing recurrence risk versus neurological function, the role of emerging tools like fluorescence for total removal, strategies for unusual cases like pineal cystic meningiomas, the need to correlate recurrence rates with tumor grade to refine prognosis and follow-up, and building consensus on whether total cyst wall resection is mandatory when tumor cells are absent or if partial excision is sufficient in some scenarios. The importance of removing the cystic wall underpins the risk reduction of recurrence. This research aims to create a single-institution retrospective cohort study of surgically treated meningioma patients between 2015 and 2021 to determine imaging and pathological features of cystic meningiomas and establish causes of recurrence.

The article argues that complete surgical resection of all components of cystic meningiomas, including the cyst walls, is critical to reducing the risk of tumor recurrence. This study provides useful clinical details on the imaging features, surgical approaches, pathological findings, and recurrence rates of cystic meningiomas, expanding knowledge that can directly improve diagnosis, treatment planning, surgical techniques to reduce recurrence risk, prognostic awareness, and management of patients with this subtype of meningioma. The data has clear practical applicability for surgeons, radiologists, and pathologists who diagnose and treat cystic meningiomas by elucidating best practices for achieving total resection and analyzing rates of neoplastic cyst wall involvement to guide biopsy and recurrence prevention when complete excision is not feasible.

MATERIALS AND METHODS

The research includes information about all patients with cystic meningioma, which were evaluated and managed over 6 years in local neurosurgical centers. The study included 24 cases of cystic meningioma, which were diagnosed among 623 surgeries for intracranial meningioma. It is corresponding to a world incidence of 3.8 % (2). CT and MRI were done in all cases before neurosurgical operations. CTs were conducted on a 64-slice multi-detector row computer tomography scan. For MRI, Siemens Symphony 1.5T was used, to complete the institutional protocol for visualizations of brain tumors: axial fluid-attenuated-inversion recovery (FLAIR); axial and sagittal T1; axial T2 Gradient-Echo; susceptibility-weighted images (SWI) after injection of intravenous contrast T1 sequence.

Surgical treatment was performed standard centered craniotomy on the place of localization of meningioma and next dissection of tumor and excision. In all operations performed, complete resection of cystic components, and remnants of the wall and dural tails were observed. If any of these components could not be removed, multiple biopsies from different sites were taken. Excision of meningioma was performed through standard microsurgical fashion. Depending on tumor consistency, location, and vascular net,

was performed first debulking after suction, sharp excision, coagulation, or ultrasonic aspiration. After this, the separation of meningioma from the brain parenchyma along the arachnoid layer was conducted, and the same manipulations were done for the structures of cysts. To avoid the injury of vascular structures and successful preservation and dissection of all veins and perforator arteries, rigorous microsurgical dissection along this separated arachnoid plane was used.

In addition, patients, who were classified as third-grade meningiomas at pathological examination, were referred for postoperative radiotherapy. All dissected tumor components, including cystic walls and dural tail, were analyzed on the presence of neoplastic cells inside the cystic walls. Results of histological analysis were categorized, depending on the histological features of meningioma to the WHO classifications (Table 1).

Table 1
World Health Organization Meningioma Classifications

WHO Grade I Benign	WHO Grade II Atypical	WHO Grade III Malignant
Meningiothelial	Chordoid	Papillary
Fibrous (fibroblastic)	Clear Cell	Rhabdoid
Transitional (mixed)	Atypical	Anaplastic
Psammomatous		
Angiomatous		
Secretory		
Lymphoplasmacyte-rich		
Metaplastic		

Source: Ostrom et al. (1).

Grade 1 meningiomas are benign and account for 80 %-90 % of cases. They exhibit compact architecture and uniform nuclei with inconspicuous nucleoli. Grade 2 or atypical meningiomas demonstrate increased mitotic activity, patternless architecture, and nuclear atypia. Grade 3 or anaplastic meningiomas are

malignant with overt anaplasia, high mitotic rate, spontaneous necrosis, and poor differentiation resembling carcinoma, melanoma, or high-grade sarcoma. Higher-grade lesions tend to be more aggressive and carry worse prognoses (1).

According to the Nauta classification, intracranial cystic meningiomas can be classified into four types (10). The Nauta classification categorizes cystic meningiomas based on their histopathological characteristics and the relationship between the cyst and the tumor. There are four recognized types: Type I, where the cyst is located outside the meningioma; Type II, in which the cyst is present within the tumor itself; Type III, characterized by a mixed pattern with both intratumoral and peritumoral cysts; and Type IV, where the meningioma itself arises from the wall of a pre-existing cyst, often described as a cystic degeneration within the tumor. Cystic meningiomas of A type contain cerebral spinal fluid and divide into A1 and A2, depending on their locations. Type B is characterized by cystic meningioma with xanthochromia fluid and divides into B1 and B2, depending on its locations. Meningioma in type C has yellow or dark fluid intratumorally. Type D contains clear fluid in peritumoral cysts, extratumoral cysts, and intratumoral cysts.

RESULTS

Research is based on the results of the treatment of 623 patients, who went through the neurosurgical operation, and in the postoperative period, on histological examination, meningioma was diagnosed. Among these 623 patients, 24 had cystic meningioma, which is related to the world incidence (3.8 %). A predominance of women (18 vs. 6) was noted.

The observed predominance of women over men in the case of cystic meningiomas aligns with general epidemiological trends seen with meningiomas. Multiple studies have pointed towards hormonal factors as a potential explanation (7,8). Estrogen and progesterone receptors are frequently found in meningioma cells, suggesting that these tumors might be influenced by sex hormones. The presence of these receptors, especially progesterone, could

potentially drive a higher incidence in women. Additionally, fluctuations in hormone levels during events like menstruation, pregnancy, and menopause can influence tumor growth. Nevertheless, men tend to experience a more aggressive progression of the disease, with a higher likelihood of tumor recurrence post-surgery. This is contrasted with women, who frequently have a milder course and a more favorable prognosis, largely attributed to hormonal influences, particularly the protective role of progesterone. Furthermore, women often present with larger cystic components within tumors than men, yet despite the size, they often respond better to treatment (10).

The average age was 48.4 years. Symptoms included: headache (21/24 - 87.5 %), focal or/and progressive neurological deficit (16/24 - 66.6 %), dizziness (12/24 - 50 %), seizures (9/24 - 37.5 %), depression syndrome (4/24 - 16.6 %). The empiric diagnostic of cystic meningioma by preoperative imaging was only in half of the cases (12/24 - 50 %). The tumor location is described in Table 2.

Table 2
Location of Tumor

Tumor localization	Total
Frontoparietal convexity	6
Temporo-occipital convexity	2
Parasagittal and falx cerebri	6
Olfactory groove	4
Sphenoid ridge	1
Petrous ridge and Petro clival	5
Total	24

Source: the material based on results of MRI.

The medium size of cystic meningioma was about 43 mm (From 32 – 104 mm). Solid portion hypointense was observed in 11 cases of the T1 sequence. In 13 cases, iso-intense appeared. In one case, scattered hyper-intensities were observed, which were confirmed as intratumoral hemorrhagic components on T2 and SWI sequences.

FLAIR showed hyper-intensity components with solid structure in 14 cases. In 6 patients, FLAIR showed iso-intensity and hypo-intensity in 4 cases. Dural sinus invasion was present on post-contrast in 3 cases, and there were no signs of infarction. Diffusion-weighted image (DWI) was performed in 16 cases. DWI showed high signal intensity if compared with the adjacent parenchyma in 9 of 16 cases. The apparent diffusion coefficient was present only in 2/16 cases of grade 1 tumors in comparison with 7/7 grades 2-3. The average apparent diffusion coefficient value was much lower in grade 2 and 3 lesion zones.

Cystic component on T1, FLAIR, and DWI was hypointense, but only 2 cases with FLAIR had isosignal. In one case, a hemorrhagic component out of the tumor tissue was present.

Multi-cystic mass was present in half of the meningiomas (12/24). More than two same cysts were found in 8 cases, and in 4 cases, different cyst types for the same type of meningioma were present. Enhancement of cyst wall observed in all types of cysts: 1, 2, and 3, and only in 4 grade of meningioma enhancement of cyst wall was absent. In one case, clear thickening of wall enhancement was observed (Figure 1). Post-contrast T1 sequence shows midline tumor of large size with mass effect around. Intense homogeneous enhancement is shown by the component with a solid structure and the thick wall of large cysts on the periphery. On the FLAIR sequence, marked edema in the surroundings and mass effect was observed. Low-intensity area reveals in susceptibility weighted sequence in relation with hemorrhagic foci inside solid tumor component.

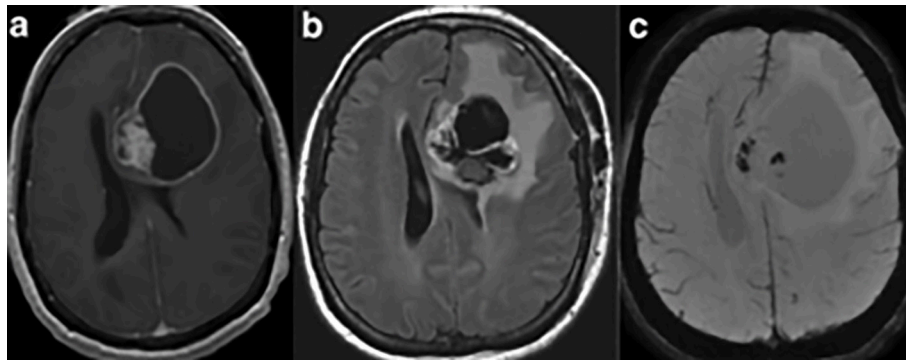


Figure 1. Cystic Meningioma of Falx Cerebri (Grade 3 According to WHO Classification): a) T1; b) FLAIR; c) Susceptibility Weighted Sequence Revealing.

The large size of cysts (more than 30 mm) was found in 6/24 cases with an average size of about 70 mm (range 32-128). In most cases (4/6) localization of such large cysts was on the convexity of hemispheres. In three of these six cases, large cysts contained structures of septum. In one case, an enhanced area inside the solid portion of the mural nodule of a large cyst was present (Figure 2). This meningioma can be characterized as 1 grade according to the WHO classification. On frontal convexity, there is a large cystic mass with a mural nodule of a small size. On T1 and T2 sequences, it is

isointense compared with the cortex. The cystic component is the same by its signal intensity to the cerebrospinal fluid. Post-contrast MRI shows mild and homogeneous enhancement of mural nodule. Also observed was no enhancement of cystic wall and cystic content.

Edema of vasogenic mechanism in nearby brain tissue was observed in 15/24 cases. In five cases, edema around peripheral cysts of a big size was observed. Vascular entrapment was observed in 6 cases. In these patients, big-size peripheral cysts with lobulated components were found.

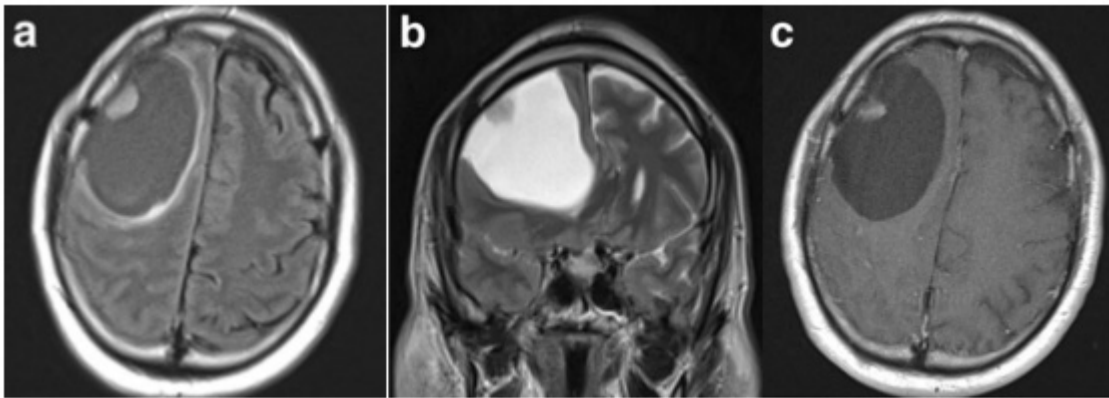


Figure 2. Picture of a Cystic Mural Nodule Inside Meningothelial-Microcystic Meningioma (Grade 1, According to WHO Classification).

Lobulated structures consisted of septum-like findings (Figure 3). Inside the peripheral cyst, structures of vascular nature were present, which were observed on axial and coronal planes during the T1 post-contrast sequence. The tail of the dural layer was also noted. In the structure of the solid component, a lot of small cysts were observed. The conclusion of radiological examinations assumes microcystic meningioma. The conclusion of pathology examinations classified this finding as meningothelial meningioma.

Calcifications of the tumor were present in 3/24 cases on CT. Hyperostosis of bone was observed in 18/24 lesions (all of them were located on convexity), including a patient with diagnosed

meningioma, which was located intraosseous outside the dural layer. Full surgical resection of meningioma and structure components of the cysts was potentially possible in 18/24 cases. Partial resection was done in 3/24 patients.

In 2/24 of the patients, it was not possible to make total or partial resections, but multiple biopsies from cystic walls were done. In one case, during the surgery, it was not possible to identify the cyst wall. After comparing the imaging aspects of the microcystic meningothelial forms, it was considered that the edema was more marked in the pure meningothelial form. Changes in the microcystic types of meningiomas were observed in a single case (Figure 3).

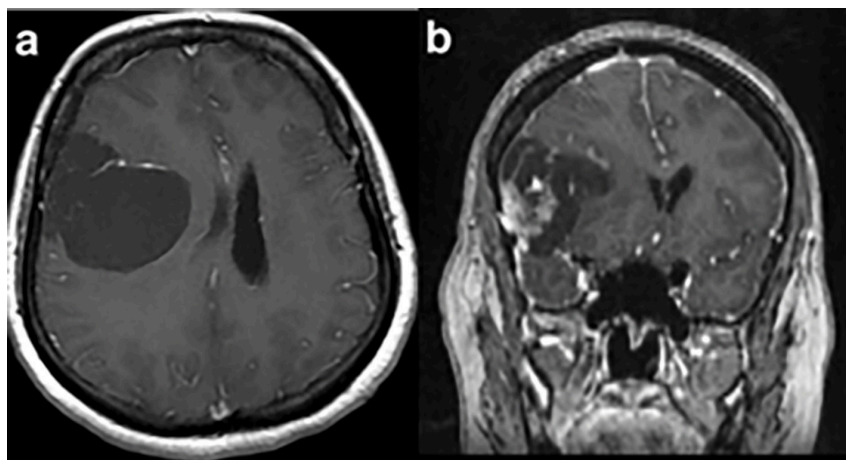


Figure 3. Meningothelial Meningioma with Peripheral Cysts and Septum-Like Components Inside.

Some of the most common and challenging surgical complications that can occur with resection of cystic meningiomas include:

- Bleeding - These tumors are often highly vascular with abnormal fragile vessels. Hemorrhage during surgery can be difficult to control.
- Cyst rupture - Accidental intraoperative rupture of the cyst capsule can lead to leakage of fluid and dissemination of tumor cells.
- Cranial nerve deficits - Cystic meningiomas near the skull base put cranial nerves at risk during dissection. This can cause postoperative neuropathies.
- Brain edema - Disrupting cyst architecture and fluid balances can exacerbate vasogenic cerebral edema. This may require urgent management.
- Infection - Cyst contents may become contaminated leading to meningitis, encephalitis, abscess, or wound infection postoperatively.
- Seizures - Cystic meningiomas have high epileptogenic potential that can cause seizures, especially with subtotal resection.
- Residual tumor - Partial or incomplete resection leaves behind tumor tissue likely to recur. Extensive invasion can prevent total removal.
- Recurrence - Even with apparent total excision, cystic meningiomas have higher recurrence rates likely due to occult spread.

Careful presurgical planning, meticulous dissection techniques preserving neurovascular structures, watertight dural closure, antibiotics, anticonvulsants, corticosteroids, and close postoperative monitoring can help minimize risks and complications following cystic meningioma surgery.

Vascular entrapment was diagnosed intraoperatively in 7 cases. Three patients had small arterial branches adherent to the cyst's wall. In one case, between the cystic part of the tumor and the solid part of the tumor, the vessel was stuck. In two cases, the opercular branch

of the middle cerebral artery which was going through the cyst and arriving in contact with the brain parenchyma was observed.

The pathological finding was summarized according to WHO classification. Grade 2 and 3 meningiomas were diagnosed in 7/24 cases. The angiomatous variant was present in one patient, and they had had radiotherapy for facial angiooma 50 years before. Inside the cyst's wall, neoplastic cells in 9/24 cases were identified. Also in three cases, meningotheliomatous cells were present. In this research, all patients' post-operative follow-ups for 36 months were done. The postoperative follow-up period of a long term was conducted in 14/24 patients for 52 months on average. Recurrence of the tumor, which requires surgery, was not observed. Three patients with grade 3 meningioma at pathology: one of them was lately diagnosed with meningeal dissemination, which resulted in hydrocephalus, and another two with papillary meningioma that disappeared.

In this research, one case of unusual location was presented. Meningioma was located in the pineal region (Figure 4). The pineal region presented a tumor, which consisted of a structure of a solid part and structure with a cystic component. This tumor is isointense compared with the cortex on the T1 sequence in the median sagittal. This tumor compresses the superior colliculi. If compared with a cerebrospinal fluid component of this cyst, it isointense on FLAIR and T2 spin-echo. The solid part of this tumor showed hyperintensity on T2 spin-echo and FLAIR and diffusion. The solid component of the structure was smaller than the cyst part. On T1 sequences in sagittal and axial projection was observed round mass lesion and quadrigeminal hollow structure, which took up the contrast intense and homogeneous. Clear attachment to the dural layer was absent, and there was no enhancement of the cyst wall. Identification of the pineal gland was not possible.

Tumoral cysts in the context of previous malignant breast carcinoma made it hard to distinguish from the raising the suspicion of metastasis. Tumor volume gradually increased over 4 years and then was made neurosurgical operation for tumor resection. After that, pathology examinations of the resected samples and a conclusion were established.

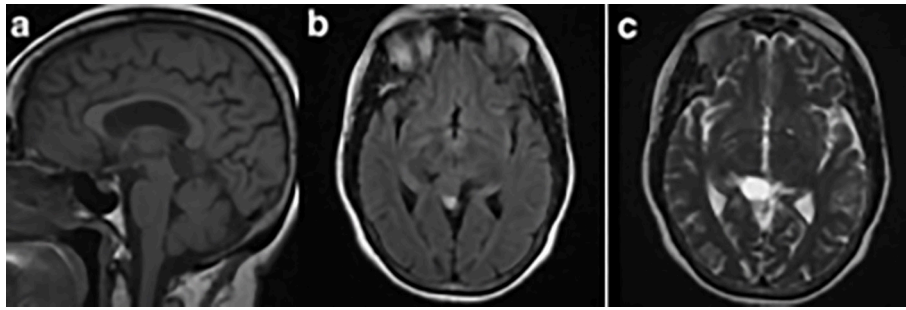


Figure 4. Meningotheelial Cystic Meningioma of the Pineal Region

From 1 % to 4 % of all intracranial tumors consist of neoplasms, which grow from the region of the pineal gland. Among them, meningiomas account for about 6-8 % (11). Most reported diagnoses are benign nature meningiomas, and the two predominant histological patterns are fibrous and meningotheelial. In this research, meningioma is considered to be of meningotheelial type.

The typical localization of meningiomas that are aroused from the pineal gland is a falcotentorial junction in the area of the velum interpositum or zone of the arachnoid envelope of the pineal gland. In some cases, they can arise from the arachnoid envelope of the pineal gland. In this research, pineal meningioma is aroused from the pineal gland. Multiplane rebuilding of 3D postcontrast T1 image can be helpful in imaging the ration with Galen vein and

attachment with falcotentoria. The cystic nature of the meningiomas no one can consider, except Li et al. (12). In that research, a database of 10 papillary meningiomas was contacted. One of these cases was the multiple cysts, which were located intra-tumoral and in the pineal region.

In this research, features of neoplastic nature in the structure of the cyst wall in 66.6 % of cases were observed (Figure 5). Due to this information, the surgical strategy was changed. It was adapted to full resection whenever it was technically possible. The technically impossible situation when performing total resection of all cystic meningioma components occurred when a suspected risk was to damage both critical structures, functional nervous area, and vascular structures of nerves.

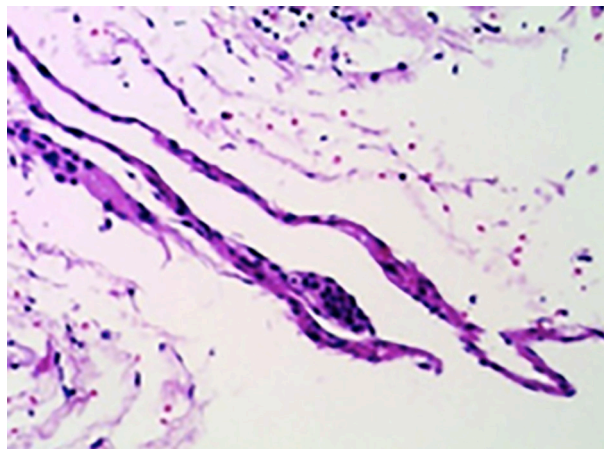


Figure 5. Wall of Cystic Component Containing Meningioma Cells. Pathology with Hematoxylin and Eosin, Magnification X200.

Recurrence in time of average following up (ratio, 36-96 month) were not observed. Special attention was paid to the segments with contrast enhancement on the image in the preoperative period. If after neurosurgical manipulations surgical remnants were still observed, (4/24 – 16.6 %) multiple biopsies of the remaining cystic wall were performed. Examination of experiences if this research concluded that full removal of meningioma with its cystic structures is primary to make recurrence rates lower.

DISCUSSION

In the past few years, the use of the new fluorescent agent 5-aminolevulinic acid (5-ALA) has shown promising results in meningioma surgery, especially in cases of bone infiltration, skull base localization, and atypical meningiomas (13). The use of 5-aminolevulinic acid (5-ALA) fluorescence imaging presents a significant advancement in treating cystic meningiomas. 5-ALA is a fluorescent dye that causes tumor cells to illuminate pink under specific light, improving the visualization of tumor margins during surgeries. This technology is particularly beneficial for cystic meningiomas, which often have indistinct boundaries and can resemble other lesions. By highlighting areas of tumor infiltration within the cyst wall, 5-ALA assists surgeons in more complete resections, potentially reducing recurrence. As this method continues to gain traction and with further refinements in fluorescence detection systems, it holds promise for optimizing the surgical removal of cystic meningiomas (13).

In this research, such a technology was not possible to be applied during the study period. Given that available clinical data has demonstrated the usefulness of 5-ALA fluorescence in identifying portions of infiltrated dura, it could potentially constitute a valuable tool for cystic meningioma surgery by providing direct visualization of infiltrated parts of the cystic wall in cases where complete cyst removal is not possible.

Cysts of intra- or peritumoral localizations remain uncommon features for meningiomas. The incidence of meningioma in worldwide

populations from 2010 to 2014 is considered to be 8.3 per 100 000 people. In the next few years, the incidence tends to rise and in 2015 the incidence was 10.82 per 100 000 (14). The same situation of meningioma incidence increasing and reported in pediatric populations but here not identify any pediatric cases.

Conventional MRI sequences are not the best way to make differentiation between meningiomas grades and it is associated with numerous complications (15). In the past few years, a lot of attention has focused on DWI signals and apparent diffusion coefficient values (16). Most meningiomas have hyper-intensity in DWI, because of their densely cellular nature, and in the present research (19/24).

The benefits of ADC coefficients in predicting the grade of meningioma are controversial (17). Benign and aggressive meningiomas can be distinguished by using DWI with high b-values. Low ADC values can improve the possibility of distinguishing grade 2 and 3 meningiomas from angiomatous and microcystic meningiomas, which can mimic malignant meningiomas. The biggest and most recent research that was published showed that grade 1 meningiomas have significantly higher ADC values if compared with grade 2 and grade 3 (18). A similar result was shown in this research. It can be supposed that prognostic value in predicting of apparent diffusional coefficient may also apply to cystic meningioma.

In 5 of 24 cases, cystic components of large size were present. Most of these cases were found of convexity. Histological types of meningioma were microcystic 1/5, meningothelial 2/5, mixed meningothelial-microcystic 1/5, and 1/5 was malignant. This finding is in concordance with previous case reports (19-23). In 3/5 patients, imaging showed inside large cysts septum-like structures. Also, the entrapment of middle-cerebral artery branches was observed. It was possible to identify cortical venous structures inside large cysts (Figure 3).

Papillary, clear cell, and angiomatous are rare pathological types. In the present research, one case of each of those has been identified. Rare malignant variant is papillary meningiomas. Papillary meningiomas account from 1 % to 2.5 % of all intracranial meningiomas.

The characteristic difference of papillary meningiomas is the heterogeneous enhancement and uncertain margins, and in most cases can help to differentiate them from typical meningiomas. Moreover, cystic components are not infrequent. In the present research, a case with heterogeneous enhancement with irregular tumor margins and heterogeneous signal on T1 and T2, which was identified as multi-cystic skull base mass, was present.

Rare variant of grade 2 represented by clear cell meningiomas. Clear cell meningioma is most frequently located in the cerebellopontine angle. In most cases, it exhibits a cystic component and strong heterogeneous enhancement with edema around the tumor. The overall recurrence rate of clear cell meningiomas is about 50 %-60 % (24). Clear cell meningioma was observed and enhancement of multi-cystic mass in cerebrum palatine angle. Clear cell meningioma was also characterized by taking up contrast inside of cystic walls, but without edema around the lesion.

Angiomatous meningioma in this research was presented as a big size structure with multi-lobulated components with clear edema around the tumor and structures of a vascular nature around it.

The variation of meningiomas with micro cysts is supposed to be low dense on CT, to have low intensity on T1 and higher on T2 imaging, and imperceptible, homogeneous enhancement because of injecting the contrast. Numerous intra-tumoral micro cysts characterized by these features and attributes.

Edema around tumors in this subgroup was reported as a severe incidence (15). In the present research, the findings of microcystic meningiomas were different: edema was absent or with very low expressiveness in the majority (4/5).

One case in this research presented very unusual imaging with a pattern of reticular honeycomb, inhomogeneous, and weak contrast enhancement.

In 50 % of cases, purulent and mixed meningiomas with microcysts were identified, compared to only 24.5 % of remaining patients. Moreover, in 2 cases, mural nodules of small size within a large cyst, characterized as microcystic

and mixed type were observed. In previous reports, the large cysts were more frequent despite the histological subtype (25).

Entrapment of structures with a vascular nature was observed in three cases inside large and with lobulated structure cysts periphery. Examinations of this case showed that mechanical blocking of cerebrospinal fluid spaces causes the cyst. This information helped to establish preoperatively whether the cystic part represents trapped cerebrospinal fluid (cysts of the arachnoid layer) or originates within the brain parenchyma (Nauta type 4 vs. type 3).

The incidence of cystic meningiomas in this cohort was 3.8 %, which is within the range of 1.6 %-10 % reported in other surgical series (26-28). This supports the rarity of these lesions relative to solid meningiomas. The hemispheric convexities were also a common localization in this and other studies (29), likely related to the prevalence of meningothelial subtype in convexity lesions which may predispose to cyst formation.

The pattern of lower ADC values differentiating higher-grade cystic meningiomas is well documented across multiple institutional datasets (30,31). The ability of advanced imaging to predict WHO grade in cystic and solid meningiomas alike underscores its value for preoperative planning.

While the 66.6 % rate of cyst wall tumor invasion was higher than some reports of up to 50 % (32), other authors have also observed invasion in over 60 % of specimens (33-35). This may relate to sampling techniques. The lack of recurrence with predominant gross total resection mirrors the general finding that cystic meningiomas likely require complete excision to minimize regrowth (36-39).

Today, the main problem of cystic meningioma surgery is the issue of excision of cystic wall components. It happens because neoplastic cells may be present at infiltrations inside the cyst wall. Such a situation will increase the risk of recurrent cystic meningioma or may cause it is spread through CSF (40). Theoretically, high recurrence risk is attributed to subtotal resection of cystic walls containing neoplastic cells (41,42). On the other hand, the identification of tumoral cells in the wall of the cysts in another research (43)

suggested that total resection is not obligatory if cysts are performed only by reactive proliferation with gliotic or fibrous tissue (44,45). Today, there is no consensus on whether complete removal is necessary.

CONCLUSION

This retrospective case series of 24 cystic meningiomas identified an incidence of 3.8 % among 623 intracranial meningiomas resected, consistent with prior data, and demonstrated a hemispheric convexity tumor localization in 25 % of cases. Apparent diffusion coefficient values were significantly lower in WHO grade 2 and 3 compared to grade 1 lesions. Complete cystic component resection was achieved in 75 % of cases, with partial resection in 12.5 % and biopsy alone in 8.3 %. Importantly, neoplastic cyst wall invasion was confirmed histologically in 66.6 % of cases. No recurrences requiring re-resection were observed over an average 49-month follow-up. Given the high rate of tumor cell invasion into the cyst walls, maximal safe surgical resection of all cystic components is recommended when anatomically and functionally feasible to minimize recurrence risk based on this study, which provides evidence supporting aggressive excision of cystic elements when plausible given lack of recurrence with predominant total resection.

Pre-operative diagnosis of meningioma can be difficult to establish if the cystic component is present. Differential diagnosis of cystic meningioma is based on the presence of such lesions, which include localizations on the dura, the presence of the dural tail, and the presence of homogenous enhancement. To reduce the risk of cystic meningioma recurrence in future investigations need to be explored alternative surgical tactics for complete resections of tumor components when the a suspected risk of damage to critical structures and functional nervous areas. Further research directions include analysis of genetic, epigenetic, and protein profiles, which could help predict recurrence risk and guide individualized treatment. For cases where open total resection risks neurological deficits, less invasive techniques like endoscopic,

radiosurgical, or cyst drainage approaches followed by radiotherapy should be evaluated in clinical trials. Standardized preoperative imaging protocols and machine learning applied to large databases may also advance diagnostic accuracy.

REFERENCES

- Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, et al. Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. *Neuro-Oncol.* 2019;21(5):1-100.
- Buerki RA, Horbinski CM, Kruser T, Horowitz PM, James CD, Lukas RV. An overview of meningiomas. *Future Oncol.* 2018;14(21):2161-2177.
- Chen TY, Lai PH, Ho JT, Wang JS, Chen WL, Pan HB, et al. Magnetic resonance imaging and diffusion-weighted images of cystic meningioma: Correlating with histopathology. *Clinic Imag.* 2004;28(1):9-10.
- Salami AA, Okunlola AI, Ajani MA, Onakpoma F. WHO classification of meningiomas-a single institutional experience. *Neurochirurgie.* 2021;67(2):119-124.
- Zhao H, Meng QL, Chen ZY. Atypical Cystic Meningioma: Report of One Case. *Zhongguo.* 2022;44(4):733-736.
- Mittal A, Layton KF, Finn SS, Snipes GJ, Opatowsky MJ. Cystic meningioma: Unusual imaging appearance of a common intracranial tumor. *Proceeding (Baylor University Medical Center).* 2010; 23:429-431.
- Garcia C, Slone S, Chau M, Neltner JH, Pittman T, Villano JL. Initial management of meningiomas: Analysis of the National Cancer Database. *Cancer Epidem.* 2019;60:16-22.
- Yamada SM, Fujimoto Y, Kawanishi Y, Shimizu K. A cystic meningioma misdiagnosed as malignant glioma by radiologic and intraoperative histological examinations. *Brain Tumor Pathol.* 2010; 27:111-115.
- Okunlola AI, Babalola OF, Okunlola CK, Akinmade A, Abiola P, Olayinka T. Awake craniotomy in neurosurgery: Shall we do it more often? *Interdisciplinary Neurosurg.* 2020;21:2-9.
- Nauta HJ, Tucker WS, Horsey WJ, Bilbao JM, Gonsalves C. Xanthochromic cysts associated with meningioma. *Neurology Neurosurg Psych.* 1979;42:529-535.
- Gendle C, Karthigeyan M, Salunke P. Pineal Region Meningioma in a Very Young Child. *Pediatr Neurosurg.* 2021;56(1):73-78.
- Li B, Tao B, Bai H, Zhong J, Wu X, Shi J, et al. Papillary meningioma: An aggressive variant

- meningioma with clinical features and treatment: a retrospective study of 10 cases. *Int J Neurosci*. 2015;26(10):878-887.
13. Foster N, Eljamel S. ALA- induced fluorescence image-guided surgery of meningiomas: A meta-analysis. *Photodiagn Photodyn Ther*. 2016;15:73-78.
 14. Francis SS, Ostrom QT, Cote DJ, Smith TR, Claus E, Barnholtz-Sloan JS. The Epidemiology of Central Nervous System Tumors. *Hematol Oncol Clin North Am*. 2022;36(1):23-42.
 15. Nowosielski M, Galldiks N, Iglseder S, Kickingereder P, von Deimling A, Bendszus M, et al. Diagnostic challenges in meningioma. *Neuro Oncology*. 2017;19(12):1588-1598.
 16. Nagano H, Sakai K, Tazoe J, Yasuike M, Akazawa K, Yamada K. Whole-tumor histogram analysis of DWI and QSI for differentiating between meningioma and schwannoma: A pilot study. *Radiology*. 2019;37(10):694-700.
 17. Xiaoi K, Qing Z, Lei H, Junlin, Z. Differentiating microcystic meningioma from atypical meningioma using diffusion-weighted imaging. *Neuroradiology*. 2020;62(5):601-607.
 18. Surov A, Ginat DT, Sanverdi E, Lim CC, Hakyemez B, Yogi A, et al. Use of diffusion-weighted imaging in differentiating between malignant and benign meningiomas. A multicenter analysis. *World Neurosurg*. 2015;88:598-602.
 19. Cheng Z, Chao Q, Zhang H, Wang DW, Shu HS. Intraventricular cystic papillary meningioma: A case report and literature review. *Med (Baltimore)*. 2020;31(31):1-5.
 20. Okunlola AI, Ibijola AA, Babalola OF, Okunlola CK, Erinomo OO. Parasagittal cystic meningioma mimicking hemangioblastoma: A case report. *Surg Neurol Int*. 2021;27(12):2-3.
 21. Lahkim M, Andour H, Laamrani FZ, Nouali HE, Fenni JE. Cystic meningioma: A case report with a literature review. *Radiology Case Report*. 2021;16(10):2958-2961.
 22. Diyora B, Kukreja S, Dhal G, Devani K, Patel M, Wankhede R. Extra-Axial Cystic Meningioma without Dural Attachment in an Adult: Case Report and Review of Literature. *Asian J Neurosurg*. 2022;17(2):173-177.
 23. Diyora BD, Dhall G, Bhende BU, Mulla M. Intraparenchymal Cystic Meningioma - A Rare Occurrence with a Clinical Significance. *Neurol India*. 2021;69(5):1442-1443.
 24. Wang XQ, Huang MZ, Zhang H, Sun FB, Tao BB, Feng BH, et al. Clear cell meningioma: Clinical features, CT, and MR imaging findings in 23 patients. *Comp Assist Tomogr*. 2014;38:200-208.
 25. Sugiyama H, Tsutsumi S, Watanabe A, Nonaka S, Okura H, Izumi H, et al. A large cystic meningioma incidentally detected during general examination for breast cancer. *Radiology*. 2022;17(5):1777-1783.
 26. Zhang D, Hu LB, Zhen JW, Zou LG, Feng XY, Wang WX, et al. MRI findings of intracranial cystic meningiomas. *Clin Radiol*. 2009;64:792-800.
 27. Zee CS, Chen T, Hinton DR, Tan M, Segall HD, Apuzzo ML. Magnetic resonance imaging of cystic meningiomas and its surgical implications. *Neurosurgery*. 1995;36:482-488.
 28. Go KO, Lee K, Heo W, Lee YS, Park YS, Kim SK, et al. Cystic Meningiomas: Correlation between Radiologic and Histopathologic Features. *Brain Tumor Res Treat*. 2018;6(1):13-21.
 29. Wang P, Han S, Liu N, Yu C, Qi X, Zhu M, et al. Peritumoral cystic meningioma: A report of two cases and review of the literature. *Exp Ther Med*. 2016;11(3):904-908.
 30. Utomo SA, Bajamal AH, Yueniwati Y, Sanjaya ID, Fauziah D. Apparent Diffusion Coefficient Values and Dynamic Contrast-Enhanced Magnetic Resonance Perfusion are Potential Predictors for Grading Meningiomas. *Int J Med Sci*. 2022;19(9):1364-1376.
 31. Saraf S, McCarthy BJ, Villano JL. Update on meningiomas. *Oncologist*. 2011;16:1604-1613.
 32. David EA, Marshall MB. Review of chest wall tumors: A diagnostic, therapeutic, and reconstructive challenge. *Semin Plast Surg*. 2011;25(1):16-24.
 33. Jang KT, Park SM, Basturk O, Bagci P, Bandyopadhyay S, Stelow EB, et al. Clinicopathologic characteristics of 29 invasive carcinomas arising in 178 pancreatic mucinous cystic neoplasms with ovarian-type stroma: implications for management and prognosis. *Am J Surg Pathol*. 2015;39(2):179-187.
 34. Al-Azzwi ZHN, Nazarov AN. Brain Tumor Classification based on Improved Stacked Ensemble Deep Learning Methods. *Asian Pacific J Cancer Prevent*. 2023;24(6):2141-2148.
 35. Ilderbayeva G, Zhetpisbaev B, Ilderbayev O, Taldykbayev Zh, Bekeeva S. Metabolic processes of organism in remote period after the combined effects of radiation and emotional stress. *Georg Med News*. 2016;(250):76-82.
 36. Diehl CD, Giordano FA, Grosu AL, Ille S, Kahl KH, Onken J, et al. Opportunities and Alternatives of Modern Radiation Oncology and Surgery for the Management of Resectable Brain Metastases. *Cancers (Basel)*. 2023;15(14):3670.
 37. Okassova AK, Ilderbayev OZ, Nursafina AZh, Zharmakhanova GM, Rakhimova BB, Bayan YT, et al. Evaluation of lipid peroxidation under immobilization stress in irradiated animals in experiment. *Open Access Macedon J Med Sci*. 2021;9:119-122.
 38. Chu ECP, Spaska A, Monov D, Kasatkin M, Stroiteleva N. Examining the correlation between

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- salivary cytokine concentrations and CRP in people experiencing social-cognitive stress. *Neurol Res.* 2023;45(2):160-165.
39. Lisnyy I, Zakalska O, Dmytriiev D, Dmytriiev K, Dobrovanov O. Pre-emptive analgesia with nonsteroidal anti-inflammatory drugs randomized, double-blind placebo-controlled study. *Lek Obz.* 2021;70(5):195-202.
40. Sagandykova NS, Fakhradiyev IR, Sajjala SR, Taukeleva SA, Shemetova DE, Saliev TM, et al. Patient-specific CFD simulation of aerodynamics for nasal pathology: A combined computational and experimental study. *Comp Meth Biomech Biomed Engin: Imag Visual.* 2021;9(5):470-479.
41. Latka D, Waligora M, Latka K, Miekisiak G, Adamski M, Kozłowska K, et al. Virtual Reality Based Simulators for Neurosurgeons - What We Have and What We Hope to Have in the Nearest Future. *Adv Intel Syst Comp.* 2018;720:1-10.
42. Nukusbekova G, Toguzbayeva D, Hashimli R, Oguz H, Taukeleva S. Reflux Symptom Index: Translation to the Kazakh Language and Validation. *J Voice.* 2022. doi:10.1016/j.jvoice.2022.07.004
43. Tang AR, Chotai S, Grisham CJ, Guidry BS, McDermott JR, Le CH, et al. Outcomes following surgical resection of cystic intracranial meningiomas. *Neurooncology.* 2022;160(1):33-40.
44. Messina A, Fogliani AM. Valproate in conversion disorder: A case report. *Case Rep Med.* 2010;2010:205702.
45. Messina A, Cucci G, Crescimanno C, Signorelli MS. Clinical anatomy of the precuneus and pathogenesis of the schizophrenia. *Anatom Sci Int.* 2023 98(4):473-481.

Mental Health Upon Return to Face-To-Face Classes: Burnout Syndrome in Basic Education Teachers

Salud Mental al Retorno a las Clases Presenciales: Síndrome de Burnout en Docentes de Educación Básica

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SUMMARY

Introduction: During the return to face-to-face classes, teachers are facing new challenges and demands because students were unable to learn adequately through the virtual modality implemented during the COVID-19 pandemic. Then, the increase in workload could affect their mental health and cause the appearance of burnout syndrome. **Objective:** Describe the level of burnout syndrome in basic education teachers upon return to face-to-face classes. **Methods:** The approach is quantitative, the design non-experimental and the descriptive type cross-sectional. The sample consisted of 170 teachers of whom applied the Maslach Burnout Inventory,

an instrument with adequate levels of validity and reliability. **Results:** It was determined that the teachers were characterized by presenting moderate levels of burnout syndrome. In the same way, they showed moderate levels of emotional exhaustion and personal accomplishment. However, they presented low levels of depersonalization. On the other hand, it was found that burnout syndrome was significantly associated with some sociodemographic and work variables such as gender, age group, employment status, and family burden of teachers ($p < 0.05$). **Conclusion:** Basic education teachers are characterized by having moderate levels of burnout syndrome during the post-pandemic context. For this reason, the Ministry of Education must design and execute policies that allow revaluing of the work that teachers have been doing and promoting the implementation of preventive and corrective programs to improve their mental health.

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RESUMEN

Introducción: Durante el retorno a las clases presenciales, los docentes están enfrentando nuevos desafíos y exigencias debido a que los estudiantes no lograron aprender de manera adecuada mediante la modalidad virtual implementada durante la pandemia por la COVID-19. Entonces, el incremento en la carga de trabajo podría afectar su salud mental y provocar la aparición del síndrome de burnout. **Objetivo:** Describir el nivel de síndrome de burnout

*en docentes de educación básica al retorno a las clases presenciales. **Métodos:** El enfoque fue cuantitativo, el diseño no experimental y el tipo descriptivo de corte transversal. La muestra fue conformada por 170 docentes a quienes se les administró el Inventario de Burnout de Maslach, instrumento con adecuados niveles de validez y confiabilidad. **Resultados:** Se determinó que los docentes presentaron niveles moderados de síndrome de burnout. Del mismo modo, mostraron niveles moderados de agotamiento emocional y realización personal, sin embargo, presentaron bajos niveles de despersonalización. Por otro lado, se halló que el síndrome de burnout se asociaba de manera significativa a algunas variables sociodemográficas y laborales como el sexo, el grupo etario, la condición laboral y la carga familiar de los docentes ($p < 0.05$). **Conclusión:** Los docentes de educación básica se caracterizan por presentar niveles moderados de síndrome de burnout durante el contexto de la pospandemia. Por ello, es necesario que el Ministerio de Educación diseñe y ejecute políticas que permitan revalorizar el trabajo que los docentes vienen realizando y promover la implementación de programas preventivos y correctivos para mejorar su salud mental.*

Palabras clave: *Síndrome de burnout, salud mental, docentes, educación básica, pospandemia, clases presenciales.*

INTRODUCTION

The COVID-19 pandemic has been a turning point in the history of humanity due to its repercussions in different areas of life. In the educational field, it provoked an unusual but necessary reform: the implementation of the virtual teaching-learning modality (1). However, in the first quarter of 2022, the number of infections and deaths caused by COVID-19 decreased significantly worldwide due to vaccination campaigns (2). In this sense, many activities that were previously carried out virtually returned in person. In Peru, the Ministry of Education established that from April 2022 classes in educational institutions return to face-to-face classes after complying with various biosafety protocols (3).

After the return to face-to-face classes, the work of teachers became more complex. Because the academic performance levels of the students

were not as desired, the learning achieved through virtual classes was insufficient. For this reason, teachers had to make a great effort, even providing more support to improve the academic performance of students. This led to an increase in their workload, and, in many cases, they carried out school reinforcement at times that were outside their working hours. Similarly, the anxiety, discouragement, and frustration of returning to on-site work drained their emotional resources while increasing their levels of mental and emotional stress and tension. In other words, a recurring phenomenon among teachers is becoming more critical: burnout syndrome (BS).

Currently, BS is the subject of much research due to its relevance and the impact it has on professionals (4). Within a historical framework, it had as its starting point the study by organizational psychologists between 1970 and 1985, with Freudenberg (5) and Maslach (6) being the main precursors of the study of this condition. It mainly affects professionals who provide services and have direct contact with other people, such as teachers, doctors, psychologists, nurses, and social workers, among others (7).

For Maslach (6), BS is a syndrome whose responses are characterized by emotional exhaustion, indifferent and unfavorable attitudes towards others, poor self-evaluation, and feelings of dissatisfaction with the work performed. Similarly, Acosta et al. (8) defined BS as a response to chronic job stress, which arises when the coping strategies that people regularly use to deal with situations that cause wear and tear in the exercise of their profession fail.

It is also argued that BS is a chronic adjustment disorder (9) and occurs when people are exposed to various stressors for a long time, whether emotional or interpersonal (10,11). Maslach and Jackson (12) established that BS is made up of three components: emotional exhaustion, depersonalization, and personal accomplishment. Emotional exhaustion refers to the drain on energy or emotional resources that causes fatigue in the person. Depersonalization is associated with the development of negative and indifferent feelings and attitudes toward other people. Personal accomplishment has to do with the cognitive self-assessment that professionals have about themselves and the work they do.

Among the main causes for a teacher to have BS are involvement in student problems, work overload, preparation of documentation and bureaucratic burden, low salary compensation, terrible working conditions, and little recognition, despite striving to improve their performance (13). However, teachers who suffer from this disease are characterized by providing poor service to students, they act with indifference and do not provide support in the tasks assigned to them. In fact, its prevalence significantly affects their performance when BS is not identified and treated on time (14).

In the context of the return to face-to-face classes, very little research has been carried out to evaluate BS in basic education teachers. Among them, in Colombian research, it was determined that the level of burnout in the sample of teachers oscillated between mild and moderate levels. The main causes were the educational lag of students and the pressure felt by teachers to fill the academic gaps generated by virtual education (15). Similarly, in Mexico, it was evaluated the impact on the mental and psychological health of teachers and students returning to face-to-face classes. They concluded that there were moderate levels of psychological discomfort, stress, and BS due to possible infections and readaptation to face-to-face (16).

This present research is relevant and original in the context of the return to face-to-face classes since it will allow the Ministry of Education and its decentralized instances to implement national, regional, and local policies to improve the working conditions in which teachers find themselves. On the other hand, the management teams of educational institutions will be able to manage and develop preventive and corrective programs to promote the mental health of teachers.

For these reasons, this research aimed to describe the level of BS in basic education teachers upon return to face-to-face classes.

METHODS

A quantitative approach was used because the research was based on numerical measurement, as well as the use of statistics to determine the

behavior patterns of the participants. Regarding the design, it was non-experimental since the BS variable was not intentionally manipulated, it was only observed. Regarding the type, it was descriptive of a cross-section, since the analysis of the characteristics of the study variable was developed and because the data collection process was carried out in a single moment, respectively (17).

The population was made up of 305 basic education teachers who worked in the city of Cusco (Peru) and the sample consisted of 170 teachers, an amount determined by probabilistic sampling with a confidence level of 95 % and a significance level of 5 %. According to Table 1, 61.8 % of the participants were women, and 38.2 % were men. Regarding the age group, 52.4 % were from 21 to 40 years old, while 47.6 % were from 41 to 64 years old. Regarding labor conditions, 57.1 % had an open-ended contract, and 42.9 % had a temporary one. Regarding the specialty, 38.8 % were teachers at Elementary school, 35.9 % of High School, and 25.3 % of Early Childhood Education. Regarding family responsibilities, 72.4 % had family responsibilities and 27.6 % did not. Regarding the highest level of study achieved, 50.6 % only achieved a bachelor's degree, 38.8 % had master's studies and only 10.6 % had a doctorate.

For data collection, a survey was prepared, which was structured in two sections. In the first section, sociodemographic and employment information was requested from the teachers (gender, age group, labor condition, level of educational system, family responsibilities, and highest level of study completed).

In the second section, the Maslach Burnout Inventory was applied, which was prepared by Maslach and Jackson (12) and evaluates the prevalence of BS caused by work activities that workers usually carry out. It is drawn up of 22 items of Likert type (never, sometimes, and always) and measures 3 dimensions: emotional exhaustion (items 1 to 9), depersonalization (items 10 to 14), and personal accomplishment (items 15 to 22). Its psychometric properties were determined in a previous investigation carried out in Peru (18), where it was found that the inventory had an adequate level of validity based on content (Aiken's $V=0.801$) and reliability ($\alpha=0.823$).

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Table 1
Sociodemographic and job characteristics of the sample

Variables	Sociodemographic and job characteristics	n= 170	%
Gender	Male	105	61.8
	Female	65	38.2
Age group	From 21 to 40 years old	89	52.4
	From 41 to 64 years old	81	47.6
Labor condition	Temporary contract	73	42.9
	Open-ended contract	97	57.1
Level of Educational System	Early Childhood Education	43	25.3
	Elementary	66	38.8
	High School	61	35.9
Family responsibilities	Yes	123	72.4
	No	47	27.6
Highest level of education completed	Bachelor	86	50.6
	Master	66	38.8
	Doctorate	18	10.6

The data collection process was carried out between November and December of the year 2022, dates in which all the Peruvian educational institutions of regular basic education were providing the educational service in person. For this, the respective authorization was requested from the Local Educational Management Unit of Cusco. Once the authorization was obtained, the permission of the management staff of each educational institution was gained and a coordination meeting with the teachers was requested to define the days of application of the data collection instruments.

For the statistical analysis, the SPSS software version 25 was used. The descriptive results were systematized in a figure and three tables, while the inferential results were obtained through the non-parametric Chi-Square (X^2) test, a statistic that allowed knowing whether the BS variable was significantly associated with the proposed sociodemographic and occupational variables.

Regarding ethical considerations, this research was carried out in accordance with the ethical principles defined by the Declaration of Helsinki and had the endorsement of the institutional ethics committee. Likewise, it should be noted that the teachers were informed about the purpose and nature of the research and gave their informed consent, ensuring the confidential, anonymous, and voluntary nature of their participation.

RESULTS

Figure 1 shows that the level of BS of 39.4 % of teachers was moderate, 31.2 % was low, and 29.4 % was high. In relation to the emotional exhaustion dimension, 40.6 % presented a moderate level, 34.1 % a high level, and 25.3 % a low level. Regarding the depersonalization dimension, 36.5 % presented a low level, 32.9 % a moderate level, and 30.6 % a high level. Concerning the personal accomplishment dimension, 45.3 % presented a moderate level, 31.2 % a low level, and 23.5 % a high level. The exposed results indicate that there is a significant percentage of teachers who presented symptoms of BS, especially in the dimension of emotional exhaustion and to a lesser extent in depersonalization and personal accomplishment.

According to Table 2, the symptoms associated with emotional exhaustion most frequently reported by teachers were feeling exhausted at the end of their workday, feeling that they reached the limit of their possibilities due to the work they do, and feeling that their work was very hard. The information described specifies that teachers would be experiencing high levels of stress due to their work, which could negatively affect their well-being and work performance.

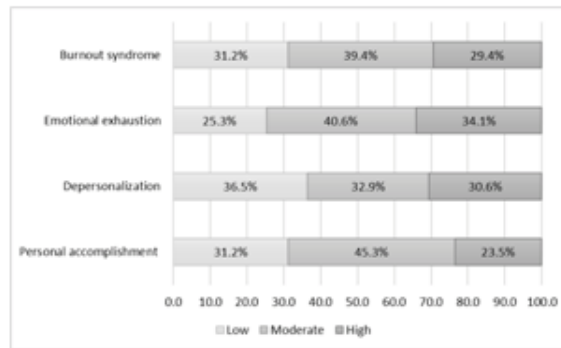


Figure 1. Descriptive results of the burnout syndrome variable and its dimensions.

Table 2
Items associated with emotional exhaustion

Items	Never		Sometimes		Always	
	n	%	n	%	n	%
I feel emotionally exhausted because of my work.	37	21.8	77	45.3	56	32.9
I feel worn out at the end of a working day.	33	19.4	72	42.4	65	38.2
I feel tired as soon as I get up in the morning and see a new working day stretched out in front of me.	50	29.4	66	38.8	54	31.8
Working with students the whole day is stressful for me.	55	32.4	69	40.6	46	27.1
I feel burned out because of my work.	40	23.5	74	43.5	56	32.9
I feel frustrated by my work.	52	30.6	73	42.9	45	26.5
I get the feeling that I work too hard.	40	23.5	68	40.0	62	36.5
Being in direct contact with students at work is too stressful.	45	26.5	69	40.6	56	32.9
At work, I feel that I have reached the limit of my possibilities.	35	20.6	55	32.4	80	47.1

Regarding Table 3, the symptoms associated with depersonalization most frequently reported by teachers were worried that their work could be hardening them emotionally, considering that they treat some students with indifference, and feeling that they are blamed for some of their

problems. The above means that teachers would be experiencing a slight feeling of detachment from their students and the work they do, a situation that would have a negative impact on the quality of teaching and the relationship between teachers and students.

Table 3
Items associated with depersonalization

Items	Never		Sometimes		Always	
	n	%	n	%	n	%
I think I treat some students with indifference.	60	35.3	55	32.4	55	32.4
I think I've been more insensitive to people since I've been doing this job.	68	40.0	62	36.5	40	23.5
I worry that this job is hardening me emotionally.	55	32.4	55	32.4	60	35.3
I really don't care what happens to some of the students I'm in charge of at the educational institution.	71	41.8	56	32.9	43	25.3
I feel like students blame me for some of their problems.	56	32.9	62	36.5	52	30.6

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In Table 4 we can see that the symptoms most frequently reported by teachers that would limit personal accomplishment were low vitality, having difficulty dealing with emotional problems at work, and creating a relaxed atmosphere

among their students. Therefore, resources and support must be provided to help them manage these symptoms and improve their emotional and mental well-being in the work environment.

Table 4

Items associated with personal accomplishment

Items	Never		Sometimes		Always	
	n	%	n	%	n	%
I can easily understand what my students think.	50	29.4	79	46.5	41	24.1
I deal very well with the problems that my students present to me.	39	22.9	85	50.0	46	27.1
I feel that I influence other people positively through my work.	46	27.1	73	42.9	51	30.0
I find myself with a lot of vitality.	74	43.5	79	46.5	17	10.0
I have the ability to create a relaxed atmosphere for my students.	56	32.9	79	46.5	35	20.6
I feel encouraged after working together with my students.	49	28.8	70	41.2	51	30.0
I have done many worthwhile things in this job.	43	25.3	62	36.5	65	38.2
I feel that I know how to adequately deal with emotional problems at work.	63	37.1	85	50.0	22	12.9

Table 5 shows that BS was significantly associated with some sociodemographic and work variables, such as gender, age group, labor conditions, and family responsibilities of teachers ($p<0.05$). In this sense, women, teachers who

were from 21 to 40 years old, those who had temporary contracts, and those who had family responsibilities presented slightly higher levels of BS compared to the other contrast groups.

Table 5

Association between burnout syndrome and sociodemographic and work-related variables

Sociodemographic and work-related variables		Burnout syndrome						p
		Low		Moderate		High		
		f	%	f	%	f	%	
Gender	Male	35	33.3	42	40.0	28	26.7	0.0001*
	Female	18	27.7	25	38.5	22	33.8	
Age group	From 21 to 40 years old	25	28.1	33	37.1	31	34.8	0.005*
	From 41 to 64 years old	28	34.6	34	42.0	19	23.5	
Labor condition	Temporary contract	22	30.1	26	35.6	25	34.2	0.001*
	Open-ended contract	31	32.0	41	42.3	25	25.8	
Level of Educational System	Early Childhood Education	14	32.6	16	37.2	13	30.2	0.055
	Elementary	19	28.8	28	42.4	19	28.8	
	High School	20	32.8	23	37.7	18	29.5	
Family responsibilities	Yes	37	30.1	46	37.4	40	32.5	0.002*
	No	16	34.0	21	44.7	10	21.3	
Highest level of education completed	Bachelor	26	30.2	34	39.5	26	30.2	0.062
	Master	21	31.8	26	39.4	19	28.8	
	Doctorate	6	33.3	7	38.9	5	27.8	

*Statistically significant association ($p<0.05$).

DISCUSSION

Currently, BS is considered a mental health problem that affects workers all over the world. This syndrome is characterized by a feeling of emotional exhaustion, depersonalization, and decreased personal accomplishment at work. In the case of teachers, BS can affect their emotional well-being and their ability to carry out their work effectively, which in turn can have a negative impact on student learning. For this reason, the present research describes the level of BS in basic education teachers upon return to face-to-face classes.

Its first finding indicates that the teachers suffered from moderate levels of BS. In this sense, teachers experienced a decrease in their energy and emotional resources due to the presence of various stressors in the educational context, one of the main ones being the increment in workload. The main symptoms associated with BS reported by teachers were feeling exhausted at the end of their workday, worrying because they perceived that their work could be hardening them emotionally, and feeling that their vitality had decreased significantly. As previously mentioned, in the post-pandemic context, the workload of teachers increased, since they had to carry out additional school activities outside of their working hours to compensate for the learning that did not materialize during the pandemic through virtual classes.

The results are in line with the work of Villarreal (15), who determined that the level of burnout in the sample of teachers was between mild and moderate levels. Among the main causes were the educational lag of students and the pressure felt by teachers to fill the academic gaps generated by virtual education. On the other hand, the level of BS found was lower than that reported by Estrada and Gallegos (18), who found that teachers were characterized by high levels of BS (42.1 %), emotional exhaustion (40.3 %), and depersonalization (37.7 %). However, they presented low levels of personal accomplishment (39.6 %). These differences can be explained by sociodemographic aspects and the academic conditions from which the data were obtained.

In this regard, it should be noted that teaching is considered a high-risk profession for BS because it demands skills and commitment to carry out various activities inside and outside the educational institution, using time that should be dedicated to rest and personal and family activities of teachers (19). In addition, the demands of the current context request that teachers train competent and comprehensive students. In this sense, the pressure that exists in them to achieve greater learning and achieve educational objectives could harm their health, both physical and mental.

Another finding indicates that BS was significantly associated with gender. This means that women presented higher levels of BS than men. Similar results were obtained in some investigations that found that there was a higher prevalence in women (18,20-22). This could be explained by the fact that women express, more frequently than men, emotional and physiological manifestations in stressful contexts (23). On the other hand, in addition to their work responsibilities, women usually assume additional tasks at home, such as family responsibilities, childcare, and other domestic activities, a situation that could affect their mental health (24).

BS was also found to be significantly associated with age. In this sense, it was determined that teachers who were from 21 to 40 years old presented higher levels of BS than teachers older than 40 years old. This is because younger teachers do not have job security. On the other hand, they may also be experiencing important changes in their personal lives, such as the transition to adulthood and the formation of their own family. These changes can increase stress and anxiety, which in turn can increase the risk of developing BS. Similar results were reported in several studies (18,20,25).

It was also found that BS was significantly associated with the labor conditions of teachers. Accordingly, the teachers who have temporary contracts showed higher levels of BS than the teachers who have open-ended contracts, a situation that is because some teachers feel worried because they do not have job stability and may feel greater pressure to demonstrate

their effectiveness and justify their short-term contract, which can increase stress and anxiety. These results are in line with other studies reported previously (18,20,26).

Finally, it was found that BS was significantly associated with the family responsibilities of teachers. The above indicates that the teachers who were responsible for the care and attention of their families experienced greater stress since they needed to balance their work and family responsibilities, which can increase their level of stress and the risk of developing BS to a greater extent. Our results diverge from some studies that stated that single people (without family responsibilities) presented higher levels of BS (27,28).

Teaching is one of the main work activities in which professionals can develop symptoms related to stress and end up suffering from BS. Teaching work requires a significant amount of time and effort, both inside and outside the classroom, which can lead to neglecting other personal or family areas due to work overload (29). Additionally, it is a profession that faces constant stressful factors, since the terrible working conditions, the high number of students per classroom, behavior problems, and friction with educational authorities and parents, among others, generate more complex situations that can significantly affect the well-being and quality of life of those who carry out this work (30,31).

Even though the present study addressed a very relevant issue associated with the mental health of teachers and important findings were made, it is necessary to specify some limitations. First, the data obtained from the teachers, who detailed the symptoms associated with BS, were based on a self-report instrument. Therefore, the results could be overestimated or underestimated. Second, the sample size is relatively small and homogeneous, which implies that caution must be exercised when interpreting the results. Consequently, it is recommended that future research use data collection instruments that complement the questionnaire to give greater objectivity to the entire process. Similarly, the size of the sample should be increased, including teachers from rural contexts and different sociocultural characteristics.

CONCLUSION

The BS in teachers is a problem that has become relevant in recent years due to its negative impact on the physical and emotional health of those who suffer from it, as well as on the quality of teaching provided to their students. It is characterized by a set of symptoms that include emotional exhaustion, depersonalization, and a decrease in personal accomplishment at work. These symptoms can be caused by various situations, such as work overload, job stress, and lack of support and recognition.

In the present study, the teachers were characterized by presenting moderate levels of BS. In the same way, they showed moderate levels of emotional exhaustion and personal accomplishment. However, they presented low levels of depersonalization. On the other hand, it was found that BS was significantly associated with some sociodemographic and work variables such as gender, age group, labor condition, and family responsibilities of teachers.

Therefore, the relevant educational authorities must establish national, regional, and local policies to improve the working conditions in which teachers work. On the other hand, the management teams of educational institutions must develop preventive and corrective programs to promote teacher well-being and consequently protect their quality of life.

REFERENCES

1. Estrada E, Gallegos N, Paredes Y, Quispe R, Córdova F. Satisfacción de los estudiantes peruanos con las clases virtuales durante la pandemia COVID-19. *Univ Soc.* 2022;14(S6):678-685.
2. Taborda A, Murillo D, Moreno C, Taborda P, Fuquen M, Díaz P, et al. Análisis de impacto presupuestal de la vacunación contra COVID-19 en América Latina. *Rev Panam Salud Pública.* 2022;46(e5):1-10.
3. Estrada E, Bautista J, Callata Z, Arce R, Quispe Y, Yabar P, et al. Concern about the spread of COVID-19 in Regular Basic Education Teachers when returning to face-to-face classes. *Behav Sci.* 2023;13(4):346.
4. Llorent V, Ruíz I. El Burnout y las variables sociodemográficas en los profesionales de la educación

- que trabajan con personas con discapacidad en Córdoba (España). *Cien Saude Colet*. 2016;21(10):3287-3295.
5. Freudenberg H. Staff burnout. *J Soc Issues*. 1974;30:159-166.
 6. Maslach C. *Burnout: The cost of caring*. New Jersey: Prentice-Hall Press; 1982.
 7. Almeida M, Oliveira N, Guimarães F, Evangelista R, Gomes A, Vieira B. Síndrome de Burnout: Un estudio con profesores. *Sal Trabaja*. 2015;23(1):19-27.
 8. Acosta J, Morales L, Álvarez G, Pino Y. Síndrome de desgaste profesional en médicos del Hospital Docente Pediátrico Cerro. *Rev Haban Cienc Méd*. 2019;18(2):336-345.
 9. Chavarría R, Colunga F, Loria J, Peláez K. Síndrome de burnout en médicos docentes de un hospital de 2° nivel en México. *Educ Médica*. 2017;18(4):254-261.
 10. Domínguez A, Velasco M, Meneses D, Guzmán G, Castro M. Síndrome de burnout en aspirantes a la carrera de Medicina. *RIEM*. 2017;6(24):242-247.
 11. Magalhães E, Machado A, Souza C, Araújo L, Moser D, Viana C. Prevalencia del síndrome de burnout entre los anestesiólogos del Distrito Federal. *Braz J Anesthesiol*. 2015;65(2):104-110.
 12. Maslach C, Jackson S. *Maslach Burnout Inventory*. California: Consulting Psychologists Press; 1986.
 13. Rodríguez E, Sánchez M. Síndrome de Burnout y variables sociodemográficas en docentes de una universidad privada de Lima. *Rev Invest Educ*. 2018;36(2):401-419.
 14. Fuster D, Jara N, Ramírez E, Maldonado H, Norabuena R, García A. Desgaste ocupacional en docentes universitarios mediante el modelo factorial confirmatorio. *Propós Represent*. 2019;7(3):198-230.
 15. Villarreal J. El Estrés y Burnout percibidos en docentes colombianos en el regreso a la presencialidad en las aulas. Un estudio exploratorio. *Rev Psicol Educ*. 2023;18(1):71-81.
 16. Armenta C, Blanco H, Castillo A. Regreso a clases, el impacto psicológico ante el confinamiento por COVID-19, la importancia de la salud mental en el proceso de aprendizaje. *Escuela Superior de Arte y Tecnología (ESAT)*. 2023;10(19):10-13.
 17. Hernández R, Mendoza, C. *Metodología de la investigación: las rutas cuantitativa, cualitativa y mixta*. México: McGraw-Hill; 2018.
 18. Estrada E, Gallegos N. Síndrome de burnout y variables sociodemográficas en docentes peruanos. *Arc Ven Farm Ter*. 2020;39(6):714-720.
 19. Rodríguez J, Guevara A, Viramontes E. 2017. Síndrome de burnout en docentes. *IE REDIECH*. 2017;8:45-67.
 20. Estrada E, Gallegos N, Parichahua J, Paredes Y, Quispe R. Síndrome de Burnout en docentes en tiempos de la pandemia de COVID-19. *Arc Ven Farm Ter*. 2022;41(5):321-326.
 21. Hernández C, Gamboa A, Prada R. Síndrome de burnout en docentes de educación básica y media en tiempos de crisis. *Bol Redipe*. 2021;10(9):472-488.
 22. Colino N, Pérez, P. El síndrome de burnout en un grupo de profesores de enseñanza secundaria en Montevideo. *CienciasPsi*. 2015;9(1):27-41.
 23. Vidal J, Muntaner A, Palou P. Diferencias de estrés y afrontamiento del mismo según el género y cómo afecta al rendimiento académico en estudiantes universitarios. *Context Educ*. 2018;0(22):181-195.
 24. Rodríguez J, Benavides E, Ornelas M, Jurado P. El burnout académico percibido en universitarios; comparaciones por género. *Form Univ*. 2019;12(5):23-30.
 25. Tacca D, Tacca A. Síndrome de Burnout y resiliencia en profesores peruanos. *Rev Psicol*. 2019;(22):11-30.
 26. Parra P, Carrión L, Gallardo K. Síndrome de Burnout en el personal docente de la Universidad Técnica Estatal de Quevedo. *LATAM*. 2022;3(2):1730-1745.
 27. Safiye T, Vukčević B, Milidrag A, Dubljanin J, Gutić A, Dubljanin D, et al. Relationship between mentalizing and teacher burnout: A cross-sectional study. *PLoS One*. 2023;18(1):e0279535.
 28. Muñoz C, Correa C, Matajudíos J. Síndrome de Burnout y estrategias de afrontamiento en docentes de primera infancia. *Espacios*. 2020;41(37):12.
 29. El-Sahili L. *Docencia: riesgos y desafíos*. México: Trillas; 2011.
 30. Peralta J. Estrés y factores psicosomáticos en docentes de una escuela normal particular: una comparación de grupos de sexos. *Kinesis*. 2018;3(3):45-53.
 31. Estrada E, Paredes Y, Quispe R. El desgaste profesional y su relación con el desempeño de los docentes de educación básica regular. *Univ Soc*. 2021;13(4):361-368.

Surgical Treatment of Abdominal Aortic Aneurysms

Tratamiento Quirúrgico de los Aneurismas de Aorta Abdominal

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SUMMARY

Introduction: Surgical treatment of abdominal aortic aneurysms poses a significant challenge in the field of vascular surgery, with numerous factors influencing operative technique and surgical outcome.

Objective: This study aimed to assess the outcomes of open surgical treatment for patients with abdominal aortic aneurysms at the Vascular Surgery Service of Mother Teresa University Hospital Centre in Tirana, and provide recommendations for improving outcomes.

Methods: A total of 206 patients who underwent transabdominal and retroperitoneal surgical access between January 2008 and December 2015 were

included in the analysis. The study evaluated the incidence of abdominal aortic aneurysms, clinical and imaging findings of the disease (ultrasound, tomographic, and arteriographic), frequency of involvement of the iliac artery in the pathological process, and postoperative complications. **Results:** Transabdominal access was the most commonly utilized, while retroperitoneal access was deemed the safest. No significant differences in recurrence rates were noted between the two approaches. The findings from this study suggest that surgery is necessary for aneurysms greater than 4.5 cm with clinical symptoms. In contrast, regular monitoring every 3 to 6 months is recommended for aneurysms smaller than 4.5 cm in the absence of clinical symptoms. The study highlights the need for ultrasound screening of the abdomen in patients over the age of 55 years referred to a vascular center with arterial hypertension, diabetes mellitus, or appropriate complaints. Further development of abdominal aortic aneurysm screening for patients over 55 years of age is warranted.

Keywords: Aortic repair; open aortic surgery, operative surgical procedures, screening program, quality of care, treatment outcome.

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RESUMEN

Introducción: El tratamiento quirúrgico de los aneurismas de aorta abdominal plantea un desafío importante en el campo de la cirugía vascular, con numerosos factores que influyen en la técnica quirúrgica y el resultado quirúrgico. **Objetivo:** El objetivo de este estudio fue evaluar los resultados del tratamiento quirúrgico abierto para pacientes

*con aneurismas aórticos abdominales en el Servicio de Cirugía Vasculardel Centro Hospitalario Universitario Madre Teresa en Tirana, y brindar recomendaciones para mejorar los resultados. **Métodos:** Se incluyeron en el análisis un total de 206 pacientes que se sometieron a un acceso quirúrgico transabdominal y retroperitoneal entre enero de 2008 y diciembre de 2015. El estudio evaluó la incidencia de aneurismas de aorta abdominal, los hallazgos clínicos e imagenológicos de la enfermedad (ecografía, tomografía y arteriografía), la frecuencia de afectación de la arteria ilíaca en el proceso patológico y las complicaciones posoperatorias. **Resultados:** El acceso transabdominal fue el más utilizado, mientras que el acceso retroperitoneal se consideró el más seguro. No se observaron diferencias significativas en las tasas de recurrencia entre los dos enfoques. Los hallazgos de este estudio sugieren que la cirugía es necesaria para los aneurismas mayores de 4,5 cm con síntomas clínicos. Por el contrario, se recomienda un control regular cada 3 a 6 meses para aneurismas menores de 4,5 cm en ausencia de síntomas clínicos. El estudio destaca la necesidad del cribado ecográfico del abdomen en pacientes mayores de 55 años derivados a un centro vascular con hipertensión arterial, diabetes mellitus o padecimientos propios. Se justifica un mayor desarrollo de la detección del aneurisma de la aorta abdominal en pacientes mayores de 55 años.*

Palabras clave: Reparación aórtica, cirugía aórtica abierta, procedimientos quirúrgicos operativos, programa de detección, calidad de atención, resultado del tratamiento.

INTRODUCTION

Abdominal aortic aneurysm (AAA) is a ticking time bomb in the abdominal cavity of over 1 % of adults worldwide (1,2). Open surgical repair of AAAs is a major procedure with its own risks, while endovascular aneurysm repair (EVAR) has lower perioperative mortality but higher long-term complications and reintervention rates. If left untreated, the ballooning weakness in the abdominal aorta can catastrophically rupture and rapidly lead to death (3,4). Despite advancements in screening and surgical techniques, AAA remains a prevalent and potentially fatal vascular disease. In the United States alone, over 15 000 deaths per year can be attributed to ruptured AAAs. Early detection and proactive surgical intervention are crucial for averting these tragic outcomes (5).

Recent studies have examined surgical outcomes and mortality rates for abdominal aortic aneurysm (AAA) repair, both open and endovascular. Despite the demonstrated prevalence of AAA, treatment outcomes vary. For instance, a nationwide prospective cohort study by Alberga et al. (6) analyzed the outcomes of endovascular treatment in 11 624 patients (74.8 %) and open intervention in 3 908 patients (25.2 %) from 2014 through 2019. They observed a decrease in total complications from 10.1 % to 7.0 %, postoperative mortality from 6.1 % to 4.6 %, and an increase in the proportion of patients with cardiac comorbidity since the creation of this nationwide initiative.

Meanwhile, Brown et al. (7) reported wide variability in risk-adjusted mortality rates (1.3 %-8.2 %) across 223 centers performing open repair from 2003-2019. The studies by Alberga et al. and Brown et al. both analyzed recent surgical trends and mortality rates, providing complementary multi-center perspectives on real-world outcomes. Meanwhile, Sharma et al. (8) and Tshomba et al. (9) drilled down on mortality and complications for specific patient subgroups. Sharma et al. reported a postoperative mortality rate of 4.1 % (n=126) in a Vascular Quality Initiative registry study of 3 078 patients who underwent elective open surgery for AAA. Tshomba et al. examined the long-term outcomes of open treatment of complex AAAs in 119 patients at a major vascular center from January 2010 to June 2016, with a mean follow-up of 76 months. They found that open repair of complex AAAs can be performed with acceptable surgical risk and consistent results, despite 37 % of deaths and 43.8 % of patients experiencing long-term chronic renal failure.

There are different views on AAA screening at both national and regional levels in many countries (10). Powell and Wanhainen (11) compared the recently published National Institute for Health and Care Services (United Kingdom) 2020 and European Society for Vascular Surgery (France) 2019 guidelines on the diagnosis and management of patients with abdominal aortic aneurysm, which contain conflicting recommendations in important areas (Table 1). The differences in the recommendable methods of treatment of juvenile aneurysms are

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similarly explained by the authors as reflecting different perspectives, methodologies, and quality assurance. Despite strong evidence supporting the need for screening to reduce mortality (12-14), there are only a few national

programs in the United States, Great Britain, Sweden, and Norway, and other countries are currently evaluating the economic effectiveness of screening programs before implementing them (4,15).

Table 1
Points of Divergence in AAA Guidelines from the UK and France

Guideline Aspect	NICE Guideline	ESVS Guideline
Screening women	Consider screening women aged ≥ 70 years with risk factors	Do not recommend population screening for women
Screening men	Recommend population screening for men aged 65-74 years	Same as NICE - recommend screening for men 65-74 years
Intervention threshold women	5.5 cm	Consider 5.0 cm
Intervention threshold men	5.5 cm	5.5 cm
Elective AAA repair women	No specific recommendation	Consider EVAR first if suitable anatomy
Elective AAA repair men	Recommend open repair first end open repair first	Recommend EVAR first for most patients
Ruptured AAA repair women	Consider EVAR first	Recommend EVAR first if suitable anatomy
Ruptured AAA repair men	Consider open repair first for men < 71 years	Recommend EVAR first if suitable anatomy
Complex/juxtarenal AAA repair	Consider open repair first	Individualized approach based on patient factors

Main differences

1. NICE focuses on cost-effectiveness and uses rigorous methodology relying heavily on randomized controlled trials (RCTs).
2. ESVS considers a wider range of evidence including recent observational studies.
3. NICE takes a UK health system perspective, and ESVS aims for the best clinical practice across Europe.
4. NICE guideline development is lengthy but multidisciplinary, ESVS is faster paced but mainly vascular surgeons.

Therefore, the problem of surgical treatment of AAAs is urgent and important for practical tasks of vascular surgery. This study aimed to analyze the surgical treatment of patients who

underwent open surgery for AAA to identify factors contributing to improved outcomes. Specifically, the task was to determine the place of AAA in the structure of vascular pathology, the frequency of concomitant obliterating pathology of the iliac and femoral segments, clinical characteristics of patients, their complaints and symptoms, imaging results of aneurysm signs using different methods, and to compare the results of transabdominal and retroperitoneal methods and their possible complications.

There is a gap in knowledge regarding the optimal surgical approach for AAA repair in terms of outcomes and complications. The purpose of this study was to compare outcomes and complications between transabdominal and retroperitoneal surgical approaches for abdominal aortic aneurysm repair in a single-center patient cohort.

MATERIALS AND METHODS

A single-center, non-randomized, retrospective study of the results of open surgical treatment of abdominal aortic aneurysms in 206 patients from January 2008 to December 2015 was performed at the Vascular Surgery Service of Mother Teresa University Hospital Centre in Tirana. The study only included patients with a histologically confirmed diagnosis of abdominal aortic aneurysm, while patients with ruptured abdominal aortic aneurysm were excluded.

Patient identification was based on the analysis of surgical logs, statistical data from medical records, and radiology imaging protocols. The data collected for each patient included demographics such as age and sex, timing of complaints before referral, comorbidities such as arterial hypertension, heart and lung diseases, diabetes mellitus, probable risk factors such as smoking, hypertension, positive family history, metabolic disorders, etc. Preoperative aneurysm imaging findings were divided into different categories based on the size of the aneurysm, which included 4 cm, 4.5 cm, 5 cm, 5.5 cm, 6 cm, 6.5 cm, 7 cm, and >7 cm. The localization of the aneurysm, involvement of iliac and femoral vessels, and aneurysm shape (sac-like, spindle-shaped, mixed) were also recorded.

The selection of the surgical intervention option for AAA was dependent on clinical features, surgery was performed using either a retroperitoneal or transabdominal approach, and the recommendations of the European Society for Vascular Surgery were followed. The surgical treatment strategy was determined and coordinated by a multidisciplinary team, which included vascular surgeons, interventional radiologists, and anesthesiologists. The date of surgery, type of surgery (transabdominal, retroperitoneal), type of first surgery and access in case of recurrence, results of the pathohistological examination, immediate and long-term results of surgery, postoperative laboratory data, postoperative complications, and their treatment were recorded. Short-term follow-up was defined as follow-up within the first year after surgery, while long-term follow-up was defined as follow-up over five years.

To analyze the data, the licensed version of the statistical program SPSS Statistics version 17 Chicago was used. Statistical analysis of indicators was carried out by studying the characteristics of the process under study, followed by the selection of indicators and their ranking by importance. The collected values of the indicators were grouped in the form of statistical tables. The results were processed by methods of descriptive statistics without testing the compared populations on the nature of the distribution. A two-sided Student's t-test was used to evaluate the statistical significance of differences between average values, followed by the comparison of the calculated value with the critical table value of the coefficient. To compare the relative frequency rates in the compared groups, we used the χ^2 (Chi-Square) goodness-of-fit test compared to the table value of the critical value.

A single-center retrospective study was chosen due to several advantages. First, it allowed access to detailed medical records and a sufficient sample size from a major vascular center. Second, it enabled analyzing real-world surgical outcomes over a 8-year period. Third, it avoided selection bias that could occur in a prospective study. Finally, it had lower costs and faster completion compared to a prospective study. However, there were also some disadvantages to this approach. First, there was potential for missing or incomplete data from the medical records. Second, findings had limited generalizability beyond this specific center. Third, there was an inability to control confounding factors or prove causation like an RCT could. Fourth, it was susceptible to biases like selection bias or reporting bias. In conclusion, a retrospective single-center study was an appropriate design to analyze surgical outcomes from this hospital's experience, although findings may not be fully generalizable. There were also limitations compared to what a prospective multicenter study could have provided.

Patients were not involved in the design, conduct, reporting, or dissemination plans of this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964

Helsinki Declaration and its later amendments or comparable ethical standards. A study was approved by the Ethics Commission of the Mother Teresa University Hospital Centre in Tirana on May 26, 2023, No 3021-A.

RESULTS

Patient characteristics

During the study period, a total of 206 patients underwent surgery for AAA and met the inclusion criteria. Of these, 188 (91.3 %) were male, and 18 (8.7 %) were female. The mean age of the patients was 67.8±5.7 years, with 67.7±5.9 years for men and 69±3.1 years for

women. There were no statistically significant differences in age between genders ($p>0.05$). Following the detection of AAA, all patients were hospitalized for surgical treatment after a thorough clinical examination based on a standard protocol. In almost all patients, there was a delay in diagnosis from 2 to 25 weeks, resulting in a difference in time from the onset of symptoms to hospitalization. On average, this time was 2.3±6.4 weeks for men and 2.5±35.2 weeks for women, with a statistically significant difference between genders ($p<0.05$). Abdominal pain was reported by 12 male patients and 6 female patients, with a statistically significant difference in the frequency of abdominal pain between genders ($\chi^2=4$, $df=1$, $p=0.05$). Detailed clinical features are provided in Table 2.

Table 2
Distributions of clinical signs

	Men	Women	Total
Clinical signs	6	0	6
Abdominal pain + lumbar pain + intermittent claudication	6	6	12
Abdominal + lumbar + back pain	8	0	8
Intermittent claudication	9	0	8
Abdominal + lumbar + chest pain	4	0	4
Epigastric + lumbar + right hypogastric pain	6	2	8
Lumbar + gluteal pain + left lower extremity	8	0	8
Colic	4	6	10
Peri umbilical pain + pelvis	24	14	38
Periabdominal and umbilical pain	104	4	108
No symptoms	178	28	206

Source: created by the authors.

Before surgery, in addition to standard clinical tests, routine instrumental studies were conducted, and specialists were consulted as necessary. All patients exhibited concomitant pathology on admission. The most common comorbidities were chronic obstructive pulmonary disease (COPD) and chronic smoker’s bronchitis (52.9 %), hypertensive disease (61.1 %), angina and postinfarct cardiosclerosis (20.4 %), vascular pathology including cerebral atherosclerosis (21.4 %), and diabetes mellitus (8.7 %, all male). This information will be considered when

distributing patients according to the types of surgical interventions performed. Among the examined patients, the following risk factors were identified: active smoking in 6 cases (2.9 %) among women and in 96 cases (4.4 %) among men; coronary heart disease of varying severity was found in 54 patients (26.2 %); mild degree obstructive diseases were found in 60 patients (29.1 %), moderate degree in 32 patients (15.5 %), and severe obstructive changes in 18 patients (8.73 %), with obstructive phenomena absent in 96 patients (46.6 %).

Confirmation of the diagnosis and follow-up imaging was performed using color Doppler echography (CDE), contrast-enhanced computed tomography (CT), and arteriography. According to standard guidelines, patients with an AAA size of 3.0-4.4 cm underwent follow-up once a year, while those with a size of 4.5-5.4 cm underwent follow-up every 3 months. Follow-up observation of the patient and recording of the results were also performed using color CDE, CT with contrast, and arteriography. The average AAA diameter was 5.8 cm in men according to CDE and 4.6 cm in women, with a statistically significant difference (p=0.05). On CT scan AAA sizes were slightly different and were 6.34 cm and 5.5 cm in men and women, respectively (p=0.05). The frequency of involvement of the underlying vessels was also analyzed, and the results are shown in Table 3.

Table 3
Prevalence of AAA and involvement of the iliac and femoral arteries

	Women	Men	Total
Femoral arteries	0 %	2.92 %	2.92 %
Iliac arteries	2.92 %	42.73 %	45.64 %
Iliac-femoral arteries	2.92 %	5.82 %	8.74 %
Without involvement arteries	0 %	0 %	38.8 %
No data	0 %	0 %	2.92 %

Source: created by the authors.

In 3.88 % of cases, there was involvement of the iliac arteries on both the right and left sides. In 2.92 % of cases, there was involvement of just the right iliac and femoral arteries. In another 3.88 % of cases, there was involvement of just the left iliac and femoral arteries. In 2.92 % of cases, there was involvement of both femoral arteries.

Characteristics of operations

The selection of the surgical intervention option for AAA was dependent on clinical features, and the recommendations of the European Society for Vascular Surgery were followed. Surgical treatment was recommended

for cases of detected or suspected aneurysm rupture, rapidly enlarging aneurysms irrespective of symptoms, aneurysms over 4.5 cm in diameter, signs of embolization, thrombosis, occlusion, and atypical aneurysm forms such as mycotic, stratifying, or circular. All these cases posed a high level of danger for the patient.

Surgery for AAA was performed using either a retroperitoneal or transabdominal approach. The transabdominal technique was performed by a median incision of the anterior abdominal wall from the xiphoid process to the symphysis, the Treitz ligament was dissected, and the retroperitoneal space was opened to the left of the aorta. If the aneurysm was infrarenal, the retroperitoneal space was dissected to expose the aorta to the level of the left renal vein, and the left renal vein was mobilized if suprarenal clamping was necessary. Distal clamping was performed below the level of the lesion. In the retroperitoneal method, the patient was laid on the right side, and access was made from the 10th intercostal space to the upper-anterior apex of the iliac bone through the lateral abdominal muscles. The left kidney was mobilized ventrally, the left ureter was visualized, and it was diverted anteriorly along with the kidney. Before aortic clamping, systemic heparin at a dose of 80–100 units/kg weight was administered, regardless of the approach. The clamping sequence was started from the distal portions of the aorta and then switched to the proximal portions to reduce the risk of distal embolization. The transabdominal route was used in 120 (58.3 %) cases, and the retroperitoneal route was used in 86 (41.7 %) cases. The use of each method depending on the clinical situation is shown in more detail in Table 4.

Anesthesia support for surgical interventions on the aorta and its branches in AAA was provided in a combined manner, including epidural anesthesia. This approach reduced the volume of narcotic analgesics used and allowed for prolonged anesthesia for several days after surgical intervention. The advantages of this approach included full protection of the patient from afferent impulses from the surgical area, adequate muscle relaxation, absence of respiratory and metabolic disorders, and reduction of surgical blood loss. The average values are shown in Table 5.

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Table 4

Distribution of patients depending on comorbidities and method of intervention

	Transabdominal procedures	Retroperitoneal procedures	Validity of the difference
Smoking	70	33	0.5
Cardiac infarction	6	12	0.05
Diabetes mellitus	8	10	0.07
Hypertension	86	40	0.05
Stenocardia	14	10	0.01
COPD	66	40	0.01
Carotid artery disease	16	8	0.02
Total	120	86	

Source: created by the authors.

Table 5

Comparative values of the mean values in both groups

	Transabdominal procedures (n=120)	Retroperitoneal procedures (n=86)	Validity of the difference
Time of operation (hours)	3.18±0.19	3.55±0.18	0.006
Intravenous analgesics (mg)	49.5±28.5	36.6±21	0.004
Epidural analgesics (mg)	56.6±9.5	39.5±6.4	0.004
Time spent in hospital (days)	11.8±2.3	7.2±1.6	0.02
Effectiveness	82.7±5.46%	85.3±4.03%	0.05

Source: created by the authors.

The maintenance of anesthesia during AAA surgeries was tailored to the specific patient, taking into account various influencing factors, including indications for the particular case, the duration of the surgical intervention, the degree of hypothermia, the level of blood loss and hemodilution, and intraoperative homeostasis results.

The choice of the optimal aortic prosthesis was based on certain requirements for its physical characteristics, including elasticity, adaptability, flexibility, ease of stitching, resistance to material separation, smooth lumen surface, and resistance to infection and thrombogenicity. It should have no toxic or allergic side effects and should be consistently available in a full range of sizes and lengths in a moderate price range. The configuration of the aortal prosthesis was dependent on the extent of the aneurysm and the

specific clinical data of the particular patient. Two types of aortic vascular prostheses were used in this study: “Dacron” – 167 (81 %) operations, and “PTFE” (polytetrafluoroethylene) – 39 (19 %) operations. No fundamental differences in the frequency or type of complications associated with the type of prosthesis used have been revealed.

The surgical procedures involved in the study included aorta-aortic lumen reconstruction in 12 cases (5.8 %), aorta-subiliac artery reconstruction in 120 cases (58.3 %), aorta-common femoral artery reconstruction in 18 cases (8.7 %), aorta-deep femoral artery reconstruction in 6 cases (2.9 %), aorta-anterior iliac artery reconstruction in 32 cases (15.5 %), aorta-both external iliac arteries reconstruction in 12 cases (5.8 %), and common iliac-external iliac artery reconstruction in 6 cases (2.9 %).

The present study utilized objective criteria derived from macroscopic CT and interventional data, as well as microscopic anatomic-pathological findings, to define aneurysms as inflammatory. The classification of inflammatory aneurysms was based on the presence of specific macroscopic features, such as thickening in the aneurysm wall, retroperitoneal fibrosis, and adhesions to neighboring organs, as well as microscopic features, including inflammatory infiltrates with plasma and lymphocytic walls, adventitial fibrosis, obliterating endarteritis, and fibrosis around nerves. These objective criteria allowed for a clear distinction between inflammatory and noninflammatory aneurysms. The inflammatory nature of AAA was observed in six patients (2.91 %) during the study, while mycotic aneurysms were encountered in two patients (0.97 %).

Characteristics of complications

Despite all the measures implemented, complications occurred during the study. Intraoperative complications were observed in 11 cases (5.3 %). Damage to the ureter occurred in 6 cases (2.6 %), requiring primary suture in 2 cases and stenting in 4 cases. Inferior vena cava damage occurred in 6 cases (2.9 %), all of which were treated with primary sutures. The duodenal injury occurred once (0.5 %) and was also sutured. These injuries were timely detected and eliminated, without affecting the further course of the operation and postoperative period in patients. Postoperative complications occurred more frequently, and their types and frequencies are presented in Table 6.

As can be seen from the table, pulmonary complications were the most common, recorded in 8 patients (8.8 %) in the retroperitoneal group and 12 patients (9.2 %) in the transabdominal group. However, this difference was not statistically significant (p=0.07). Cardiovascular complications occurred in 6 patients (13.3 %) in the retroperitoneal group compared to 10 patients (15.8 %) in the transabdominal group, with a statistically significant difference (p=0.004). Gastrointestinal complications were observed in 5 patients (5.8 %) in the retroperitoneal group compared to 15 patients (12.5 %) in

Table 6

Type and frequency of postoperative complications

	Complications
Pulmonary complications	20 (9.7%)
Cardiovascular complications	16 (7.8%)
Gastrointestinal complications	20 (9.7%)
Postoperative hernia	11 (5.3%)
Hemorrhagic complications	11 (5.3%)
Thromboembolia	11 (5.3%)
Bedsore	12 (5.8%)

Source: created by the authors.

the transabdominal group, with a statistically significant difference (p=0.002). Postoperative hernia developed in 6 patients (6.9 %) in the retroperitoneal group compared to 5 patients (4.2 %) in the transabdominal group, without a statistically significant difference (p=0.5). Hypotension and drainage bleeding were observed in 6 cases (9.5 %) in the transabdominal group and 5 cases (11.1 %) in the retroperitoneal group, without a statistically significant difference. Bedsore and wounds of the sacrum and gluteal muscles were observed in 7 patients (11.1 %) in the transabdominal group and 4 patients (8.8 %) in the retroperitoneal group, without a statistically significant difference. Acute thromboembolism of the femoral artery was observed in 6 cases (9.5 %) in the transabdominal group and 3 cases (6.6 %) in the retroperitoneal group, without a statistically significant difference. The surgery time for retroperitoneal interventions averaged 3.55 hours, while for transabdominal interventions, it was 3.18 hours, with a statistically significant difference (p=0.06).

Thirty-one repeated interventions were performed to eliminate complications: nephrectomy (1 case, 0.5 %), colostomy (6 cases, 2.9 %), catheter thrombectomy (12 cases, 5.8 %), iliofemoral arterial shunt (4 cases, 1.9 %), femoral arterial shunt (6 cases, 2.9 %), relaparotomy and abdominal revision (2 cases, 0.9 %).

The transabdominal approach requires more extensive abdominal exposure and manipulation which can increase stress on the cardiovascular system, especially in patients with pre-existing cardiac conditions. The increased surgical

trauma may lead to greater hemodynamic instability intra-operatively and a higher risk of events like myocardial ischemia or infarction postoperatively.

Gastrointestinal complications occurred more often after transabdominal procedures (12.5 % vs. 5.8 % for retroperitoneal). The transabdominal technique requires more intestinal manipulation and retraction which can disrupt bowel function after surgery, increasing the risk of ileus, nausea/vomiting, etc. Dividing the posterior peritoneum also compromises the bowel blood supply.

The transabdominal incision and opening of the peritoneum breach two additional tissue planes compared to the retroperitoneal approach. This greater surgical trauma predisposes to increased pain, ileus, infection, and other wound-related complications that may prolong recovery. The transabdominal technique has greater potential for direct injury to intra-abdominal organs like the bowel, spleen, or liver which could lead to increased complications if unrecognized or not repaired appropriately.

DISCUSSION

The present study investigated the impact of various complications on the outcomes of surgical treatment for AAA. While some complications are difficult to prevent, particularly in high-risk cases with concomitant pathology, most can be significantly reduced by improving surgical technique. In the analysis of 214 patients who underwent open planned surgical treatment for AAA between January 2012 and December 2021 (16), in-hospital mortality within 30 days was 1.9 %. Using multivariate logistic regression was identified chronic obstructive pulmonary disease (COPD) was the only predictor significantly associated with mortality ($p=0.015$).

This study found a postoperative mortality rate of 4 %, which is within the range reported in the literature for planned open treatment of AAA (1-8 %). For example, a recent large comparative analysis (7) of 67 073 surgical procedures for AAA performed between 2003 and 2019 found mortality rates ranging from 1.3 % to 8.2 %. Only 4.9 % of the 223 hospitals performing surgical procedures during this period performed ≥ 15

of them per year. The authors of the analysis observed a trend of decreasing mortality with increasing annual volume of surgery, with each additional case associated with a 0.012 % decrease in mortality ($p=0.05$). To achieve acceptable outcomes, the minimum abdominal aortic aneurysm repair volume for a specific surgical team should be between 9 and 13 operations per year (8), and at least 18 operations per year for the hospital as a whole. Vascular Surgery Services of Mother Teresa University Hospital Centre in Tirana's average annual number of surgeries is 12.1. The mortality rates for centers with a low volume of surgeries should be treated with caution since much of the variability in these results will be statistical noise rather than true differences in the quality of treatment at the center level. These findings are consistent with a similar analysis of the centralization of surgical treatment for AAA in Catalonia, Spain (17) which found a significant reduction in overall mortality after complete centralization (4.7 % versus 2.0 %, $p<0.001$), particularly for open operations (8.7 % versus 3.6 %, $p=0.005$). To achieve the best long-term outcome, open surgical treatment of ABA should be performed in centers with a high volume of aortic surgery and tailored to the individual patient (9,18).

Endovascular aneurysm repair has become a priority in vascular surgery and the main method of AAA treatment due to its ability to reduce procedure time, surgical complications, and length of hospital stay (2,6). As a result, it has significantly replaced open intervention techniques in the treatment of AAA (3,14).

While EVAR has become the predominant method for elective AAA repair, open surgical repair still plays an important role in certain circumstances. EVAR offers benefits including shorter hospital stays, lower perioperative mortality, and quicker recovery times. However, EVAR also has drawbacks such as the need for long-term surveillance, higher re-intervention rates, and inferior long-term aneurysm-related mortality compared to open repair. Open surgery may be preferred for patients with hostile neck anatomy unsuitable for EVAR, those with large or complex AAAs, or young and healthy patients expected to outlive the durability of endograft. The choice between open and endovascular repair is made based on a detailed assessment of patient

risk factors, anatomy, and life expectancy. In general, authors aim to reserve open repair for younger, low-risk surgical candidates expected to benefit from the more durable results. For older or higher-risk patients with suitable anatomy, the main default strategy is EVAR to minimize perioperative morbidity and mortality.

A retrospective cohort study (19) compared perioperative data and complications of open operations for AAA performed at Ottawa Hospital from 2014 to 2017 (n=49) and from 2005 to 2007 (n=53). The study found that the number of open AAA surgeries decreased by 61 %, anesthesia time and time in the operating room increased, and complications in anatomically similar patients increased. These results suggest a decline in the level of preparedness of the specialized institution for the open treatment of AAA and the postoperative care of such patients as a result of a decrease in the number of surgeries performed.

Treatment of recurrent AAA is usually difficult, and perioperative mortality in such cases is significantly increased compared with primary treatment (1,4,20). This study found slightly higher postoperative complication rates (15.2 %) than reported in the literature, but they did not contribute to increased mortality. The 5-year survival rates at the Vascular Surgery Service of Mother Teresa University Hospital Centre in Tirana were high, ranging from 60 % to 75 %.

The issue of mycotic abdominal aortic aneurysm (AAA) has been discussed in the literature. However, due to its rarity, there are limited studies available to establish a consensus on its treatment and management (21-23). According to the 2016 Dutch Audit of Surgical Aneurysms, 26 cases of mycotic AAA were identified, representing 0.7 % of all reported AAA cases (21). Monthly mortality among these patients was 7.7 %, with one patient dying within the first day after surgery, representing 9.1 % of cases. Re-hospitalization within a year was observed in 36.4 % of the cases. In a retrospective review of treatment for patients with an infectious nature of AAA from 2002 to 2020, open surgical procedures were performed in 66 patients with a median follow-up of 26.5 months (13-66 months). The overall in-hospital mortality was 27.9 % (23). A retrospective

analysis of case histories reported that 17 open surgeries for mycotic AAA were performed at a single tertiary vascular center from 2001 to 2018. The 1-year overall survival rate was 94.1 %, while the 3-year survival rate was 81.8 %, and the 5-year survival rate was 75.0 %. The curves of overall and recurrence-free survival showed no statistically significant differences depending on the type of intervention (22,24,25). Although the small number of patients in this study does not allow for significant statistical conclusions, it is evident that individually planned surgical treatment with adequate antibiotic therapy can achieve acceptable results in this group of patients.

Despite reliable data supporting the need for screening to prevent rupture and reduce mortality in patients with AAA, the condition continues to pose a serious risk (15,26-28). Screening is economically effective, even with an AAA prevalence as low as 0.5 % (4). However, Dansey et al. (14) analyzed the U.S. National Inpatient Sample from 2004 to 2015 and identified 46 191 patients scheduled for AAA surgery, of whom 59 % did not meet the screening criteria. Among these, 27 653 (63 %) were over 75 years old, 10 603 (24 %) were under 65 years old, and 16 103 (36 %) were women (29). The authors recommended that consideration be given to broadening the screening criteria to include individual women and a broader age range. Kapila et al. (15) recommend screening men and women aged 65-80 years and first-degree relatives, while Dansey et al. (14) recommend screening smoking men over 55 years of age and all patients with a family history of AAA.

Nayeemuddin et al. (30) reviewed imaging and management of complications from open surgical repair of AAA. They noted that while patients undergoing EVAR are routinely followed up with imaging to detect complications, those with open repair typically do not receive imaging follow-up. However, this study and others demonstrate that open repair can also lead to postoperative complications (31,32). Nayeemuddin et al. (30) highlighted how increased use of CT angiography has enabled better identification of complications after open AAA repair. Similar to their findings, this single-center study was able to characterize a range of complications through the utilization of

imaging modalities like CT and color Doppler ultrasound. Further research on larger scales can help provide more robust data on the rates of various complications following open AAA repair.

Swerdlow et al. (33) discussed the dramatic shift towards endovascular aneurysm repair (EVAR) and away from open repair over the past two decades. As they noted, EVAR has become the predominant technique for AAA treatment due to advantages like shorter hospital stays and lower perioperative mortality. The decrease in open repairs has correspondingly led to diminished technical proficiency and preparedness for managing complications (34,35), as evidenced by studies like Nayeemuddin et al. (30). However, Swerdlow et al. (33) caution against the overuse of EVAR, as younger, healthier patients may benefit more from the durability of open repair in the long run. They emphasize that open repair remains an essential treatment modality for certain patients and situations. Maintaining capabilities for both open and endovascular repair is important, as this study shows open AAA surgery still has a role despite the rise of EVAR. Individualized assessment of patient risk factors and anatomy can help determine the optimal approach (36).

Given the patient characteristics in the current study, it would be reasonable to consider the feasibility of screening those over 55 years of age. If modern surgical treatment of AAA can be performed in a safer manner, the benefits of screening and subsequent surgical intervention may be greater than traditionally thought.

CONCLUSIONS

Abdominal aortic aneurysms are more prevalent in men aged 55-75 years and account for 3 %-5 % of vascular surgery cases. This study found a delay in diagnosis after the onset of symptoms. The transabdominal surgical approach was more commonly used, but the retroperitoneal approach had lower complication rates. There was no significant difference in recurrence rates between the two techniques. For inflammatory and mycotic aneurysms, the transabdominal approach gave better outcomes. The retroperitoneal approach reduced pain

severity, complications, hospital stay, and costs. Mortality rates within 1 month and 1 year were similar for both surgical techniques.

In addition, the study has a number of limitations. Key limitations of the study include:

1. Single-center retrospective study with a relatively small sample size (n=206). The results may not be generalizable to other hospitals/regions. A multi-center study could provide more robust results.
2. Lack of a control group for comparison. Having a group of patients who received alternative treatment or no treatment would allow stronger conclusions about the impact of the surgical interventions.
3. No data on long-term survival, quality of life, or aneurysm-related mortality after hospital discharge. This information would provide valuable insights into the long-term efficacy of interventions.

Based on these findings, surgical treatment may be recommended for abdominal aortic aneurysms larger than 4.5 cm and in the presence of clinical symptoms. Observation tactics with visual monitoring every 3 or 6 months may be considered if the aneurysm is smaller than 4.5 cm and there are no clinical complaints. Any physician in the area, whether general surgeon or urologist, cardiologist or pathologist, encountering a patient over 55 years of age with arterial hypertension, diabetes mellitus, a history of smoking, and unspecified abdominal pain of indefinite or stabbing nature, should recommend an abdominal ultrasound in addition to the appropriate investigations indicated by the treatment protocol. A strategy of continuous monitoring of the patient by improving functional vital signs is advisable only in cases where the risk of lethal outcomes after and during surgery is too high. In all other cases of abdominal aortic aneurysms, surgical treatment should be strongly recommended. Finally, given the clinical benefits of using surgical treatment of asymptomatic aneurysms to reduce mortality, it is necessary to conduct an economic assessment of the feasibility of abdominal aortic aneurysms screening in the population over 55 years of age of both sexes.

REFERENCES

1. Sakalihasan N, Michel JB, Katsargyris A, Kuivaniemi H, Defraigne JO. Abdominal aortic aneurysms. *Nature Rev Dis Primers*. 2008;4:34.
2. Blackstock CD, Jackson BM. Open surgical repair of abdominal aortic aneurysms maintains a pivotal role in the endovascular era. *Semin Intervent Radiol*. 2020;37(4):346-355.
3. Witheford M, Brandsma A, Mastracci TM, Prent A. Era of endovascular aortic aneurysm repair is linked to preoperative anatomic severity and perioperative patient outcomes. *J Vasc Surg*. 2022;75(1):126-135.
4. Kessler V, Klopff J, Eilenberg W, Neumayer C, Brostjan C. AAA revisited: A comprehensive review of risk factors, management, and hallmarks of pathogenesis. *Biomedicines*. 2022;10(1):94.
5. Castro-Ferreira R, Lachat M, Schneider PA, Freitas A, Leite-Moreira A, Sampaio SM. Disparities in contemporary treatment rates of abdominal aortic aneurysms across Western countries. *Eu J Vasc Endovasc Surg*. 2019;58(2):200-205.
6. Alberga AJ, Karthaus EG, Wilschut JA, de Bruin JL, Akkersdijk GP, Geelkerken RH. Dutch Society of Vascular Surgery, Steering Committee of the Dutch Surgical Aneurysm Audit, and the Dutch Institute for Clinical Auditing. Treatment outcome trends for non-ruptured abdominal aortic aneurysms: A nationwide prospective cohort study. *Eur J Vasc Endovasc Surg*. 2022;63(2):275-283.
7. Brown CS, Montgomery JR, Kim GY, Kemp MT, Osborne NH. Reliability of hospital-level mortality in abdominal aortic aneurysm repair. *J Vasc Surg*. 2022;75(2):535-542.
8. Sharma G, Madenci AL, Wanis KN, Comment LA, Lotto CE, Shah SK. Association and interplay of surgeon and hospital volume with mortality after open abdominal aortic aneurysm repair in the modern era. *J Vasc Surg*. 2021;73(5):1593-1602.
9. Tshomba Y, Sica S, Minelli F, Ferraresi M, de Waure C, Donati T. Long-term results of complex abdominal aortic aneurysm open repair. *J Personalized Med*. 2022;12(10):1630.
10. Pratesi C, Esposito D, Apostolou D, Attisani L, Bellosta R, Benedetto F. Italian Guidelines for Vascular Surgery Collaborators – AAA Group. Guidelines on the management of abdominal aortic aneurysms: Updates from the Italian Society of Vascular and Endovascular Surgery (SICVE). *J Cardiovasc Surg*. 2022;63(3):328-352.
11. Powell JT, Wanhainen A. Analysis of the differences between the ESVS 2019 and NICE 2020 guidelines for abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2020;60(1):7-15.
12. Carnevale M.L, Koleilat I, Lipsitz EC, Friedmann P, Indes JE. Extended screening guidelines for the diagnosis of abdominal aortic aneurysm. *J Vasc Surg*. 2020;72(6):1917-1926.
13. O'Donnell TFX, Schermerhorn ML. Abdominal aortic aneurysm screening guidelines: United States Preventative Services Task Force and Society for Vascular Surgery. *J Vasc Surg*. 2020;71(5):1457-1458.
14. Dansey KD, V arkevisser RRB, Swerdlow NJ, Li C, de Guerre LEVM, Liang P. Epidemiology of endovascular and open repair for abdominal aortic aneurysms in the United States from 2004 to 2015 and implications for screening. *J Vasc Surg*. 2021;74(2):414-424.
15. Kapila V, Jetty P, Wooster D, Vucemilo V, Dubois L. Canadian Society for Vascular Surgery. Screening for abdominal aortic aneurysms in Canada: 2020 review and position statement of the Canadian Society for Vascular Surgery. *Canadian J Surg*. 2021;64(5):461-466.
16. Ibrahim A, Yordanov MD, Hasso M, Heine B, Oberhuber A. Open treatment of abdominal aortic aneurysm in the endovascular era. *J Clin Med*. 2022;11(11):3050.
17. Tripodi P, Mestres G, Riambau V. Vascular Advisory Committee – Catalan Health Service. Impact of centralisation on abdominal aortic aneurysm repair outcomes: Early experience in Catalonia. *Eur J Vasc Endovasc Surg*. 2020;60(4):531-538.
18. Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA. The Society for Vascular Surgery practices guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2-77.
19. Kinio A, Ramsay T, Jetty P, Nagpal S. Declining institutional memory of open abdominal aortic aneurysm repair. *J Vasc Surg*. 2021;73(3):889-895.
20. Park JK, Kang J, Kim YW, Kim DI, Heo SH, Gil E. Outcomes after elective open abdominal aortic aneurysm repair in octogenarians compared to younger patients in Korea. *J Korean Med Science*. 2021;36(47):e314.
21. Dang Q, Stadius van Eps RG, Wever JJ, Veger HTC. Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit, and the Dutch Institute for Clinical Auditing. Nationwide study of the treatment of mycotic abdominal aortic aneurysms comparing open and endovascular repair in The Netherlands. *J Vasc Surg*. 2020;72(2):531-540.
22. Premnath S, Zaver V, Hostalery A, Rowlands T, Quarmby J, Singh S. Mycotic abdominal aortic aneurysms – A tertiary center experience and

SURGICAL TREATMENT OF ABDOMINAL AORTIC ANEURYSMS

- formulation of a management protocol. *Ann Vasc Surg.* 2021;74:246-257.
23. Touma J, Couture T, Davaine JM, de Boissieu P, Oubaya N, Michel C. Mycotic/infective native aortic aneurysms: Results after preferential use of open surgery and arterial allografts. *Eur J Vasc Endovasc Surg.* 2022;63(3):475-483.
 24. Turgunov Y, Shakeyev K, Sharapatov Y, Lavrinenko A, Pronkin E. The Model of Acute Obstructive Pyelonephritis for Studying Bacterial Translocation of *E. coli* from Gastroenteric Tract. *Open Access Macedon J Med Sci.* 2022;10:232-235.
 25. Tamm TI, Datsenko BM, Nepomniashchii VV, Kramarenko KA, Zakharchuk AP, Mamontov IN, et al. Diagnostics and tactics of treatment in patients with acute pancreatitis complicated by jaundice syndrome. *Klin Khirurg / Ministerstvo okhorony zdorov'ia Ukraïny, Naukove tovarystvo khirurgiv Ukraïny.* 2009;(7-8):122-123.
 26. Kamilova U, Ermekbaeva A, Nuritdinov N, Khamraev A, Zakirova G. Occurrence of comorbid diseases in patients after COVID-19. *J Med Life.* 2023;16(3):447-450.
 27. Dobrovanov O, Králinský K. Sonographic screening of congenital kidney malformations in Slovakia. *Lek Obz.* 2018;67(12):426-429.
 28. Semianiv M, Sydorчук L, Fedonyuk L, Nebesna Z, Kamyshnyi O, Sydorчук A, et al. Metabolic and hormonal prognostic markers of essential arterial hypertension considering the genes polymorphism AGTR1 (rs5186) and VDR (rs2228570). *Roman J Diabet Nutrit Metabol Dis.* 2021;28(3):284-291.
 29. Sakibaev KS, Nikityuk DB, Atabaev IN, Sattarov AE, Nuruev MK. Somatotypological features of the physique of ethnic Kyrgyz women of different ages. *Asia Life Sci.* 2020;Suppl 22(2):S185-S200.
 30. Nayeemuddin M, Pherwani AD, Asquith JR. Imaging and management of complications of open surgical repair of abdominal aortic aneurysms. *Clin Radiol.* 2012;67(8):802-814.
 31. Phuangrach N, Sarakarn P. Using Multilevel Negative Binomial Modeling to Detect Active Smoking in Colorectal Cancer Screening. *Asian Pacific J Cancer Prevent.* 2023;24(8):2823-2827.
 32. Lisnyy I, Zakalska O, Dmytriiev D, Dmytriiev K, Dobrovanov O. Pre-emptive analgesia with nonsteroidal anti-inflammatory drugs randomized, double-blind placebo-controlled study. *Lek Obz.* 2021;70(5):195-202.
 33. Swerdlow NJ, Wu WW, Schermerhorn ML. Open and Endovascular Management of Aortic Aneurysms. *Circ Res.* 2019;124(4):647-661.
 34. Zyuzkov GN, Miroshnichenko LA, Polykova TY, Simanina EV. Regulation of functions of regeneration-competent cells of nerve tissue in ethanol-induced neurodegeneration by erk1/2 and p38 inhibitors. *Azerb Pharm Pharmacother J.* 2022;22(1):42-46.
 35. Imashev M, Fursov A, Imasheva B, Fursov R, Kuspaev Y, Kovalenko T, et al. Gastroduodenal bleeding and perforation in diabetic patients with metabolic syndrome (The results of a 15-year observation of city residents with intensive urbanization). *Iran J Publ Health.* 2019;48(10):1786-1793.
 36. Arapbaevna KZ, Ardak A, Abzhanovna AG, Bahitkerevna DA, Uringalievna BA, Izbasarovna KE, et al. Modern diagnostic approaches for early detection of antiphospholipid syndrome. *Arch Venez Farmacol Therapeut.* 2021;40(2):178-186.

Immediate Results of Orthotopic Intracorporeal Ileoneocystoplasty in the Modification of the Clinic

Resultados Inmediatos de la Ileoneocistoplastia Intracorpórea Ortotópica en la Modificación de la Clínica

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SUMMARY

Relevance: Bladder cancer remains an urgent problem in the field of oncological urology, which requires great attention and additional clinical trials. Based on information from the World Health Organization, bladder cancer ranks 10th in the overall prevalence of all cancer pathologies worldwide in 2022 with an upward trend. **Objective:** This study aimed to evaluate the improved reconstructive stage of radical cystectomy for neocyst formation in patients with muscle-invasive bladder cancer. **Results:** A study involving 9 patients undergoing orthotopic ileoneocystoplasty revealed that all maintained normal urinary function. The procedure showed promise in mitigating its radical nature through positive changes, aided by advanced suture techniques that reduced surgical duration and minimized tissue traumatism and scarring. Additionally, its adaptability to various Radical Cystectomy approaches suggests its potential as a versatile option in urological surgery.

Conclusion: During the postoperative observation in patients, authors noted the absence of problems with self-controlled urination, violations of the tightness of the vesicourethral anastomosis, or metabolic changes due to the removal of the ileum part of the small intestine. In all cases, the neocyst functioned normally and the patients had no complaints about the radical nature of this method of surgery.

Keywords: Muscle-invasive bladder cancer, neobladder, radical cystectomy, neovesica, urinary diversion.

RESUMEN

Relevancia: El cáncer de vejiga sigue siendo un problema urgente en el campo de la urología oncológica, que requiere gran atención y ensayos clínicos adicionales. Según datos de la Organización Mundial de la Salud, en 2022 el cáncer de vejiga ocupará el 10º lugar en la prevalencia global de todas las patologías oncológicas a nivel mundial, con una tendencia al alza. **Objetivo:** Este estudio tuvo como objetivo evaluar la etapa reconstructiva mejorada de la cistectomía radical para la formación de neoquistes en pacientes con cáncer de vejiga músculo-invasivo.

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Resultados: *El estudio que incluyó a 9 pacientes sometidos a ileoneocistoplastia ortotópica reveló que todos mantuvieron una función urinaria normal. El procedimiento resultó prometedor al mitigar su naturaleza radical mediante cambios positivos, ayudado por técnicas de sutura avanzadas que redujeron la duración quirúrgica y minimizaron el traumatismo tisular y la cicatrización. Además, su adaptabilidad a diversos abordajes de cistectomía radical sugiere su potencial como opción versátil en cirugía urológica.* **Conclusiones:** *Durante la observación postoperatoria de los pacientes, los autores observaron la ausencia de problemas con la micción autocontrolada, violaciones de la estanqueidad de la anastomosis vesico-uretral o cambios metabólicos debidos a la extirpación de la parte del íleon del intestino delgado. En todos los casos, el neoquiste funcionaba con normalidad y los pacientes no tenían quejas sobre el carácter radical de este método de cirugía.*

Palabras clave: *Cáncer de vejiga músculo-invasivo, neovejiga, cistectomía radical, neovesica, derivación urinaria.*

INTRODUCTION

The statistics show that about one-third of 600 thousand already diagnosed cases of bladder cancer (BC) will be fatal. Diagnostic problems often arise on the way to successful treatment of this disease because the main diagnostic method is cystoscopy, which is an invasive and expensive procedure. Most cases of BC are diagnosed in the early stages, but about 25 % are detected already in the period of muscle-invasive BC (MIBC), which significantly reduces the chances of patients' recovery (1). At the initial stages of oncogenesis, the cancer cells do not affect the muscle layer of the bladder and this stage, called muscle non-invasive BC (MNBC), has the best prospects for recovery. With the progression of MNBC, the cancer cells reach the muscle membrane and according to morphological features, this stage is classified as MIBC. In cases of MIBC, radical cystectomy (RCE) is widely used, in which the bladder is completely taken out and the urostoma is removed. Studer et al. (2) developed the method of forming a neocyst, an artificial orthotopic bladder, built from the small intestine and directly connected to the urethra, which made a notable discovery in the field of urology. However, a

significant drawback of this intervention was the difficulty in bringing the left ureter under the sigmoid mesentery to create a ureteral-enteric anastomosis. The intracorporeal technique was carried out in 2011 at the Carolina University headed by surgeon Jonsson et al. (3). The main adaptation to the "traditional" ileoneocystoplasty was in conducting the ileourethral anastomosis as the first step of reconstruction, which helped to create a tight anastomosis without tension.

Improving the quality of life of MIBC patients remains an urgent problem. The RCE involves the absolute removal of the bladder together with the organs and lymph nodes located nearby. An uncommon method of orthotopic ileoneocystoplasty is a modified robot-assisted U-shaped neobladder, which was developed to facilitate the creation of a cystourethral anastomosis in extracorporeal reconstruction, first performed by Hu et al. (4). When using a Y-shaped ileal orthotopic artificial bladder after previous pelvic exenteration performed by Martínez-Gómez et al. (5), there were also cases of frequent urinary incontinence, especially at night, which is a typical problem after neocyst creation during RCE. If the authors talk about the complications of RCE, it is worth mentioning the occurrence of such a rare pathology as the formation of ileal neobladder fistulas (ileal fistula), which requires fistulectomy, partial ileostomy and creation of ileal "end to end" anastomosis. Lu et al. (6) conducted research on this complication in 2022. This phenomenon usually occurs a long time after orthotopic neocystoplasty and undergoes effective treatment by surgical intervention methods.

Currently, the "golden standard" for creating an orthotopic artificial bladder is the use of ileal segments, but sigmoid segments are less commonly used. In 2019, El-Helaly et al. (7) investigated in detail the differences in postoperative periods after neocystoplasty with two different segments of the small intestine: ileal and sigmoid. In general, there was no fundamental difference in the intraoperative and postoperative period in ileal or sigmoid neobladder, the complications occurred with the same frequency in both groups with no significant variations in urination. The only difference was the lower frequency of nocturnal urination in patients with ileocyst than in patients

who underwent sigmoid neocystoplasty. This observation favours ileoneocystoplasty as the most optimal type of urine derivation with further improvement in the living conditions of an MIBC patient. The main reason for this choice is the absence of urostomas, which significantly worsens the psycho-emotional state and life quality of the patient as it necessitates constant care and treatment.

The purpose of this study was to evaluate the effectiveness of MIBC treatment notably by creating an artificial reservoir for urine derivation from small intestine segments of the patients and to study urination and other urinary system functions in the postoperative period. In addition, due to the formation of the neobladder in the usual place and its binding to the functionally healthy external bladder sphincter, the patient can perform self-controlled urination, which is a positive aspect after RCE.

MATERIALS AND METHODS

Nine patients with MIBC in the clinical stage T2aN0M0-T3bN0M0 were eligible for the study based on the Academician Vozianov Institute of Urology of the National Academy of Medical Sciences of Ukraine. All patients were males, aged 45 to 85 years, examined in the medical institution during 2019-2020. All subjects underwent cystectomy and lymphadenectomy by laparoscopy, but one-third of patients underwent open bladder resection in other hospitals. Two patients were subject to intracorporeal ileoneocystoplasty and six received a change of access from the midline laparotomy. All operations were carried out in the Trendelenburg position using combined peridural intravenous anesthesia with endotracheal intubation. First, the surgeons removed the bladder and then proceeded to the resection of regional lymph nodes and prostate gland along with seminal vesicles. Next, an ileal segment approximately 50 cm long was isolated and brought to the pelvic cavity, with subsequent restoration of the small intestine integrity. The first step in creating the neocyst was to mark two inflection points 15 cm from the opposite ends of the segment with betadine solution (Figure 1), marked 4 and 5 respectively.

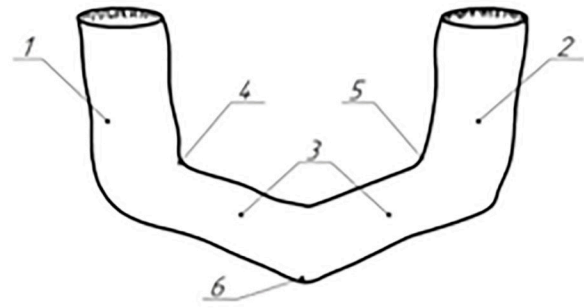


Figure 1. Isolation of the ileal segment.

Note: 1 – right segment; 2 – left segment; 3 – middle segment; 4 – the first inflection point; 5 – the second inflection point; 6 – the sagging point. Source: Vozianov et al. (8).

The ligature holders (suture material Vicryl 4/0) were applied to two defined points and the nondetubularized ends of the ileum graft were transferred to the vertical position (Figure 1 – 1, 2). The same betadine solution was used to dot the area of sagging in the projection of the middle ileal segment (Figure 1 – 6). The next step was to give a spherical shape of the bladder to the two isolated parts of the ileal segment along the counter-mesenteric edge, while the central part was placed asymmetrically, having previously made a 5 cm long midline incision 0.7-0.8 cm from the duplicate peritoneum. From the middle segment, the authors moved back to the counter mesenteric edge, and an integral intestinal lamina was formed (Figure 2) due to this manipulation, which had a cervical strip (Figures 1 – 6).

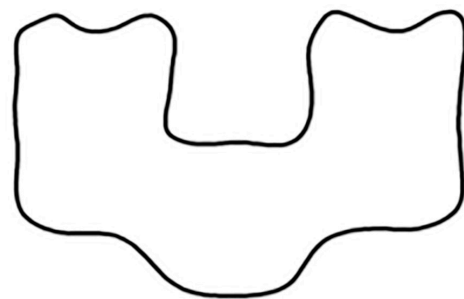


Figure 2. Detubularization of the ileal segment. Source: Vozianov et al. (8).

Using the *Hendo-60-3,0A* stapler or continuous suture *V-Lock 2/0* the median edges of the two segments were connected to the upper edge of the central part of the graft (Figure 3 – 3).

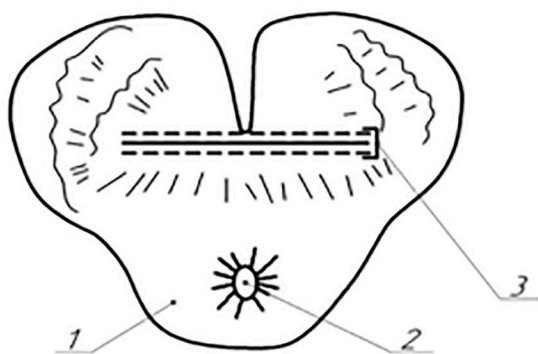


Figure 3. Formation of the bladder neck.
 Note: 1 – cervical flap; 2 – hole in the projection of the sag point (tank neck hole); 3 – the line of fixation of the medial edge of the right and left segments to the upper edge of the middle segment. Source: Vozianov et al. (8).

An opening with a diameter of 0.6-0.8 cm was formed in the marked area of the sagged neobladder (Figure 3 – 2). With the same mechanism, the authors joined the upper thirds of the lateral margin of two ileal segments using intestinal suture *V-Lock 2/0* or stapler *Hendo-60-3,0A*, forming the aboral and adoral intestinal openings. The diameter of the neocyst neck orifice was increased to 1.0-1.5 cm and a Foley genitourinary catheter (Ch 26-30) was inserted into the created hole, formed hemispheres were turned outward and tubularized on the catheter tube, making 3-5 knot sutures *Vicryl 5/0* on the front and rear surfaces. The neobladder neck was duplicated with two nodular mucosal-muscular sutures *Vicryl 3/0*, superimposed in parallel to its axis (Figure 4 - 1).

The formed neobladder neck and the membranous part of the urethra were sutured with six knotted sutures *Vicryl 2/0*, forming a vesicourethral anastomosis (Figure 4 – 2). When performing this manoeuvre, the front edge of the strip (Figure 4 – 3) was shifted in caudo-ventral direction during cervical suturing and in cranio-dorsal direction during urethral ligature suturing (Figure 4 – 2 and Figure 4). The ureters on the posterolateral plane of the neobladder underwent anastomosis with suture material *Vicryl 4/0* (Figure 5 – 1, 2).

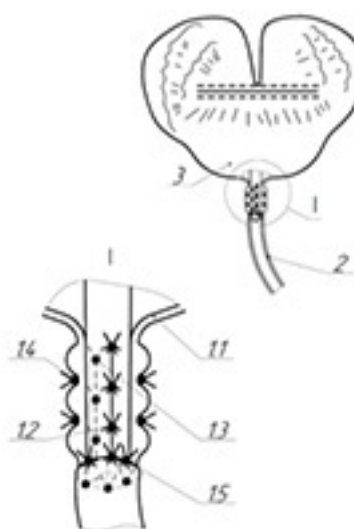


Figure 4. Duplication of the bladder neck.
 Note: 1 – vesico-urethral segment (the outlined fragment includes the reconstructed bladder neck and vesico-urethral anastomosis); 2 – posterior urethra; 3 – cervical flap; 1.1 – bladder neck; 1.2 – front tubular seams; 1.3 – rear tubularizing seams; 1.4 – side duplication seams; 1.5 – vesicourethral anastomosis. Source: Vozianov et al. (8).

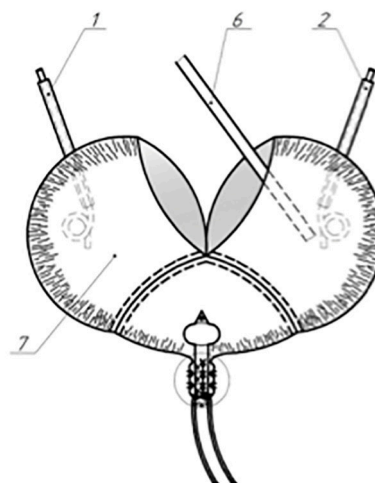


Figure 5. Formation of uretero-neovesica anastomosis.
 Note: 1 – right ureter (drained); 2 – left ureter (drained); 3 – intestinal reservoir; 4 – reconstructed vesico-urethral segment; 5 – membranous urethra (catheterized). Source: Vozianov et al. (8).

The unadhered edge of the cervical strip and the neck of the reservoir itself are connected with the lower thirds of the lateral side of two ileum grafts, and the pre-formed intestinal openings are sealed with an intestinal stapler *Hendo-60-3,5A* or a continuous suture *V-Lock 2/0*. It is also important to insert a cystostomy drain Ch 22-24 into the aboral opening before the sealing stage (Figure 5 – 6). The final stage of ileoneocystoplasty is the closure of the visceral peritoneum defect of the anterior surface area of the neocyst, where the sutures of the ileal segments are located, followed by the installation of pelvic drains (Figure 6).

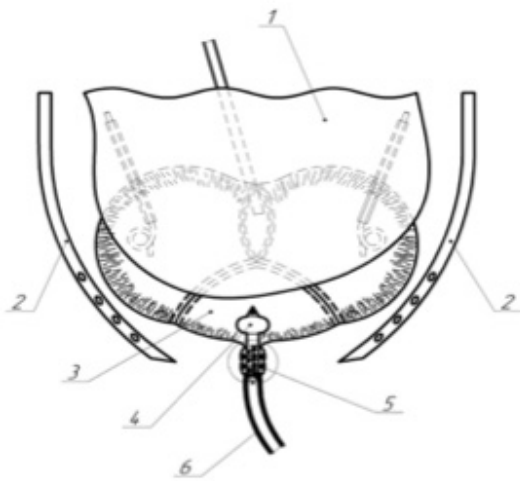


Figure 6. Peritonization and installation of pelvic drains. Note: 1 – peritoneum (after the reversible peritonosis maneuver); 2 – pelvic drains; 3 – urethral catheter balloon; 4 – intestinal bladder; 5 – reconstructed vesico-urethral segment (the outlined fragment includes the reconstructed bladder neck and vesico-urethral anastomosis); 6 – urethra (catheterized). Source: Vozianov et al. (8).

The example for this study was orthotopic artificial ileoneocystoplasty carried out by Studer et al. (2), which was described in his work in 1989. However, the development of modern medicine helps to reduce traumatism from surgical interventions, using minimally invasive methods and improving the quality of life of the patients, involving new approaches of creating artificial reservoirs for urine derivation.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. A study was approved by the National Academy of Medical Sciences of Ukraine.

RESULTS

To form and compare the findings of the study based on the postoperative period, all patients were divided into two groups: the patients who underwent bladder reconstruction by standard open surgical access and the patients who underwent intracorporeal ileoneocystoplasty using the laparoscopic method. The first group included seven patients, and the second group had two (Table 1).

Key eligibility criteria for surgery included preoperative transurethral biopsy and screening. These assessments histologically confirmed the invasion of tumor cells into the bladder's muscle layer, demonstrating malignancy with high specificity and sensitivity. This confirmation served as the primary indication for orthotopic ileoneocystoplasty. It is also worth mentioning that now there are techniques for conducting RCE, in which men retain the prostate, but only if the cancer process has not damaged its anatomical structures. The controversy surrounding this topic stems from the fact that it has both benefits and risks. On one hand, it raises the risk of cancer recurrence in the urethra. On the other hand, it enhances patients' quality of life by not causing erectile dysfunction and facilitating postoperative recovery and social adaptation.

To assess the quality and benefits of the artificial bladder method, authors evaluated the following indicators: neobladder volume, the act of urination, its frequency per day and cases of urinary incontinence, the presence or absence of narrowing of the vesicourethral anastomosis, as well as its impermeability. At the same time, the neocyst volume was initially determined directly during the surgery, and then the final measurements were made after 6 months to compare with the initial value. For

IMMEDIATE RESULTS OF ORTHOTOPIC INTRACORPOREAL ILEONEOCYSTOPLASTY

Table 1
Comparison of ileoneocystoplasty results in the postoperative period (p<0.05)*

Indicators	Open RCE	Laparoscopic RCE
The volume of the artificial bladder, mL:		
– intraoperatively	180 ± 23	160 ± 50
– in 6 months	420 ± 68	380 ± 50
Postoperative period in a medical institution, days	14.2 ± 4.2	7.2 ± 1.5
Time of urine derivation stage, h	1.5 ± 0.5	2.5 ± 0.5
The process of urination	Preserved	Preserved
Tightness of vesico-urethral anastomosis	Tightness is preserved	Tightness is preserved
Stenosis of vesico-urethral anastomosis	Not applicable	Not applicable
Stress urinary incontinence	1/7 in the daytime and at night	2/2 at night

Note: * – the difference between two groups is relative.

Source: S.O. Vozianov et al. (8).

example, in the group of patients who underwent an open cystectomy, the volume of the artificial reservoir was on average 180 mL with a possible error of 23 mL, and six months later its volume increased by 240 mL, amounting to 420 mL with an error of 68 mL. In patients who underwent RCE by laparoscopic method, the volume of the neobladder during surgery was 160 mL, and after 6 months, it increased by 220 mL, and in both cases, the difference was ±50 mL. In summary, the second group of patients had a significantly shorter hospital stay after surgery compared to the first group. However, the patients who underwent ileoneocystoplasty through open surgical access experienced a longer recovery period with a higher risk of complications. In general, the period of rehabilitation after RCE and ileoneocystoplasty was much longer in patients who underwent a full incision to access the abdominal cavity than in patients who were subject to minimally invasive surgical techniques that provided minimal trauma and intervention in the body. In addition, the emergence of new innovative methods of creating surgical sutures such as intestinal sutures and sutures with a surgical stapler can significantly reduce the time of surgical intervention.

It is advisable to clarify that two patients had previously undergone open bladder resection in other hospitals, which could also affect the recovery rates in the postoperative phase. After ileoneocystoplasty, all patients

were subject to periodical monitoring to detect timely postoperative complications or other abnormalities that could be associated with the intervention. The investigators reported self-controlled urination in both groups, which is the main goal in the search for new methods of bladder reconstruction in people suffering from MIBC. The kidneys also showed no accumulation of urine, which could be evidenced by the dilation of the collecting tubes, renal cups, and pelvis (hydronephrosis). The impermeability of the vesicourethral anastomosis was intact with no constriction detected in further examinations. This can be explainable by the addition of standard ileoneocystoplasty with a new method of forming the neck of the artificial “neovesica” bladder, which eliminates the possibility of tension of the vesico-urethral anastomosis. This disadvantage of ileoneocystoplasty in Studer’s surgery was the impetus for scientists to conduct clinical studies to find a solution to this complication. The main reasons for the tension of the vesicourethral anastomosis are short mesentery of the intestine, insufficient length of the membranous part of the urethra, and adhesions of the small intestine and pelvis due to previous surgical interventions when in such cases it is possible to form an anastomosis in a more bent position. Shortening of the membranous part of the urethra in men occurs due to enlargement of the prostate gland, which is removed during RCE, or it may be due to congenital anatomical features that are not

considered pathology. In these complications, the tightness of the vesicourethral anastomosis may be compromised, which subsequently leads to its stenosis, and, as a result, urination disorders. To reduce the probability of tension of the vesicourethral anastomosis, it is necessary to choose the ileal segment with the largest number of mesenteries (2).

When using the laparoscopic method during the formation of the urethra-ileal anastomosis, there are several difficulties: insufficient visualization, occurring with open surgical access, and the possibility of mesentery tension or anastomosis caused by the artificial bladder passing to the free end of the urethra without the help of hands. In addition, when evaluating the data on stress urinary incontinence, the authors noted that in the group that underwent laparoscopic RCE, both patients had incontinence at night. In the first group, this disorder was observed only in one patient but both during the day and at night. Urinary incontinence at night is associated with the fact that the pressure inside the urethra decreases, and the pressure in the neobladder begins to exceed the resistance capability of the urethral sphincter. This can be explainable by a violation of the vesicoureteral reflux, which in healthy people is responsible for increasing the tone of the urethral constrictor muscle. In general, problems with urination in patients with the removed bladder are explainable by the fact that RCE violates the integrity of the reflex arc and the very morphology of the genitourinary system, which are responsible for the act of urination. In addition, nocturia can be associated with a decrease in neocyst volume, compared to a healthy bladder, where the volume can reach 750 mL.

The metabolic acidosis caused by an extremely large ileal segment (up to 65 cm) removed from the small intestine is also considered a possible complication after artificial orthotopic ileoneocystoplasty. This resulted from metabolic changes that can further lead to renal failure, but in the early and late postoperative periods, these changes did not show in any of the patients. Therefore, an urgent problem for the field of oncological urology is also the search for options to reduce the length of the ileum graft to lower or eliminate the likelihood of metabolic changes in the gastrointestinal tract. However, the reduction

of the segment used for the artificial reservoir can lead to a decrease in the neocyst volume and the creation of subsequent problems with urinary retention and prolonged act of urination. In both groups of patients, this complication did not take place, which is also a positive side of the conducted intracorporeal ileoneocystoplasty.

When conducting cyst prostatectomy in men, it is possible to combine it with nerve-preserving techniques, which helps to preserve erectile function in patients to whom RCE is indicated. This positively contributes to the psychological and emotional aspects of recovery and partially eliminates the negative side of the radical nature of this surgical intervention. The patients also underwent RCE, which involves the removal of regional groups of lymph nodes. The lymph dissection can significantly increase the overall duration of surgery. However, the lack of convincing clinical trials complicates the debate about the need for lymph node resection in RCE.

When performing ileoneocystoplasty, the main problem could be the peristalsis of the ileum graft, but the crossing of the antimesenteric facet and cross-connection of the ends of the ileal segment can compensate for this, as explained in the method of Goodwin et al. (9). The main improvement and modification to standard methods of ileoneocystoplasty was the use of a new "neovesica" technology in the reconstructive stage during the formation of the neck of the urinary neobladder, associated with the elimination of tension of the vesico-urethral anastomosis.

The method of creating an artificial bladder generally helps to preserve the process of natural and most importantly controlled urination, owing to the preservation of the urinary tract structure, and the absence of artificial urine receivers and drain devices. In addition, the technique of ileoneocystoplasty is quite simple and clear in the course of work. However, along with the obvious advantages of this surgical intervention, there are also several contraindications, which include the widespread dissemination of oncological process, the proliferation of cancer cells of the bladder neck in female patients, and the urethra in men, impaired renal function, impaired gastrointestinal tract, and disorder of functional capacity of the external urethral opening and its permeability.

DISCUSSION

There are many approaches to urine derivation used after RCE. Here are the major ones: the imposition of direct ureteral anastomoses, which leads to urine diversion to the intestine, the formation of ileal conduit with the withdrawal of a “wet stoma” and the withdrawal of a “dry stoma” in the formation of artificial urine reservoirs from the detubularized parts of the small intestine. However, the most common option adopted in ileoneocystoplasty is the creation of an artificial orthotopic bladder.

As noted in the previous sections, the main complication in the creation of an artificial bladder is the tension of the vesicourethral anastomosis with the possibility of its tension in the subsequent postoperative period. The research took place to improve the technique “*non-hole*”, used in the creation of urethral anastomosis. The essence of this improvement is that the caudal part of the intestinal lamina is anastomosed directly to the urethra with wrapping sutures before attaching the ureters to the artificial reservoir. It starts from 6 o'clock and continues clockwise to 12 o'clock, the next stitch also starts from the previous place but with a change of direction counterclockwise. In this study, the surgeons used a special needle holder with a remote end bent at an angle of 120 degrees. The absence of serious complications in the postoperative period generally favors this modification, but this technique requires further clinical studies to form more accurate and reasonable conclusions (10). In addition, it will be advisable to apply two sutures between the neobladder and the pelvic floor on the side of the anastomosis itself to reduce the tension in the vesicourethral anastomosis, as described in the standard technique of ileoneocystoplasty according to Pavlović et al. (11). Some scientists talk about the need to preserve the neurovascular bundle for further urination without striking deviations. Boccafoschi et al. (12) described the role of preservation of the neurovascular bundle in the further process of urination of patients after RCE and the creation of an artificial reservoir in detail in 1993.

In the present study, all patients had preserved the functional capacity of the urethral sphincter, but there are also cases of urinary incontinence

of neurogenic origin. These conditions allow the use of artificial urethral sphincters, applied to the bulbous part of the urethra. The only disadvantage is the possibility of damage to the urinary tract or bladder, which can further lead to infectious diseases of the excretory system, necrosis, and the return of urinary incontinence (13). In this case, there is an urgent need for repeated surgical intervention, which entails negative consequences in the recovery period. However, the study of the technology of implantation of artificial urethral sphincters is insufficient, which makes widespread use of this method impossible, not to mention a wide range of postoperative complications and side effects, confirmed during clinical trials by Si-Chiang et al. (14) and Chung (15), who studied modern surgical devices for stress urinary incontinence.

A rather interesting method of creating an ileobladder is its orthotopic spiral modelling with urethral re-implantation was described in the scientific article by Zhong et al. (16). In achieving this at the design stage, the graft was connected “spirally” and then the surgeon performed anastomosis of the urethra, which was previously “turned outward”, holding the artificial reservoir with the help of a urinary stent, using the technique of reflux-free papilla with a disconnected cuff and applying absorbable surgical material to create a suture. After performing this method of ileoneocystoplasty in selected patients, the specialists observed that the functional results in the long-term postoperative period are satisfactory, but the immediate complications after surgery are difficult to control. Quite a positive aspect of this study was also the fact that the scientists were able to significantly reduce the length of the ileum graft (up to 40-45 cm), which eliminates the risk of metabolic acidosis among the possible complications (17).

Miki et al. (18) also conducted a study aimed at stabilizing the neobladder, as well as avoiding the tension of the anastomosis by the method of temporary tension of the anastomosis site itself. For this purpose, patients were divided into two groups: one part of the patients underwent vesicourethral anastomosis intracorporeally with 4 knotted sutures and the second part underwent modified manipulation of anastomosis formation. A loop suture was made at 5 o'clock in the bladder neck and then

the reservoir was transferred to the pelvic cavity. The Foley urinary catheter was inserted through the urethra and the last loop of suture was fixed to its end, and the neocyst was placed closer to the urethra, by excessively tensioning the Foley catheter, and the bladder neck was moved to a stable position (19). This tension particularly makes it easier for surgeons to find the neck of the neobladder, and the loop suture keeps the necessary tension during the formation of the vesicourethral anastomosis, later removed at the end of neocystoplasty. When using the described modification, there is a significant reduction in the required time of surgery and the absence of severe complications after the intervention, but these changes have not been popularized in urology due to the lack of clinical studies. From January 2014 to December 2018, on the premises of Nanchang University, Yu et al. (20) conducted a study to compare the performance of the vesicourethral anastomosis laparoscopically and the performance of the same anastomosis, but with tension and ligation and using only one Foley catheter. In conclusion, vesicourethral anastomosis with tension and ligation offers several advantages. It's easier for surgeons to learn, more practical, and more convenient, and it also significantly reduces surgical intervention time compared to the laparoscopic approach.

Urinary incontinence can also be associated with a reduction in the length of the urethra, which leads to changes in its normal functioning (21). It is also worth mentioning that urine detention can be affected when the perineum is lowered down during orthotopic neo-cystoplasty because the anterior part of the sacroiliac ligaments supporting its fixed position is cut (22-24). Authors believe that it is necessary to create a "secondary sphincter", stitching the middle part of the rectal elevator muscle in addition to the edges of the anastomosis to correct this defect. At the same time, the urethra maintains a good position in the abdominal cavity, preventing tension of the anastomosis. Boccafoschi et al. (12) described a "secondary sphincter" technique and all indications and contraindications in a detailed study. The authors emphasize that damage to the spongy part of the urethra should be avoided during this manipulation because it can come out of the pelvic floor, which will lead to a violation of its blood supply.

In Germany, Horstmann et al. (25) conducted a study in which they compared two anastomosis methods using robot assisted RCE with neocystoplasty in detail. In the first method, they used 6-knot sutures, and the second method was similar to this study with the formation of vesicourethral anastomosis using a vicryl suture. In the same way, a continuous suture is started at the 6 o'clock mark and, the formed artificial reservoir and urethra are sutured in the clockwise direction to the 12 o'clock mark, and then the second hemisphere of the vesicourethral anastomosis is created in the counter-clockwise direction. After comparing these two techniques, the surgeons found no striking differences between them, and the postoperative period was favorable in both groups of patients. Koie et al. (26) studied the positive outcomes of automated RCE with intracorporeal cystoplasty. They found that automating the reconstruction process had several benefits, including reduced fluid loss, reduced blood loss, and faster recovery of small intestine function. Similarly, Albisinni et al. (27), conducted a systematic review and concluded that robot-assisted RCE with ileoneocystoplasty offers the typical advantages of minimally invasive surgery. They suggested that this method of surgery is not inferior to open surgical access.

Mineo Bianchi et al. (28) proposed a method of muscular-fascial reconstruction when performing the vesicourethral anastomosis. A study examined 42 clinical cases of patients with BC who had previously undergone robot-assisted RCE and intracorporeal ileoneocystoplasty. Afterwards, these patients underwent recto-prostatic fascia reconstruction using a spiked suture in two directions. After analysing data on daytime and nighttime urination at 3-, 6-, and 12-months post-surgery, researchers found that urinary retention improved significantly. Notably, this improvement was more pronounced in younger patients (29,30).

There is also a way to create a vesicourethral anastomosis with the CAPIO device, which automatically sews the urethra with a neobladder, studied by Badawy et al. (31). The patients who underwent RCE with neocystoplasty were also divided into two groups but without significant differences in any parameters. Some patients were sutured using the standard method,

while others received sutures using the CAPIO suture device. In the first group, creating the anastomosis took nearly ten minutes longer than in the second group, significantly extending the overall surgical procedure. Moreover, the second group experienced significantly less blood loss. When comparing the postoperative period, the researchers noted fewer cases of uncontrolled urination in the group that underwent anastomosis with the apparatus compared to the group with the traditional suturing technique. Therefore, this device directly affects the anastomosis by preventing scarring in the area of the anastomosis, which can spread to the urethral sphincter, disrupting the process of its closure (32-36).

When studying the scheme of “traditional” ileoneocystoplasty, introduced by Hamada et al. (37), it can be also noticed that they used only an instrumental method of intestinal margins matching, which can be justified by insufficiently developed surgical instruments at that time. During the period of the introduction of new technologies, it will be more expedient to use less traumatic methods of surgical stapling (e.g., intestinal staplers) and reduce the invasiveness of the operation, compensated by robot-assisted and laparoscopic operations (38-41).

CONCLUSIONS

After a detailed study of all clinical cases of 9 patients who underwent orthotopic ileoneocystoplasty, it can be concluded that the function of the urinary system was preserved in all patients and a number of improvements and changes compensated the radical nature of the surgery during the operation. Due to the use of the latest techniques of intestinal suture formation, namely intestinal suture *V-Lock 2/0* or joining tissues with an intestinal stapler *Hendo-60-3,0A*, the overall duration of the surgical intervention is significantly reduced, as well as traumatism and subsequent scarring of tissues, as is the case with standard suturing methods. In addition, this method of orthotopic ileoneocystoplasty helps to reduce its technology to a single component when using different approaches in the performance of RCE. Using the “neovesica” method for a vesicourethral anastomosis reduces the risk of tension and, therefore, lowers the chances of long-

term issues like night-time urinary incontinence or urinary control problems.

Notably, this aspect in the postoperative period improves the overall physical and psycho-emotional well-being of patients, contributing to faster recovery and recovery after RCE. In addition, a significant reduction in the length of the ileal intestinal segment (up to 50 cm), which is removed to create an artificial bladder reduces the risk of metabolic complications associated with disorders of the small intestine, which can lead to metabolic acidosis in patients. Intracorporeal orthotopic ileoneocystoplasty has its advantages, but its adoption is limited due to the lack of minimally invasive equipment and its high cost. As a result, classical ileoneocystoplasty with open surgical access is more commonly used. In summary, further clinical studies with a larger patient sample are required to draw definitive conclusions. Additionally, there is a need for advancements in orthotopic bladder surgery techniques to minimize post-operative complications and adverse outcomes commonly observed in patients undergoing this procedure.

REFERENCES

1. Bladder cancer. 2022. <https://www.iarc.who.int/cancer-type/bladder-cancer/>.
2. Studer UE, Ackermann D, Casanova GA, Zingg EJ. Three years' experience with an ileal low-pressure bladder substitute. *Br J Urol.* 1989;63:43-52.
3. Jonsson MN, Adding LC, Hosseini A, Schumacher MC, Volz D, Nilsson A, et al. Robot-assisted radical cystectomy with intracorporeal urinary diversion in patients with transitional cell carcinoma of the bladder. *Eur Uro.* 2011;60(5):1066-1073.
4. Hu SW, Wu CC, Chen KC, Ho CH. 2019. Modified U-Shaped ileal neobladder designed for facilitating neobladder-urethral anastomosis in extracorporeal reconstruction after robotic-assisted radical cystectomy. *J Cancer Res Ther.* 2019;15:51-55.
5. Martínez-Gómez C, Angeles MA, Migliorelli F, Martínez A, Bernard M, Ferron G. Creation of a Y-shaped ileal orthotopic neobladder after an anterior pelvic exenteration in 10 logical steps. *In J Gynecol Cancer.* 2020;30(1):152-153.
6. Lu D, Wu Y, Liao S, Xie X, Zhu D, Ye Sh. Delayed ileal neobladder fistula caused by bladder stones: A case report. *BMS Urol.* 2022;22:87.

7. El-Helaly HA, Saifelnasr MK, Mohamed KM, Abdelaziz AS, Youssef HA. Outcome of orthotopic sigmoid versus ileal neobladder reconstruction. *Urol Ann.* 2019;11(2):204-210.
8. Vozianov SO, Shamraev SM, Leonenko AM, Vasileva VD, Shamraeva DM, Ridchenko MA, et al. Immediate results of orthotopic intracorporeal ileoneocystoplasty. *Urol.* 2021;25(3):203-209.
9. Goodwin WE, Winter CC, Barker WF. "Cup-patch" technique of ileocystoplasty for bladder enlargement or partial substitution. *J Urol.* 2002;168(2):667-670.
10. Hou GL, Li YH, Zhang ZL, Xiong YH, Chen XF, Yao K, et al. A modified technique for neourethral anastomosis in orthotopic neobladder reconstruction. *Urol.* 2009;74(5):1145-1149.
11. Pavlović K, Hrkać A, Kožul IS, Zalihić D, Zalihić A, Gilja I. Long-term results of augmentation ileocystoplasty in spinal cord injury patients. *Cent European J Urol.* 2021;74(2):178-184.
12. Boccafoschi C, Annoscia S, Lozzi C, Signorello D. Vesico-urethral and entero-urethral anastomosis: Anatomic-surgical considerations and technical note. *Arch Ital Urol Androl.* 1993;65(5):563-569.
13. Palleschi G, Cardi A, Falsaperla M. Urodynamic assessment of orthotopic urinary diversions. *Front Urol.* 2022;2:885826.
14. Si-Chiang V, Ginsberg DA, Teruya KK, Boyd SD. Outcomes of artificial urinary sphincter placement in men after radical cystectomy and orthotopic urinary diversions for the treatment of stress urinary incontinence: The University of Southern California experience. *Urol.* 2012;79(6):1397-1401.
15. Chung E. Contemporary surgical devices for male stress urinary incontinence: A review of technological advances in current continence surgery. *Transl Andrology Urol.* 2017;6(2):112-121.
16. Zhong H, Shen Y, Yao Z, Chen X, Gao J, Xiang A, et al. Long-term outcome of spiral ileal neobladder with orthotopic ureteral reimplantation. *In Urol Nephrol.* 2020;52(1):41-49.
17. Wang L, Hussein AA, Guru K, Li Q. Robotic ileal ureter with bladder augmentation in a modified Studer fashion for a long ureteral stricture and small bladder. *Urol Video J.* 2022;16:100182.
18. Miki J, Yanagisawa T, Tsuzuki S, Kimura T, Kishimoto K, Egawa S. 2017. Improved technique for intracorporeal neobladder-urethral anastomosis in laparoscopic radical cystectomy. *In J Urol.* 2017;4(4):330-331.
19. Reifsnnyder JE, Hanna MK. Advances in bladder substitution and creation of neobladders in children. *F1000Res.* 2019; 8:F1000 Faculty Rev-1992.
20. Yu Z, Huang J, Deng H, Zeng Z, Deng L, Xu X, et al. A novel neobladder-urethral drag-and-bond anastomosis technique during laparoscopic radical cystectomy for ileal orthotopic neobladder: Surgical technique and initial research. *Cancer Manage Res.* 2021;13:2909-2915.
21. Fathi R. Optimization of urolithiasis treatment and diagnosis in the Turkestan region. *J Med Life.* 2022;15(3):344-349.
22. Luciani LG, Mattevi D, Cai T, Malossini G. Robotics in Urology: No More Shadows? *Uro.* 2021;1(4):254-265.
23. Dobrovanov O, Králinský K, Kovalchuk VP. Ethiological agents of urinal infections and microbial resistance: Retrospective study. *Lek Obz.* 2019;(7):186-190.
24. Dobrovanov OY. Efficacy and sensitivity of prenatal and postnatal ultrasound screening of congenital developmental anomalies of kidneys in Slovakia. *Wiad Lek.* 2021;74(3 cz 1):450-454.
25. Horstmann M, Kurz M, Padevit C, Horton K, John H. Technique of the urethral anastomosis in orthotopic neo-bladder following robot-assisted radical cystectomy (RARC). *Aktuel Urol.* 2013;44(2):137-140.
26. Koie T, Ohyama C, Makiyama K, Shimazui T, Miyagawa T, Mizutani K, et al. Utility of robot-assisted radical cystectomy with intracorporeal urinary diversion for muscle-invasive bladder cancer. *In J Urol.* 2019;26(3):334-340.
27. Albisinni S, Vecchia A, Aoun F, Diamand R, Esperto F, Porpiglia F, et al. A systematic review and meta-analysis comparing the outcomes of open and robotic assisted radical cystectomy. *Minerva Urol Nephrol.* 2019;71(6):553-568.
28. Mineo Bianchi F, Romagnoli D, D'Agostino D, Salvaggio A, Giampaoli M, Corsi P, et al. Posterior muscle-fascial reconstruction and knotless urethro-neobladder anastomosis during robot-assisted radical cystectomy: Description of the technique and its impact on urinary continence. *Arch Ital Urol Androl.* 2019;91(1):5-10.
29. Lukyanenko N, Lenha E, Spaska A, Klets T, Shevchenko T. Tactics for treating young children with pyelonephritis and vesicoureteral reflux associated with impaired fibrillogenesis. *Mol Cell Biochem.* 2023;478(3):531-538.
30. Lukyanenko NS, Imanmadiyeva DM, Dolinnaya VT, Spaska A. "Clinical masks" of congenital malformations of urinary system in children of early age. *Int J Health Sci.* 2021;5(3):244-251.
31. Badawy AA, Saleem MD, El-Baset EA, Morsi ES. Decreasing operative time and incontinence rates in patients treated with radical cystectomy and urethral diversion: A prospective randomized trial using a new suturing device (CAPIO). *In J Nephrol.* 2012;44(3):769-774.

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32. Luciani LG, Mattevi D, Cai T, Malossini G. Robotics in Urology: No More Shadows? *Uro*. 2021;1(4):254-265.
33. Tusupbekova MM, Sharapatov YA, Pronkin EA, Lavrinenko AV, Turgunov YM. Comparative study of morphological changes in the kidney and ureter of a rabbit with various methods of infection. *Clin Exper Morphol*. 2022;11(1):62-72.
34. Sharapatov Y, Turgunov Y, Lavrinenko A. Pathogenic mechanisms of acute obstructive pyelonephritis. *Open Access Maced J Med Sci*. 2021;9(F):124-128.
35. Zulkhash N, Shanazarov N, Kissikova S, Kamelova G, Ospanova G. Review of prognostic factors for kidney transplant survival. *Urologia*. 2023;3915603231183754.
36. Nuradilova D, Kaliyeva L, Vaitkiene D, Kalimoldayeva S, Issenova S. Urogenital mixed infections in reproductive aged women with pelvic inflammatory disease. *Georg Med News*. 2021;(312):114-118.
37. Hamada A, Razdan S, Etafy MH, Fagin R, Razdan S. Early return of continence in patients undergoing robot-assisted laparoscopic prostatectomy using modified maximal urethral length preservation technique. *J Endourol*. 2014;28(8):930-938.
38. Koraitim MM, Atta MA, Foda MK. Orthotopic bladder substitution in men revisited: Identification of continence predictors. *J Urol*. 2006;176(5):2081-2084.
39. Yokota N, Ito F, Ishikawa T, Yamashita K, Nakazawa H. Neobladder-rectal fistula as early postoperative complication of radical cystectomy and orthotopic neobladder construction. *Nihon Hinyokika Gakkai Zasshi*. 2013;104(4):616-619.
40. Bhongir AV, Sampath S, Bonthapally RK, Gudivada KK, Ramaswamy G. Sequential Application and Post-Test Probability for Screening of Bladder Cancer Using Urinary Proteomic Biomarkers: A Review based Probabilistic Analysis. *Asian Pacif J Cancer Prevent*. 2023;24(6):2021-2027.
41. Grishin A, Spaska A, Kayumova L. Correction of overactive bladder with botulinum toxin type A (BTX-A). *Toxic*. 2021;200:96-101.

Sexual Disorders in Women: Causes and their Correction

Trastornos Sexuales en la Mujer: Causas y su Corrección

Liana Spytka

SUMMARY

Introduction: Difficulties caused by sexual disorders can lead to psychological problems in women associated with feelings of loneliness, shame, alienation, conflicts, and physical and psychological violence, therefore this issue needs detailed consideration. This research was conducted since sexual health is an integral part of a woman's life and inextricably affects psychological well-being, a sense of happiness, and quality of life. **Objectives:** The research aimed to identify the prerequisites for the occurrence of sexual disorders and to select methods for effective psychocorrection. **Methods:** Several research methods were used in the work, such as dialectical, interpretive, synthesis and analysis, and questionnaire. The causes of sexual dysfunctions in women were analyzed, the relationship with psychological, physiological, and interpersonal factors was described, and the diagnostic criteria of certain types of disorders and their prevalence were given. The consequences of sexual disorders on the general psychological state of women and their relationships with partners are emphasized. An empirical study was conducted among women

with sexual disorders of different age categories to determine the relationship between their psychological state mechanisms, strategies for coping with stressful situations, and the development of sexual dysfunctions.

Results: The results showed that women with sexual disorders have pronounced psychological protection mechanisms such as compensation and substitution, and as a strategy for overcoming difficulties, they mainly choose distancing. This indicates the occurrence of sexual dysfunctions, mainly due to the inability to deal with stressful situations and avoid their resolution. Based on the obtained data, the main elements, and stages of psychological correction of disorders were determined. The practical significance of the research lies in the development of effective criteria for the diagnosis and successful treatment of sexual dysfunctions in women.

Keywords: Sexual life, psychocorrection, sexual dysfunction, preventive care, women's health, FSD.

RESUMEN

Introducción: Las dificultades provocadas por los trastornos sexuales pueden derivar en problemas psicológicos en las mujeres asociados a sentimientos de soledad, vergüenza, alienación, conflictos y violencia física y psicológica, por lo que este tema necesita una consideración detallada. Se realiza esta investigación ya que la salud sexual es una parte integral de la vida de una mujer y afecta inextricablemente el bienestar psicológico, la sensación de felicidad y la calidad de vida. **Objetivos:** La investigación tuvo como objetivo identificar los requisitos previos para la aparición de trastornos sexuales y seleccionar métodos para una psicocorrección eficaz. **Métodos:**

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*Se utilizaron varios métodos de investigación, como el dialéctico, el interpretativo, el de síntesis y análisis y el cuestionario. Se analizaron las causas de las disfunciones sexuales en la mujer, se describió la relación con factores psicológicos, fisiológicos e interpersonales y se dieron los criterios diagnósticos de determinados tipos de trastornos y su prevalencia. Se destacan las consecuencias de los trastornos sexuales sobre el estado psicológico general de la mujer y sus relaciones con la pareja. Se realizó un estudio empírico entre mujeres con trastornos sexuales de diferentes categorías de edad para determinar la relación entre los mecanismos de su estado psicológico, las estrategias para afrontar situaciones estresantes y el desarrollo de disfunciones sexuales. **Resultados:** Los resultados mostraron que las mujeres con trastornos sexuales tienen pronunciados mecanismos de protección psicológica como la compensación y la sustitución, y como estrategia para superar las dificultades eligen principalmente el distanciamiento. Esto indica la aparición de disfunciones sexuales, principalmente por la incapacidad de afrontar situaciones estresantes y evitar su resolución. A partir de los datos obtenidos se determinaron los principales elementos y etapas de la corrección psicológica de los trastornos. La importancia práctica de la investigación radica en el desarrollo de criterios eficaces para el diagnóstico y tratamiento exitoso de las disfunciones sexuales en las mujeres.*

Palabras clave: *Vida sexual, psicocorrección, disfunción sexual, cuidados preventivos, salud de la mujer, DSF.*

INTRODUCTION

Sexual desire is defined as an urge to engage in sexual activity or an interest in a partner. It can be dyadic, that is, there is an interest in actions with another person, or solitary (1). Sexual disorders in women are a common form of pathology and are a serious public health problem, as they occur in about 41.5 % of premenopausal women (2). Sexual function is an important part of life, so it has a direct impact on a woman's well-being. Sexual dysfunctions are a heterogeneous group of disorders, the characteristic features of which are significant impairment of a woman's ability to feel sexual pleasure or to respond sexually. Sexual reactions have a biological basis, so they interact with intrapersonal, interpersonal, and cultural aspects of life and sexual disorders are formed because of somatic and mental factors.

Female sexuality is a combination of sexual function, sexual identity, and sexual relations. It is formed throughout life under the influence of several factors: interpersonal communication, age characteristics, sexual and reproductive health, and social factors. A complex of emotional, somatic, social, and intellectual aspects forms sexual health, which affects the enrichment of the personality, the development of sociability, and general psycho-emotional well-being.

World Health Organization (WHO) distinguishes the following components of sexual health: general well-being; security, respect, and freedom from violence and discrimination, respect for human rights; relevance of sexual health throughout life, not only during the reproductive period; a variety of forms of sexual self-expression and sexuality (3). Sexual health depends on the availability of reliable information about sex, risks and consequences, access to services related to sexual health, and living in a supportive environment. According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (4), there are the following types of sexual disorders in women: sexual interest disorder (arousal), orgasm disorder, and genital-pelvic pain disorder (penetration). The formation of sexuality is a complex process in psychosexual and somatosexual directions, which begins in the embryonic period of ontogenesis and ends with puberty. Since the birth of a child, his psychosexual development is influenced by psychological factors, such as sexual orientation, gender-role behavior, sexual self-awareness, as well as social norms of behavior, school, family, children's and youth groups, and mass media. Gross deformations can occur when the early stages of psychosexual development are disturbed (5).

Several modern researchers have studied the issue of female sexual dysfunction and its impact on the general well-being of women. Falyova (6) analyzed approaches to the study of sexual disorders and their impact on psychosomatic health, emphasizing the need for preventive measures, psycho-correction of emotional states such as anxiety, stress, and depression, correction of attitudes about sex, as they increase the likelihood of developing psychosomatic diseases. Kocharyan (7) identified

a number of psychoemotional factors that are the cause of hypoactive sex drive in women, and also compared data on hyposexual behavior in different ethnic regions and found that East Asian women have lower sex drive compared to women of Canadian origin. Gerasimenko (8) studied the impact of post-traumatic stress disorder (PTSD) on the sexual sphere of the personality it was determined that 95.4 % of women with PTSD have an insufficient level of sexual communication, which was the result of a constellation of pathopsychological and negative socio-psychological factors. In their research, Grigorenko et al. (9) studied sexual dysfunctions in women of different ages, where also analysed the classification of female sexual dysfunction (FSD) and the causes of its occurrence, as well as emphasized the importance of taking an interdisciplinary approach when evaluating and treating sexual dysfunctions in women. It was stated that a collaborative effort between multiple specialties is necessary to make accurate diagnoses and choose personalized, targeted treatments for each woman. Kowalewska et al. (10) conducted an online-based survey, aimed at examining the correlates of compulsive sexual behaviors (CSB) with sociodemographic and sexual history characteristics in Polish women. The obtained results showed that excessive pornography use was the strongest predictor of CSB symptoms, and divorced or separated women and those who were single exhibited higher CSB symptom severity in contrast to their married or informally involved counterparts. A study conducted by Efrati et al. (11) showed that young women with substance use disorders displayed higher levels of compulsive sexual behavior disorder symptoms and engaged in more risky sexual behaviors compared to women without substance use disorders. The compulsive sexual behaviors explain the relationship between substance use and risky sex in these women. All the addictive behaviors were associated with a history of childhood emotional abuse.

Contemporary research on FSD takes a comprehensive view, considering biological, psychological, and sociocultural factors. Studies explore the role of neurobiology, psychological elements such as body image and mental health, relationship dynamics, cultural impacts, and varied treatment strategies. Inclusivity,

technology-based interventions, and the enduring effects of FSD on women's holistic wellness are focal points, revealing a nuanced and progressive comprehension of this intricate matter. However, discrepancies exist in the classification of FSD, with variations in definitions and diagnostic criteria. Moreover, cultural differences and societal norms lead to divergent perspectives on what constitutes normal sexual function, adding to the contradictions within this multifaceted field.

While many studies have examined different facets of sexual dysfunction in women, there is still a need for research that comprehensively explores how women's psychological factors, sexual attitudes, and emotional states all interact together to impact the development and worsening of sexual disorders. Developing tailored psychotherapy approaches that address these diverse interacting influences is also needed.

This study aimed to determine the factors causing sexual disorders and to identify methods for their correction. Several tasks were performed: approaches to the study of sexual problems on women's psychosomatic health were analyzed; the importance of the study of sexual dysfunctions was emphasized; the relationship between attitudes towards sex and the current psychoemotional state was established; determined intrapsychological factors that influence the occurrence of sexual disorders; methods of psychocorrection of female sexual dysfunction were given.

MATERIALS AND METHODS

To achieve the goals of the research several methods were used, which made it possible to analyze the problems of sexual disorders in women, in particular of a psychological nature, as well as to identify methods for the prevention and correction of sexual dysfunctions. Through synthesis and analysis, scientific and theoretical concepts were studied, which revealed the essence of female sexual dysfunction and its development, types, and nature of manifestation, causes of occurrence, and concepts of treatment. The theoretical data obtained during the research provided the basis for further study of the problems and factors of the occurrence of female sexual

disorders. 40 women aged 18-45, who had sexual disorders, took part in the study by questionnaire. The participants filled out questionnaires through Google Forms, using only initials to denote themselves to preserve anonymity. Before the questionnaire, the participants were informed about the objectives of the study and gave their consent to data processing. The average time to fill out the questionnaire was 30 minutes.

Since sexual dysfunctions often arise due to depression and psycho-emotional factors, the first method for the study was the questionnaire “Index of lifestyles” by Plutchik–Kellerman (12) to identify the dominant mechanisms of mental protection in women, study the hierarchy of the psychological protection system and assess the overall intensity of all mechanisms. The methodology was developed based on the generated characteristics of 16 self-defense mechanisms, which over time were revised and reduced to 8 main mechanisms, namely: displacement, denial, substitution, projection, compensation, reactive formation, regression, and rationalization. At the same time, compensation and rationalization stand out as the most constructive forms of protection, and projection and displacement—as the most destructive. Currently, a version of 92 statements is used, to which it is necessary to answer “Yes” or “No” depending on whether the respondent agrees with them.

In the study, it was also important to determine the behavior of women, their ability, and ways of getting out of crisis situations, one of which is problems of a sexual nature, to rationally select methods for correcting sexual dysfunctions that arose because of psychological problems. For this, the questionnaire “Coping Strategies” by Lazarus and Folkman (13), is designed to identify coping mechanisms and methods of overcoming difficulties in a number of areas of mental activity. The questionnaire consists of 50 statements that must be rated from 0 to 3 depending on how much the respondent agrees with them. The methodology makes it possible to identify behavioral strategies that a person prefers in difficult life situations, among which the following are defined: confrontational coping, self-control, distancing, acceptance of responsibility, search for social support, escape avoidance, positive reappraisal, and problem-solving planning.

The dialectical method made it possible to reveal the relationship between the development of sexual dysfunction and the methods of mental protection that dominate the interviewed women, as well as their ability and methods to overcome stressful situations. The interpretive method helped to combine the received data and data from previous studies to determine the most effective factors contributing to the process of prevention and correction of female sexual dysfunctions.

RESULTS

Female sexual dysfunctions (FSD) are a single diagnosis that denotes the number of sexual disorders in women, which include disorders of desire, disorders of arousal, disorders of achieving orgasm, and the presence of sexual pain. A broad classification of female sexual disorders includes disorders of both physiological and psychological direction (9). These encompass various sexual disorders, such as decreased interest and desire within relationships, aversion to sexual activity, reduced cognitive and genital arousal, unwanted spontaneous genital arousal, female orgasmic issues, and painful intercourse conditions. A separate type of sexual disorder also includes compulsive sexual behavior (CSB), which is currently under-researched in women compared to men (10). It is excessive use of pornographic content, impulsive participation in risky sexual relationships, and uncontrolled use of paid sexual services.

There are different origins of female sexual disorders. One of them is psychogenic factors, which are manifested more often in women due to increased vulnerability, emotionality, and sensitivity, and therefore are more pathogenic than in men, and cause inhibition of sexual manifestations or become a priority in intermediate states. There can be different reasons and conditions for the occurrence of sexual pathology in women: FSD can appear as an independent disease with somatic well-being, not related to a disease of the body; may be the result of external causes and constitutional factors; may be the result of a disease of the body. There is also a narrower term for sexual disorders – hypoactive sex drive disorder (HSDD), which

refers specifically to elements of desire, interest in sex, or libido (14).

Currently, there is no single approach to determining the psychological causes of FSD, but a number of researchers have studied this issue. Based on work with patients, Kocharyan (7) identified factors for women, including negative partner influences (husband’s unemployment or dominance), dissatisfaction with partner’s appearance, outside romantic interests, loss of sexual allure due to dependency, unmet sexual needs, sexual reproaches, and conflicts with in-laws.

According to the Diagnostic and Statistical Manual of Mental Disorders (4), female sexual disorders can arise from various factors including a partner’s health or sexual problems, a woman’s history of trauma or negative body image, mismatched libidos, or poor communication within a relationship, and cultural or religious views about sexuality.

Friedmann and Cwikel (1) argued that psychosocial factors that can provoke hyposexual disorders include difficulties in communication, destructive previous or current relationships, deficiencies in sexual education, and sexual misinformation. Negative and emotional factors are also distinguished, which include distracting thoughts about appearance, memories of previous unsuccessful attempts at intimacy, and anxiety about sexual activity. Since the emotional and interpersonal component of emotional closeness is more important for women than for men, the above factors hinder their sexual arousal and satisfaction. For women, sexual response is more important in psycho-emotional terms than in physical terms, in particular, because of the need for a relationship with a partner. Therefore,

for them, sexual games, and signs of attention from a partner play an important role as stimuli in arousal, which, as a result, strengthens the feeling of unity and responsibility in the relationship. Women’s sex drive depends on the emotions associated with sexual relations, so they are more likely to be satisfied if they have a close relationship with their partner.

The opposite of reduced sex drive is hypersexuality in women, which has only recently begun to receive due attention and discussion. According to studies (10), only 31 % of women seek help for hypersexual behavior. The strongest predictor among symptoms of hypersexuality was problematic viewing of pornography. This problem was observed more among single women, divorced, and those who live apart from their partner than among those who are married or in informal relationships. The severity of hypersexual behavior directly depends on the number of sexual contacts but does not depend on the age of the first sexual relationship. From the above, it can be concluded that the aetiology of FSD includes many factors, such as psychological, interpersonal, psychological, and sociocultural.

When investigating the causes of sexual disorders and choosing rational methods of treatment, it is important to study the general psychological state of women. Since FSDs are inextricably linked to psychological factors, particularly those related to stress and depression (15), it was decided to study the mechanisms of psychological protection in women. The study was conducted among 40 women with diagnosed sexual behavior disorders aged 18-45. For this, the “Index of lifestyles” method by Plutchika–Kellerman (12) was used (Figure 1).

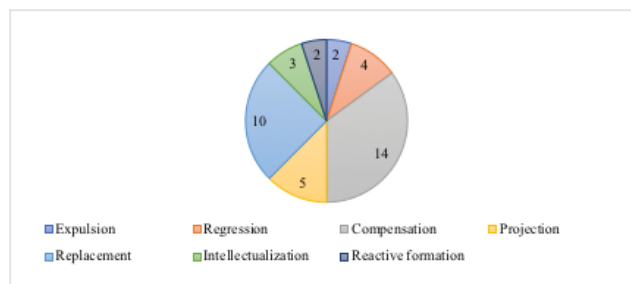


Figure 1. The results of the “Index of lifestyles” method by Plutchika –Kellerman (12).

As can be seen from the results, compensation, and substitution are dominant mechanisms of psychological protection in most women, and regression and projection are used to a lesser extent. Compensation manifests itself in finding a replacement for a real or unreal defect, hiding the shortcomings of an intolerable feeling with other qualities through fantasies, and “putting on” the characteristics, behavior, and values of another person. Compensation can act as a form of protection against the feeling of inferiority, which is typical for women with sexual disorders that arise because of dissatisfaction with their external qualities. Substitution manifests itself in the release of oppression, most often through anger, which is directed at people or objects that are less dangerous or more accessible than those that cause negative feelings.

In this way, women can use the sexual energy that they cannot release in their sexual life in useful affairs, and hobbies. Although this does not save them from the problem of FSD, but only allows them to divert attention from it. Violation of sexual function for a woman’s personality has a negative character, as it increases the feeling of inferiority and can lead to a violation of interpersonal relations with a partner. What methods women choose to overcome difficulties in their lives can also show strategies for further therapy of sexual dysfunctions. This led to the implementation of the “Coping strategy” by Lazarus and Folkman (13), a technique to determine which coping mechanisms women with FSD prefer.

As can be seen from the results, the prevailing strategies in women are equally distancing, acceptance of responsibility, and planning to solve the problem (Figure 2). Thus, considering the

results of both methods, it is possible to confirm once again that a large part of women with sexual dysfunctions, when aware of the problem, have the desire to switch to another type of activity, which can only deepen the problem if ignored. However, a significant part is still ready to take responsibility and look for ways to solve it.

A Pearson correlation analysis showed a 0.2 coefficient between coping strategies and defense mechanisms, indicating unconscious influences of defenses on behavior, reasoning, and situation acceptance. For example, compensation and substitution as protection combined with distancing as a coping method explain the prevailing desire of women to avoid the issue of sexual problems, which in the future may lead to worse consequences for their psycho-emotional state. Therefore, psychotherapeutic measures occupy a special place in the system of treatment of various forms of sexual pathologies in women, and they should have a systematic therapeutic effect.

Given women’s emotional sensitivity and vulnerability, treating FSD should involve principles like addressing their personality, active participation, cooperation with professionals, holistic life focus, combining biological and psychological approaches, shifting self-perception, and following a sequenced treatment process. In the therapy of sexual disorders, the key task is to normalize emotional reactions, eliminate functional disorders, and increase endurance in relation to the mental effects of stressful situations on a woman’s life. Rational therapy should consider both the physical features of the body and the personality itself with its individual characteristics, as they affect a woman’s ability to focus on therapy, to be

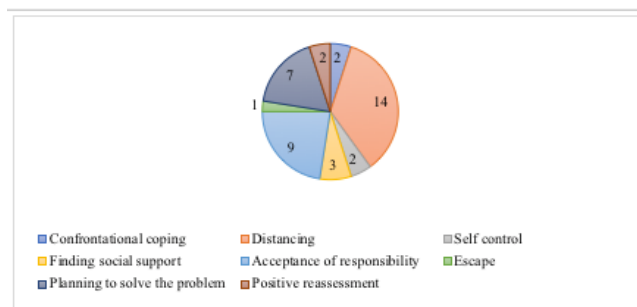


Figure 2. Results of the “Coping strategy” by Lazarus and Folkman (13) technique.

influenced by it. Therefore, it is important to identify the causes of suffering and to study the influence of unconscious and conscious mental reactions on them.

There are a number of methods of therapeutic interventions in the treatment of FSD (5):

- Drug therapy, which is effective in cases where disorders arise on an organic basis.
- Physiotherapy, which is used to treat disorders of an organic and functional nature.
- Training methods that are particularly effective for the treatment of sexual disorders of the functional type and when working with couples (relaxation training, the program of Masters and Johnson, systematic desensitization, emotional training, aversion treatment);
- Hypnotherapy and autogenic training.
- Psychotherapy, which sometimes becomes the only form of treatment for FSD or plays the most significant role in a systemic approach (non-hypnotic suggestive psychotherapy, meditation methods, rational psychotherapy methods).
- Partner and group psychotherapy.

A separate method is the use of cognitive behavioral therapy (CBT), which can be effective both under the supervision of a psychotherapist and when working independently (16). CBT can be delivered in an individual, group, or couples format, with the involvement of all participants being an important prerequisite for successful treatment. Behavioral, cognitive, and emotional aspects are the main components of cognitive-behavioral therapy. Negative thoughts about sexual intimacy increase anxiety, negatively affect a woman's psychological and emotional state and lead to avoidance and tension, which provokes even more negative thoughts, as if in a closed circle.

Therapy aimed at cognition should include a reinterpretation, psychoeducation, cognitive restructuring, validation of taking responsibility for one's pleasure, non-evaluative awareness, and distancing from thoughts. For the development of emotional perception, and management of anxieties that may arise as a cause or consequence

of sexual disorders, important components are relaxation training and stress reduction methods. Step-by-step exposure and communication skills training are effective for correcting behavioral aspects. Psychotherapy for FSD will be effective if it consists of the main mandatory steps: formation of healthy psychological attitudes through psychotherapeutic conversations, elimination of neurotic reactions caused by the personal reaction of women with disorders to their own sexual inferiority; and restoration of sexual function. Thus, the effective treatment of women's sexual disorders is inextricably linked to the psychological aspects of their personality and must consider the general psycho-emotional state of a woman when selecting therapy methods.

DISCUSSION

Sexual disorders in women can have both a psychological and a physiological nature, as well as be complex. It is important to have clear diagnostic criteria by which to determine the presence of dysfunctions in sexual health in a case. The causes of psychological or interpersonal dysfunctions are low self-esteem and negative body image, inaccurate or unrealistic sexual desires, false expectations, unrealistic standards and assumptions, partner monitoring and self-monitoring, inadequate skills and knowledge for emotional and physical relaxation, lack of deep sexual knowledge, insufficient skills for self-pleasure, experience of violence and abuse, mistrust, and alienation of a partner.

Inadequate strategies for managing life stress can be identified as a separate reason. As the results of "Coping Strategies" by Lazarus and Folkman (13) showed, most women in their lives choose strategies related to distancing themselves from problems. This applies not only to sexual dysfunctions, but also to other stressful situations that arise in life: conflicts, mistrust, alienation, weak communication skills, and previous relationship experience. It is especially critical when it concerns the relationship with the partner and directly affects the sexual relationship with him. According to the biopsychological model of understanding the sexual response of a person, which was presented by Rosen and Barsky (17), it combines many aetiological

factors: interpersonal, such as the quality of past and present relationships, psychological, which includes anxiety and depression, physiological and biological, related to physical health, neurobiology, endocrine functions, sociocultural factors that depend on upbringing, cultural norms, and expectations. Combined, all of this affects a woman's sexual response.

The circular model by Basson (18) shows that emotional closeness and relationship satisfaction are important components of sexual relationships in women, and the need for closeness is an integral motive for accepting sexual stimuli. Orgasm is not necessarily the goal of sexual intercourse for women, but rather the emotional satisfaction of feeling close and connected with a partner. Several reasons encourage women to have sex: physical pleasure, the desire to please a partner and express their affection for him, to raise their self-esteem, to feel wanted, and to distract themselves from negative thoughts. As for the latter, this echoes the results of the "Index of Lifestyles" method by Plutchik-Kellerman (12), according to which women tend to use the compensation mechanism for psychological protection. In many cases, sex for them acts to "block" stressful life situations or anxiety. In the case when sexual relations themselves become the cause of anxiety and depression, women compensate or replace them with other types of activities, often ignoring the existence of a problem and not paying much attention to it. This complicates the diagnosis of sexual disorders and their subsequent treatment, which has a negative impact on the general psycho-emotional state of women.

The reason for this negative phenomenon can be the taboo of the subject of sex and its concealment from society until recently, since for many centuries it was perceived only as a means of procreation, while other types of sexual stimulation were considered sinful, and in some places became a reason for imprisonment (19). Nowadays, the view of sex and sexuality has changed, although in some cultures it is still a matter of shame. This is demonstrated in the study of scientists from Bahrain, Alselaiti et al. (20), who studied the extent to which the male-oriented Arab culture affects the quality of Arab women's sexual lives, the prevalence of sexual dysfunctions among them, and the frequency of seeking medical attention with this

problem. Thus, it was determined that 43 % of the 360 surveyed women had problems with sexual contact. In particular, 37 % of women with disorders noted difficulties with sexual desire. The reasons for the high level of FSD were the polygamous relationships of men, the lack of gender equality, and the directly proportional dependence of the number of detected disorders on the age of women. The worst thing is that 96 % of women did not ask doctors about sexual difficulties, and 87 % did not dare to discuss their problems with doctors. This again confirms the results obtained during the study cited in the article that numerous modern women still prefer to distance themselves from the problem of FSD in case of their occurrence. However, the frequency of manifestation of certain mechanisms of psychological protection and strategies for overcoming stressful situations also depends on aspects of the cultural environment in which women are located (21,22).

A study of sexual dysfunction among middle-aged and elderly Chinese women by Zhu et al. (23), confirmed the relationship between the increasing age of women and the risk of developing sexual disorders. In particular, 58 % of women had certain sexual difficulties related to both physical factors (dyspareunia, dysphoria, other diseases of the body not related to sexual function) and the presence of sexual dysfunction of the partner, due to which 39 % of the surveyed women completely stopped sex life (24). Lammerink et al. (25) also noted the decrease in sexual desire with age, they studied the sexual functioning of Dutch women. According to their results, one in four women between the ages of 20 and 80 had some problems in their sex lives, but despite a decline in sexual activity and functioning with age, sexual satisfaction showed a slight decline.

The presence of other diseases of the body and drug therapy also have a significant impact on FSD. Camara et al. (26) investigated the risk of sexual dysfunction in HIV-infected women from Conakry. They found the connection of disorders not only with the adoption of antiretroviral therapy, but also with other factors, such as the absence of marriage, and the age of 35 years and older, which were associated with hormonal changes in the aging process. The work also noted the importance of sensitizing doctors

and people supervising HIV-infected women to assess possible sexual disorders in their patients during routine consultations and as part of HIV treatment programs.

The issue of compulsive sexual behavior disorder was raised by Efrati et al. (11), who studied this question among women who were dependent on the use of psychoactive substances and who had experienced early psychological trauma. It has been determined that chemical dependencies are often combined with other mental disorders and addictive behaviors, one of the main types of which is compulsive sexual behavior disorder. This was because the precursors of this disorder and addictions have the same nature of occurrence. And the main ones are children's injuries, and the accumulation of negative life events over time. This once again confirms the need for psychological therapy and correction, firstly, of women's depressive and anxious states to overcome various manifestations of female sexual disorders (27,28).

As emphasized by McCool-Myers et al. (29), in treatment and correctional work with women with sexual dysfunctions, health workers should be aware of risk factors for women of reproductive age, and prevention strategies should have an impact on factors such as physical activity, access to sex education, empowerment of women regardless of age and cultural background. Among the significant risk factors for the appearance of FSD, poor physical and psychological health, stress, traumatic operations on the genitals, dissatisfaction with relationships, religiosity, and violence were highlighted. At the same time, among the factors that could have a preventive effect, physical exercises, established intimate communication, sexual education, and older age at marriage were emphasized (30).

Female sexual dysfunction has a strong impact on women's reproductive and sexual lives, where social, psychological, and biological factors play a role (31). The conducted research and analysis of the works of other scientists showed the interdependence of the psycho-emotional state of women and the development of sexual disorders, as well as the influence of psychological protection mechanisms and strategies for overcoming stress on the effectiveness of corrective and therapeutic therapy.

CONCLUSIONS

Sexual health is an integral complex of interacting elements of sexuality: biological, psychological, social, and socio-psychological, which ensure adequate sexual behavior and relationships, sexual harmony, and adaptation to a partner. The reasons for the development of sexual disorders in women can be different. Among the main ones, psychogenic factors that negatively affect sexual manifestations can be distinguished, and in women who are more emotional, sensitive, and vulnerable, they take on more threatening forms. Although there is currently no single approach to determining the psychological causes of FSD, some researchers have singled out the following: partner factors related to the partner's health and sexuality; individual vulnerability; negative attitude towards one's own body and appearance in general; stress, psychological exhaustion and burnout; strained relations with a partner, sexual disharmony in activities and desires; violation of interpersonal communication; cultural and religious factors; early trauma and trauma related to violence. Women's sexual desire depends on emotions, so the important role for them is not so much physical pleasure from sexual intercourse as the feeling of closeness with their partner, which they seek to get through sexual games and signs of attention from their partner.

The aetiology of FSD includes many factors, such as psychological, physical, interpersonal, psychological, and sociocultural. The study described in the article demonstrated that women with sexual disorders tend to use compensation and substitution as a psychological defense mechanism, and distancing as a coping strategy. This makes it difficult to diagnose and treat the problem, as women still often avoid it. Psychotherapeutic measures in the treatment of sexual disorders in women should be aimed at correcting personal reactions when pathology is detected and preventing the emergence of an inferiority complex, considering the individual and general emotional characteristics of each woman. At the same time, it is important to observe the principles of phasing, consistency, and ethics. Correction should consist of three important steps: formation of healthy psychological attitudes,

elimination of neurotic reactions, restoration, and activation of sexual functions. The sample of this research only included women aged 18–45 with diagnosed sexual disorders, which are a specific subset of the female population. The findings may not apply to women outside this age range or women without sexual disorders. However, the exploration of coping mechanisms and defense mechanisms employed by women with sexual disorders offers insights into how these strategies influence their responses and common emotional states. The article's integration of diverse therapeutic approaches like drug therapy, physiotherapy, cognitive-behavioral therapy (CBT), and psychotherapy underscores the complexity of addressing FSD and offers a more holistic view of potential treatment ways, that can be applied to the larger number of the female population. Further research with larger, more diverse samples would be needed to determine if the patterns observed here generalize robustly to the overall female population. This article expanded the knowledge of women's sexual psychology. It provided a foundation for future research and clinical practice in this area, guiding the development of more effective strategies for addressing the complex challenges faced by women with sexual disorders.

REFERENCES

- Friedmann E, Cwikel J. Women and men's perspectives on the factors related to women's dyadic sexual desire, and on the treatment of hypoactive sexual desire disorder. *J Clin Med*. 2021;10(22):5321.
- McCool ME, Zuelke A, Theurich MA, Knuettel H, Ricci C, Apfelbacher C. Prevalence of female sexual dysfunction among premenopausal women: A systematic review and meta-analysis of observational studies. *Sexual Med Rev*. 2016;4(3):197-212.
- Sexual health. 2023. <https://cutt.ly/q7B1gEj>.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Washington: American Psychiatric Publishing, 2013.
- Dronova VL, Kornienko SM. Clinical-anamnestic features and quality of life in women with endometrial pathology on the background of uterine myoma. *Med Perspektivi*. 2017;22(1):81-88.
- Falyova OE. The relationship between attitudes towards sex and the current psycho-emotional state of women with different family status. *Med Psychol*. 2015;4(40):10-14.
- Kocharyan G. Hypoactive sexual desire due to physiological conditions, influences of social and psychological factors, disregard for sexual needs of a woman. *Health of Man*. 2022;3:56-65.
- Gerasimenko LO. Motivational aspects of sexual behavior in women with post-traumatic stress disorders. *Herald Prob Biol Med*. 2014;2(4):107-111.
- Grigorenko VM, Romashchenko OV, Melnikov SM, Bilogolovka VV, Myronenko NO, Dzuraeva LS. Sexual dysfunctions in women of different ages. *Men's Health, Gender and Psychosomatic Medicine*. 2023;1-2(14-15):68-75.
- Kowalewska E, Gola M, Lew-Starowicz M, Kraus SW. Predictors of compulsive sexual behavior among treatment-seeking women. *Sexual Med*. 2022;10(4):100525.
- Efrati Y, Goldman K, Levin K, Rosca P. Early-life trauma, negative and positive life events, compulsive sexual behavior disorder and risky sexual action tendencies among young women with substance use disorder. *Addictive Behaviors*. 2022;133:107379.
- Plutchik R, Kellerman H, Conte HR. *A structural theory of ego defenses and emotions*. New York: Plenum; 1979.
- Lazarus R, Folkman S. *Stress, appraisal, and coping*. New York: Springer Publishing Co.; 1984.
- Pyke RE. Decisions on measures of hypoactive sexual desire disorder in women: A history, with grounds to consider clinical judgment. *Sexual Med Rev*. 2021;9(2):186-193.
- Alidost F, Pakzad R, Dolatian M, Abdi F. Sexual dysfunction among women of reproductive age: A systematic review and meta-analysis. *Internat J Reprod BioMed (IJRM)*. 2021;19(5):421-432.
- Stephenson KR, Zippa N, Brotto LA. Feasibility of a cognitive behavioral online intervention for women with Sexual Interest/Arousal Disorder. *Clin Psychol*. 2021;77(9):1877-1893.
- Rosen RC, Barseky JL. Normal sexual response in women. *Obstet Gynecol Clin North Am*. 2006;33(4):515-526.
- Basson R. The female sexual response: A different model. *J Sex Marital Therapy*. 2020;26(1):51-65.
- Poslavska OV, Shponka IS, Babiy HS. The diagnostic value of the p16ink marker for verification of tumors of unknown primary site in women with isolated lesion of inguinal lymph nodes. *Med Perspektivi*. 2019;24(2):13-19.
- Alselaiti M, Saleh MA, Muhammed H, Attallah E, Dayoub N. Prevalence of female sexual dysfunction and barriers to seeking primary health care treatment

- in an Arab male-centered regime. *Open Access Macedonian J Med Scienc.* 2022;10(E):493-497.
21. Chorna VV, Makhniuk VM, Khliestova SS, Gumeniuk NI, Chaika HV. Attitude of health care workers in the field of mental health to their health. *Med Perspektivi.* 2021;26(2):188-196.
 22. Orupabo CD, Odoya CG. Anthropometric variables in breast lesions of women of reproductive age in University of Port Harcourt Teaching Hospital. *Internat J Med Medical Res.* 2023;8(2):18-23.
 23. Zhu Y, Yang X, Fan X, Sun Y, Tan C, Wang Y, et al. Decreased sexual desire among middle-aged and old women in China and factors influencing it: A questionnaire-based study. *Evidence-Based Complemen Alternat Med.* 2021;1:6649242.
 24. Astakhov VM, Batsylyeva OV, Puz IV, Shudrikova NV. Features of the organization of medical and psychological assistance in the situation of perinatal losses (literature review). *Med Perspektivi.* 2022;27(3):44-50.
 25. Lammerink EAG, de Bock GH, Pascal A, van Beek AP, van den Bergh ACM, Sattler MGA, et al. A survey of female sexual functioning in the general Dutch population. *J Sexual Med.* 2017;14(7):937-949.
 26. Camara A, Tounkara TM, Delamou A, Baldé R, Leno NN, Kuotu GC, et al. Prevalence and risk factors of female sexual dysfunction among women infected with HIV in Conakry. *Clin Epidemiol Global Health.* 2021;12:100828.
 27. Beniuk VO, Ginzburg VG, Vygivska LM, Maidanyk IV, Chorna OO, Oleshko VF, et al. Assessment of correction effectiveness of psychoemotional state in pregnant women after application of assisted reproductive technologies. *Med Perspektivi.* 2021;26(4):131-138.
 28. Kulyk II, Khmil SV. Endometriosis-associated infertility: the role of hormones and its correction. *Internat J Med Medical Res.* 2021;6(2):5-10.
 29. McCool-Myers M, Theurich M, Zuelke A, Knuettel H, Apfelbacher C. Predictors of female sexual dysfunction: A systematic review and qualitative analysis through gender inequality paradigms. *BMC Women's Health.* 2018;18:108.
 30. Heryak SM, Humenna IY. Instrumental and diagnostic criteria of hemodynamic disorders and endothelial dysfunction correction in pregnant with arterial hypertension. *Internat J Med Medical Res.* 2015;1(1):30-34.
 31. Slyva AF, Selskyy PR, Kuziv OY, Slyva VV. The state of cellular immunity in pre- and menopausal women with hyperplastic endometrial processes. *J Med Biol Res.* 2020;2:29-36.

Behaviors Linked to the Acceptance of Vaccinations Aiming to Expedite COVID-19 Management Within the Citta Sub-District of Soppeng District, Indonesia

Comportamientos Asociados con la Aceptación de la Vacunación como un Esfuerzo para Acelerar El Manejo del COVID-19 en el Sub-Distrito De Citta, del Distrito De Soppeng, Indonesia

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SUMMARY

Background: COVID-19 is a respiratory disease that spread massively in 219 countries leading to a pandemic. Vaccination is a prevention strategy in the epidemiology approach by analyzing behavioral determinants related to vaccination acceptance of COVID-19. This study aims to analyze the association between behavioral determinants with the vaccination's acceptance of COVID-19 in Citta District, Soppeng Regency. **Method:** A cross-sectional study design was carried out on 333 people. Cluster sampling was applied as the sampling technique. Data analysis used the Chi-Square test and logistic regression. **Results:** A significant relationship was found between behavioral determinants and acceptance of the COVID-19 vaccine,

including access to information ($p=0.013$) and the role of health workers ($p=0.003$). Whereas gender, education, occupational, knowledge, attitudes, and family support were not related to the COVID-19 vaccination acceptance. Multivariate analysis results showed that access to information ($p=0.004$: OR 2.129: 95 % CI: 1.272-3.563) and the role of health workers ($p=0.001$: OR 0.444: 95 % CI: 0.278-0.707) were most related with the 1st booster COVID-19 vaccination effectiveness. **Conclusion:** The role of health workers associated with COVID-19 vaccination acceptance is related to the information that can be obtained and accessed by the community. **Suggestions:** It is expected that health workers will act more actively in capturing the public and be more informative and open to the public regarding information.

Keywords: Vaccine-Acceptance, COVID-19, Behavior, Information.

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RESUMEN

Antecedentes: La COVID-19 es una enfermedad respiratoria que se propagó ampliamente en 219 países, lo que llevó a una pandemia. La vacunación es una estrategia de prevención en el enfoque epidemiológico al analizar los determinantes conductuales relacionados con la aceptación de las vacunas contra la COVID-19. Este estudio tiene como objetivo analizar la asociación entre los determinantes conductuales y la aceptación de las vacunas COVID-19 en el Distrito de Citta, Regencia de Soppeng. **Método:** Se llevó a cabo un diseño de estudio transversal con un total de 333 personas. Se aplicó un muestreo por conglomerados como técnica de muestreo. El análisis de datos utilizó la prueba de Chi-Cuadrado y la regresión logística. **Resultados:** Se encontró una relación significativa entre los determinantes conductuales y la aceptación de la vacuna COVID-19, incluido el acceso a la información ($p=0.013$) y el papel de los trabajadores de la salud ($p=0.003$). Mientras que el género, la educación, la ocupación, el conocimiento, las actitudes y el apoyo familiar no se relacionaron con la aceptación de la vacuna COVID-19. El resultado del análisis multivariante mostró que el acceso a la información ($p=0.004$: OR 2.129; IC del 95 %: 1.272-3.563) y el papel de los trabajadores de la salud ($p=0.001$: OR 0.444; IC del 95 %: 0.278-0.707) estaban más relacionados con la efectividad de la primera dosis de la vacuna COVID-19. **Conclusión:** El papel de los trabajadores de la salud se asocia con la aceptación de la vacuna COVID-19, lo que se relaciona con la información que la comunidad puede obtener y acceder. **Sugerencias:** Se espera que los trabajadores de la salud actúen de manera más activa para captar al público y sean más informativos y abiertos al público en cuanto a la información.

Palabras clave: Aceptación de la vacuna, COVID-19, comportamiento, información.

INTRODUCTION

The World Health Organization (WHO) reports that globally the number of confirmed cases of COVID-19 is 276 436 619 people with a total death of 5 374 744 people or a mortality rate of 1.9 %. Based on WHO data, it was known that there were 219 countries infected with coronavirus with 180 of them experiencing local transmission (1).

Globally, the number of COVID-19 cases in women and men is relatively the same, namely

50.4 % and 47.6 %, respectively. In Southeast Asia itself, the number of confirmed COVID-19 cases was 44 865 441 people with a total death of 718 368 people or with a mortality ratio of 1.6 %. As of December 26, 2021, based on data from the Ministry of Health of the Republic of Indonesia, it was known that the number of confirmed cases to date is 4 261 759, with a cure rate of 96.5 % or 4 113 049 people and the number of cases that have died is 144 055 people or with a percentage of 3.4 % and active cases of 0.1 % or as many as 4 655 cases (2).

According to data from South Sulawesi on the COVID-19 response, the number of confirmed cases in Soppeng regency was 2 397 cases with a total recovery percentage of 97.2 % or 2 331 recovered cases and 66 deaths or 2.8 %. In addition, based on data from the Indonesian Ministry of Health, the Soppeng district is one of the regions experiencing local transmission. In handling and preventing COVID-19 disease, the government is currently massively protecting the community by launching programs such as 5M (using masks, maintaining distance, washing hands, avoiding crowds, and reducing mobility), 3T (testing, tracing, and treatment) as well as vaccination. These efforts are made to protect and guard people from the spread of the coronavirus.

Vaccination is considered one of the government's efforts to form immunity against existing viruses. COVID-19 vaccination aims to form antibodies resistant to the coronavirus (3). Vaccination is carried out to form herd immunity as one of the efforts to control and prevent COVID-19. The expected vaccination coverage is 70 %-80 % to create herd immunity (4).

Based on data from the Ministry of Health, the coverage of the 3rd dose of COVID-19 vaccination in Indonesia, as of September 27, 2022, had reached 26.98 % (Ministry of Health, 2021). Based on WHO data, only around 39.44 per 100 population have received the complete dose of vaccine from January 13th, 2021 to December 20th, 2021 (World Health Organization (WHO), 2021). COVID-19 vaccination coverage with the 3rd dose in South Sulawesi Province reached 14.26 % as of September 27, 2022. Vaccination coverage in Soppeng for the first dose of vaccine was 87.43 % the second dose was 69.61 % and the third dose third at 15.99 % as of September 27, 2021 (Ministry of Health, 2021) (6).

Based on the latest data on the achievements of the COVID-19 vaccination in every district in Soppeng Regency on March 30th, 2022, it was found that there were three districts with low vaccination achievement, namely Citta District, Liliriaja District, and Gandra District. Citta District was the district with the lowest vaccination, with the achievement of vaccine dose 1 was 76.04 %, vaccine dose 2 was 48.71 %, and dose 3 was 4.58 % (Soppeng Regency Government, 2022) (7).

Vaccination efforts carried out by the government received various responses in the Soppeng community, including areas with high vaccination coverage rates in South Sulawesi. Yet, this high coverage was not contributed by every district as happened in Citta District where the coverage of the 3rd dose vaccine is still low at 4.58 %.

Community behavior in receiving vaccinations is a determinant that affects the achievement of the expected target of the 3rd dose of vaccination. Lawrence Green's Behavior Change Theory (1980) explained that behavior change is influenced by three factors, namely predisposing factors such as age, education, occupation, attitudes, actions, and so on. It is supporting factors such as support for access to information facilities and infrastructure—reinforcing factors such as family support and the role of health workers (8).

The study conducted by the Determinants of Community Willingness to Receive COVID-19 Vaccination in Central Sulawesi showed that the factors influencing people's willingness to receive the Central Sulawesi COVID-19 vaccination such as age, occupation, marital status, religion, and ethnicity had a relationship with vaccines acceptance in the community. Meanwhile, based on the logistic regression multivariate test results, it was shown that Supporting factors and religion are the determinants most related to people's willingness to receive the COVID-19 vaccination in Central Sulawesi (9).

Another study regarding the analysis of COVID-19 vaccination acceptance among the community shows that acceptance of vaccines in the community is influenced by knowledge, availability of access to information, and

family support for COVID-19 vaccination acceptance (10).

As one of the areas in Soppeng District with low coverage of the 3rd dose of vaccination, the study aimed to examine the community behavior towards vaccination, especially the relationship between the behavioral determinants and the vaccination acceptance in the community in Citta District, Soppeng Regency.

MATERIALS AND METHODS

This study implemented an analytic observational study with a cross-sectional study design and was conducted in Citta District, Soppeng Regency.

The sample was 333 people. Data was collected from COVID-19 vaccination coverage using questionnaires. Cluster sampling was applied as the sampling technique, with inclusion criteria, namely residents of Citta District, aged 18-60 years, willing to become informants and have carried out the 2nd dose of COVID-19 vaccination.

This study used secondary data from vaccination coverage reports for each sub-district in Soppeng Regency and primary data in the form of a questionnaire containing demographic data and the variables studied.

Granting permission to conduct the study was obtained through a certificate from the Department of Epidemiology, Faculty of Public Health, Hasanuddin University with number: 21273/UN4.14.1/PT.01.04/2023. Further, in conducting this study, the researchers also obtained approval from the Ethic Committee of the Hasanuddin University Health Faculty with the number: 3267/UN4.14.1/TP.01.02/2023 on April 10, 2023.

Data Analysis

Data processing and analysis were carried out using the SPSS version 24 program. Bivariate analysis using the Chi-Square test was implemented to find out which variables

had a significant relationship with COVID-19 vaccination acceptance and multivariate analysis using multiple logistic regression tests with the enter method was also applied to find out which variables were most related to the COVID-19 vaccination acceptance.

RESULTS

Sample Characteristics

Table 1 shows that respondents have almost the same proportion of females (49.8 %) and males (50.2 %). Most of the respondents are aged 18-29 years (15.3 %). Most respondents (36.0 %) did not finish school/elementary school. Most of the respondents (31.5 %) work as housewives.

Table 1
Respondents' Demographic Characteristics

Characteristics	N	%
Gender		
Male	167	50.2
Female	166	49.8
Age group (Year)		
<=29	148	44.4
30-49	134	40.2
>=50	51	15.3
Level of determinant o		
Primary education	120	36.0
Secondary Education	103	30.9
Higher Education	51	15.3
Undergraduate/ Bachelor/Master	59	17.7
Occupation		
Farmer	92	27.6
Civil Servant	32	9.6
Employed in the private sector	70	21.0
Learner	34	10.2
Housewife	105	31.5
Booster Vaccine Acceptance		
Yes	133	39.9
No	200	60.1

Table 2 shows that most of the respondents (75.1 %) have less knowledge about receiving booster vaccines. This study also found that most respondents (63.1 %) had a poor attitude regarding receiving booster vaccines. Most of

the respondents (73.9 %) had good access to information about booster vaccine acceptance and some respondents (45.9 %) considered the role of health workers to be good about booster vaccine acceptance.

Table 2
Distribution of Respondents Based on Research Variables

Independent Variable	Total n = 333	Percentage (%)
Knowledge		
Good	83	24.9
Poor	250	75.1
Attitude		
Good	123	36.9
Poor	210	63.1
Access to Information		
Good	246	73.9
Poor	87	26.1
Family Support		
Good	64	19.2
Poor	269	80.8
Role of Health Workers		
Good	153	45.9
Poor	180	54.1

Table 3 indicates that access to information and the role of health workers are significantly related to booster vaccine acceptance. While for gender, education, employment status, knowledge, attitudes, and family support variables, there is no significant relationship with booster vaccine acceptance.

Access to information is significantly related to booster vaccine acceptance with a p-value of 0.013. Most respondents (62.4 %) had good access to information, but they did not receive booster vaccines. In addition to access to information, the role of health workers is also significantly related to booster vaccine acceptance with a p-value of 0.003. Most of the respondents (49.0 %) considered the health workers had a good role and they received booster vaccines. In addition, most women (62.7 %) chose not to receive booster vaccines, while most respondents (41.3 %) with less family support received booster vaccines.

BEHAVIORS LINKED TO THE ACCEPTANCE OF VACCINATIONS

Table 3
Relationship between Independent Variables and Dependent Variables

Independent Variable	COVID-19		Vaccines Acceptance		Total		p-value
	Succeed		Not Succeed		n	%	
	n	%	n	%			
Gender							
Male	71	42.5	96	57.5	167	100	0.395
Female	62	37.3	104	62.7	166	100	
Level of Education							
No study/primary education	46	38.3	74	61.7	120	100	0.883
Secondary education	43	41.7	60	58.3	103	100	
Higher education	22	43.1	29	56.9	51	100	
Undergraduate/ Bachelor/Master	22	37.3	37	62.7	59	100	
Occupation							
Farmer	42	45.7	50	54.3	92	100	0.086
Civil Servant	12	37.5	20	62.5	32	100	
Employed in the private sector	27	38.6	43	61.4	70	100	
Student	19	55.9	15	44.1	34	100	
Housewife	33	31.4	72	68.6	105	100	
Knowledge							
Good	38	45.8	45	54.2	83	100	0.261
Poor	95	38.0	155	62.0	250	100	
Attitude							
Good	54	43.9	69	56.1	123	100	0.311
Poor	79	37.6	131	62.4	210	100	
Action							
Good	21	32.8	43	67.2	64	100	0.249
Poor	112	41.6	157	58.4	269	100	
Access to Information							
Good	88	35.8	158	62.4	246	100	0.013
Poor	45	51.7	42	48.3	87	100	
Family Support							
Good	22	34.4	42	65.6	64	100	0.385
Poor	111	41.3	158	58.7	269	100	
Role of Health Worker							
Good	75	49.0	78	51.0	153	100	0.003
Poor	58	32.2	122	67.8	180	100	

Table 4 shows that access to information and the role of health workers are most related to booster vaccine acceptance, while work and knowledge are not significantly related to booster vaccine acceptance.

This study found that access to information has a value of $p=0.004$ with an OR value of 2.129 greater than 1 which is a risk factor and significant because the lower value is 1.272 and the upper is 3.563 which does not contain a value

of 1. This can be explained since respondents who can access information have 2,129 times the risk of not receiving the COVID-19 vaccine. The health worker role variable has a value of $p = 0.001$ with an OR value of 0.444 where less than 1 is a protective factor and is significant because the lower value is 0.278 and the upper is 0.707 which does not contain a value of 1. This means that respondents who do not feel the role of health workers have 0.444 times the risk of not receiving the COVID-19 vaccine.

Table 4

Results of Multivariate Analysis of Behavioral Determinants with Acceptance of COVID-19 Vaccination

Variables	B	Sig.	Exp (B)	95% CI	
				Lower	Upper
Occupation	-0.117	0.121	0.889	0.767	1.031
Knowledge	-0.034	0.902	0.966	0.560	1.668
Access to Information	0.756	0.004	2.129	1.272	3.563
Role of Health Worker	-0.813	0.001	0.444	0.278	0.707

DISCUSSION

This study found that the variables of access to information and the role of health workers were related to COVID-19 vaccination acceptance in Citta District. In line with this study, a study on acceptance of the COVID-19 vaccine conducted in Saudi Arabia shows that health workers and the mass media have been identified as important sources of health information for the general public in the acceptance of the COVID-19 vaccine (11).

A study conducted in India regarding acceptance and concerns about the COVID-19 vaccine showed that around 42 % reported having received knowledge about vaccination through print media and 55 % through social media (12). This is in line with this study where it is known that access to information is related to the COVID-19 vaccination acceptance in Citta District Soppeng Regency in which 62.4 % of respondents with good access to information did not receive booster vaccines due to the large amount of information circulating about the adverse effects of vaccines and the community's inability to filter the information obtained. In concordance with this, a study conducted on acceptance and attitudes toward COVID-19 vaccines: A cross-sectional study from Jordan, shows that mistrust of any source of information about COVID-19 is 0.271 greater (13).

The local government according to district policy conducts mobile vaccinations aimed at those who have limited access to the nearest health service to carry out vaccinations accompanied by the Indonesian Army and Police. This was carried out as an effort to deal with problems

related to access to information for booster vaccine acceptance and as an effort to accelerate the handling of COVID-19 in Citta District as well as reaching a wider range of residents who have limited access to health services.

The media is a party that should provide a valid source in educating the public about the COVID-19 vaccination because misinformation that spreads through various media channels can have a major impact on acceptance of the COVID-19 vaccine. In addition, sources of misinformation and conspiratorial beliefs spread through various media channels can also reduce the acceptance of the COVID-19 vaccine.

The role of health workers in driving factors is to encourage someone to act. Based on this study, it is known that the role of health workers has a relationship with COVID-19 vaccination acceptance in Citta District. These results are in line with a study conducted by the Ministry of Health, which found that around 79 % of respondents trusted more on health workers and medical workers 57 % seeking information about everything related to vaccinations. About 54 % of the most trusted sources of information about the COVID-19 vaccine are healthcare providers and health workers (13). Therefore, they can also maximize the role of health workers in conveying information about the COVID-19 vaccination.

These findings are against the results found in a previous study conducted by Rawung et al., who found that the role of health workers has no relationship with acceptance of the COVID-19 vaccination because the role of health workers can be replaced by social media which currently greatly influences a person's actions (14). However, in a study conducted by

Motta et al. (15), doctors and other health workers were identified as potential communicators in conveying messages that emphasized the medical and social benefits of the COVID-19 vaccine that could be disseminated effectively. Therefore, health workers must be careful in encouraging public confidence in the COVID-19 vaccination and minimizing misinformation, because refusal of vaccines can strengthen an outbreak (16).

Based on further analysis, the study found that access to information is a risk factor that influences booster vaccine acceptance, and the role of health workers is protective of booster vaccine acceptance in Citta District, Soppeng Regency. In line with this, government programs should aim at developing effective COVID-19 vaccination strategies, including tailor-made communication approaches, to ensure that all people in all locations have access to accurate information about vaccine safety and effectiveness.

Soppeng District government program such as door-to-door vaccination needs to be carried out, apart from involving health workers as vaccination officers. The involvement of health workers as a means of information can also be fulfilled, considering the level of public trust in the role of health workers is quite good.

This is in line with research conducted by UNICEF where the community makes health workers or medical staff a determinant in making decisions to vaccinate against COVID-19, followed by the role of family members in influencing vaccine acceptance (17). Nuzhath et al. found that misinformation was the main factor influencing people's acceptance of vaccinations. There were 32.47% of respondents who were not willing to receive vaccinations due to misinformation obtained through the mass media (18). With these results of the study, it is expected that future government programs will target how to provide access to accurate and reliable information to the public through the utilization of existing health human resources.

In addition to supporting the desired acceleration, the factors utilization such as human resources by involving vaccinators from primary level health facilities to hospitals, availability

of vaccines, distribution, and ease of access to vaccinations as well as assistance from related parties such as the Indonesian Army and Police should be carried out.

CONCLUSIONS AND RECOMMENDATIONS

Access to information and the role of health workers are the variables most related to the COVID-19 vaccination acceptance in Citta District, Soppeng Regency. Access to information in research is a risk factor and the role of officers is protective.

This is closely related to misinformation circulating in the community obtained from unreliable sources. It is important the role of health workers to provide education and explanations of information regarding news related to the COVID-19 vaccine circulating in the community and to collaborate with the government to provide accurate information media so that it can be accessed by the community. Thus, there are no errors in receiving information in the community, and this can help accelerate the handling of COVID-19 in Citta District, Soppeng Regency

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REFERENCES

1. World Health Organization. COVID-19 Response Fund WHO Coronavirus (COVID-19) Dashboard. 2021. Available from: <https://covid19.who.int/table>
2. Ministry of Health, Directorate General of Disease Prevention and Control, Directorate of Surveillance and Health Quarantine. Emerging Infections: Latest Official Information Media on Emerging Infectious Diseases. Jakarta; 2021. Available from: <https://infeksiemerging.kemkes.go.id/dashboard/COVID-19>

3. Dinar RE. COVID-19 Vaccine the Mandatory Book You Need to Know. In: Prabawati TA, editor. Yogyakarta: Rapha Publishing; 2021.
4. Palutturi S, Syam A, Arifin MA, Asnawi A. COVID-19 Indonesia Needs Us. Yogyakarta: Learning Library; 2020.
5. Ministry of Health. National COVID-19 vaccination. 2021. Available from: <https://vaksin.kemkes.go.id/#/vaccines>
6. Indonesian Ministry of Health. Current Situation of Coronavirus Disease (COVID-19) Development April 23, 2021. *Emerging Infections*. 2021. Available from: <https://covid19.kemkes.go.id/situasi-infeksi-emerging/situasi-terkini-perkembangan-coronavirus-disease-COVID-19-23-april-2021>
7. Government of Soppeng Regency. Achievement of COVID-19 Vaccination in Soppeng Regency on March 30, 2022. Soppeng; 2022.
8. Green LW, Kreuter M, Deeds SG, Partridge KB. Health education planning: A diagnostic approach. In: *Health education planning: A diagnostic approach*. 1980.p.306.
9. Ichsan DS, Hafid F, Ramadhan K, Taqwin T. Determinants of Community Willingness to receive COVID-19 Vaccination in Central Sulawesi. *Poltekita J Health Science*. 2021;15(1):1-11.
10. Lasmita Y, Misnaniarti M, Idris H. Analysis of Acceptance of COVID-19 Vaccination among the Community. *J Kesmas (Public Health) Khatulistiwa*. 2021;8(4):195.
11. Qattan AMN, Alshareef N, Alsharqi O, Al Rahahleh N, Chirwa GC, Al-Hanawi MK. Acceptability of a COVID-19 Vaccine Among Healthcare Workers in the Kingdom of Saudi Arabia. *Front Med*. 2021;8:1-12.
12. Anil A, Sharafudeen S, Krishna A, Rajendran R, James J, Kuruvilla S, et al. Acceptance and concerns regarding COVID-19 vaccine in Kerala, India. *Public Heal Toxicol*. 2021;1(1):1-6.
13. El-Elimat T, AbuAlSamen MM, Almomani BA, Al-Sawalha NA, Alali FQ. Acceptance and attitudes toward COVID-19 vaccines: A cross-sectional study from Jordan. *PLoS One*. 2021;16(April 4):1-15.
14. Rawung GM, Kaunang WPJ, Mantjoro EM. The Relationship of Knowledge, Family Support, and the Role of Health Workers with the Acceptance of COVID-19 Vaccination by The Community in the Paniki Bawah District. *Prepotif. J Public Health*. 2023;7(1):727-740.
15. Encouraging COVID-19 Vaccine Uptake Through Effective Health Communication. *Front Polit Sci*. 2021;3:1-12.
16. Malik AA, McFadden SAM, Elharake J, Omer SB. Determinants of COVID-19 vaccine acceptance in the US. *E Clin Med*. 2020;26:100495.
17. Pane M, Windyaningsih C. Puskesmas and Health Offices in Controlling the COVID-19 Pandemic Ministry of Health of the Republic of Indonesia Jakarta 2020. 2020.
18. Nuzhath T, Tasnim S, Sanjwal RK, Trisha NF, Rahman M, Mahmud SMF, et al. COVID-19 vaccination hesitancy, misinformation and conspiracy theories on social media: A content analysis of Twitter data. 2020.

Infective Endocarditis in the Colombian Caribbean Region: Clinical Profile, Microbiological Insights, and Risk Factors for Mortality

Endocarditis Infecciosa en la Región Caribe Colombiana: Perfil Clínico, Conocimientos Microbiológicos y Factores de Riesgo de Mortalidad

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SUMMARY

Background: Infective endocarditis (IE) is defined as the infectious and inflammatory process of the heart's internal structures. It can be caused by a broad group of bacteria and, rarely, fungi, with potentially life-threatening consequences. **Objective:** To profile bacterial resistance and identify mortality risk factors in IE patients. **Methods:** This cross-sectional study included clinically diagnosed IE patients. Sociodemographic, comorbidity, clinical, and microbiological data were recorded. Descriptive analyses, Chi-Square/Fisher's exact tests, and Student's *t*-tests examined variables in relation to IE outcomes (survival vs. mortality). Multivariate logistic regression calculated odds ratios and confidence intervals. **Results:** We enrolled 39 patients (mean age

51 ± 19.5 years, 54 % male). Common comorbidities included acute kidney injury (AKI) (46 %), heart failure (26 %), and ischemic stroke (21 %). Deceased patients had higher rates of fatigue ($p=0.03$), lower limb edema ($p=0.01$), and AKI ($p=0.01$) than survivors. Fifteen (38 %) patients had positive cultures; *Staphylococcus aureus* predominated in survivors (13 %) and deceased (13 %) patients ($p=0.06$). Multi-drug-resistant bacteria were found in six (15 %) patients, and one (2.6 %) had Extensively Drug-Resistant bacteria. Multivariate Logistic Regression indicated that lower limb edema (OR 8.6, 95 % CI 1.5–49, $p=0.01$), and AKI (OR 7.8, 95 % CI 1.65–37.2, $p=0.01$) increased mortality risk in IE patients. **Conclusion:** In this study, lower limb edema and AKI were significant predictors of mortality in IE patients, emphasizing their clinical importance in IE progression and resolution. Further research should explore additional variables and risk factors to enhance our ability to predict and manage outcomes in this population.

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RESUMEN

Antecedentes: La endocarditis infecciosa (EI) se define como el proceso infeccioso e inflamatorio de las estructuras internas del corazón. Puede ser causada por un amplio grupo de bacterias y, rara vez, por hongos, con consecuencias potencialmente mortales. **Objetivo:** perfilar la resistencia bacteriana e identificar factores de riesgo de mortalidad en pacientes con EI. **Métodos:** Este estudio transversal incluyó pacientes con EI clínicamente diagnosticada. Se registraron datos sociodemográficos, de comorbilidad, clínicos y microbiológicos. Los análisis descriptivos, las pruebas de Chi-Cuadrado/exactas de Fisher y las pruebas t de Student examinaron las variables en relación con los resultados de IE (supervivencia versus mortalidad). La regresión logística multivariada calculó los Odds ratios y los intervalos de confianza. **Resultados:** Se incluyeron 39 pacientes (edad media $51 \pm 19,5$ años, 54 % hombres). Las comorbilidades comunes incluyeron lesión renal aguda (IRA) (46 %), insuficiencia cardíaca (26 %) y accidente cerebrovascular isquémico (21 %). Los pacientes fallecidos tuvieron tasas más altas de fatiga ($p=0,03$), edema de miembros inferiores ($p=0,01$) y IRA ($p=0,01$) que los supervivientes. Quince (38 %) pacientes tuvieron cultivos positivos; *Staphylococcus aureus* predominó en los pacientes sobrevivientes (13 %) y fallecidos (13 %) ($p=0,06$). Se encontraron bacterias multirresistentes en seis (15 %) pacientes y uno (2,6 %) tenía bacterias extremadamente resistentes a los medicamentos. La regresión logística multivariada indicó que el edema de las extremidades inferiores (OR 8,6, IC 95 % 1,5–49, $p = 0,01$) y la IRA (OR 7,8, IC 95 % 1,65–37,2, $p = 0,01$) aumentaron el riesgo de mortalidad en pacientes con EI. **Conclusión:** En este estudio, el edema de las extremidades inferiores y la IRA fueron predictores significativos de mortalidad en pacientes con EI, enfatizando su importancia clínica en la progresión y resolución de la EI. Investigaciones adicionales deberían explorar variables y factores de riesgo adicionales para mejorar nuestra capacidad de predecir y gestionar los resultados en esta población.

Palabras clave: Endocarditis infecciosa, resultado, resistencia antimicrobiana, insuficiencia cardíaca.

INTRODUCTION

Infective endocarditis (IE) is a disease that primarily affects internal structures of the heart, such as the cardiac endothelium itself, as well as native or prosthetic valves, resulting from a bacterial or fungal infection. Its presentation can

range from acute to subacute (1). It is closely associated with healthcare practices, with the placement of central venous catheters and dental procedures being among the leading risk factors for developing this cardiac infection. However, patients with intravenous drug use, congenital defects, degenerative heart diseases, among others, can also develop IE (2–4).

Complications arising from IE can be catastrophic and result in high morbidity and mortality, despite its diagnosis and management having been established in clinical practice guidelines for several years (5). Additionally, these complications impose significant costs on the healthcare system, as they lead to physical disabilities that can impact the employment status of those affected and their substantial socioeconomic burden on the population. Hospital-acquired infections follow a more severe and increasing pattern in terms of occurrence, mainly due to the frequent need for invasive procedures in complicated patients who require closer monitoring of their condition (6–8).

IE primarily affects middle-aged individuals, with an average age of 55 years, and the gender distribution is marked by 68 % in males and 32 % in females. At the time of diagnosis, up to 40 % of patients with IE have no comorbidities. However, up to 10% of patients diagnosed with congestive heart failure can have IE (8). This is likely due to valvular anatomy degeneration; nevertheless, the epidemiological profile of this disease is not yet clearly understood (9).

In Latin America, including Colombia, it was observed that IE predominantly affects males in up to 68.5 % of the cases. Valvulopathies were the most frequent risk factor (24.3 %). Regarding microbiological characteristics, the most prevalent isolated microorganisms were *Staphylococcus aureus* (27.3 %), followed by viridans group streptococci (VGS) in up to 26.7 % of the cases with IE (10).

In the Colombian Caribbean Region, especially in Barranquilla city, epidemiological reports of IE are outdated and scarce. This implies that establishing the infectious profile of a rare but necessary pathology can be complex. This study aimed to characterize the bacterial resistance profile in patients diagnosed with infective endocarditis at a hospital reference

center in Barranquilla and to identify risk factors associated with mortality in this population.

METHODS

A cross-sectional study was conducted, enrolling clinically diagnosed IE patients hospitalized at a reference hospital center in Barranquilla, Atlántico, Colombia between 2017 and 2022. Sociodemographic, comorbidity, and clinical characteristics were collected. A database was designed, incorporating admission data, and this information was cross-referenced with culture data.

Data distribution was assessed using the Shapiro-Wilk test, confirming the parametric nature of the data for subsequent analysis. Measures of central tendency (mean and standard deviation) were calculated for quantitative variables, while for categorical variables, absolute and relative frequencies were determined. Means obtained by patients were compared based on the outcome (Survivor vs. Deceased) using the Student's t-test. The Chi-Square test or Fisher's exact test was employed to analyze categorical variables, depending on the distribution compliance of the categories.

A multivariate logistic regression model was constructed to identify potential risk factors for mortality. The model was selected and adjusted using the Backward method, considering the minimum number of variables necessary. Adjusted Odds Ratios were reported along with 95 % confidence intervals. A p-value < 0.05 was considered statistically significant. The statistical software used in this study was R-CRAN VERSION 4.3.0 (11).

RESULTS

Thirty-nine patients with IE were enrolled in the study. The average age was 51 ± 19.5 years. The most common age group was adults (44 %) (27 - 59 years) (Table 1). In this study, 54 % of the patients were male, with a male-to-female ratio of 6 to 5. No significant difference was

found between age and sex ($p=0.8$) (Figure 1). Acute kidney injury (AKI) (49 %) was the most common comorbidity, followed by heart failure (26 %) and ischemic stroke (21 %) (Table 1).

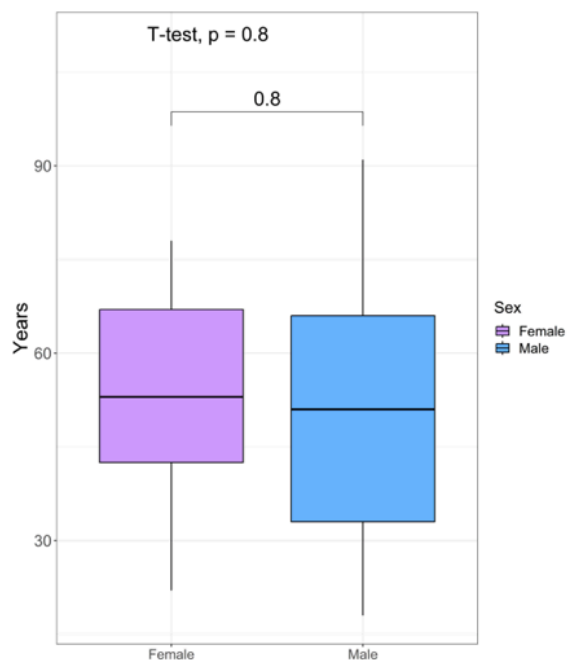


Figure 1. Distribution of the age (in years) of patients with IE by gender.

Comorbidities and Outcomes

In this study, we compared the frequency of comorbidities in patients with IE based on the outcome (Survivors vs. Deceased) (Table 1). No significant differences were identified in the frequency of ischemic stroke ($p = 0.7$), hemorrhagic stroke ($p = 0.4$), heart failure ($p = 0.5$), pulmonary embolism ($p = 0.4$), and splenomegaly ($p = 0.4$) between survivors and deceased cases. However, a notable association was observed between AKI and mortality, with a higher prevalence in deceased patients (73 % vs. 33 %, $p = 0.02$) (Figure 2) (Table 1).

Table 1

Sociodemographic Characteristics and Comorbidities in Survivor vs. Deceased Patients with Infective Endocarditis

Characteristic	Overall (n=39) ¹	Deceased (n=15) ¹	Survivor (n=24) ¹	p-value
Age	51 ± 19.5	54 ± 20.6	50 ± 17	0.6 ²
Sex				>0.9 ³
Female	18 (46 %)	7 (47 %)	11 (46 %)	
Male	21 (54 %)	8 (53 %)	13 (54 %)	
Age Group				0.6 ⁴
Adulthood	17 (44 %)	7 (47 %)	10 (42 %)	
Elderly	16 (41 %)	7 (47 %)	9 (38 %)	
Youth	6 (15 %)	1 (6.7 %)	5 (21 %)	
Comorbidities and clinical findings				
HF	10 (26 %)	5 (33 %)	5 (21 %)	0.5 ⁴
IS	8 (21 %)	4 (27 %)	4 (17 %)	0.7 ⁴
ICH	1 (2.6 %)	1 (6.7 %)	0 (0 %)	0.4 ⁴
Abscesses	1 (2.6 %)	0 (0 %)	1 (4.2 %)	>0.9 ⁴
Pulmonary Embolism	1 (2.6 %)	1 (6.7 %)	0 (0 %)	0.4 ⁴
AKI	19 (49 %)	11 (73 %)	8 (33 %)	0.015 ³
Splenomegaly	1 (2.6 %)	1 (6.7 %)	0 (0 %)	0.4 ⁴

HF: Heart failure, IS: Ischemic Stroke, ICH: Intracerebral Hemorrhage, AKI: Acute Kidney Injury

¹ Mean (SD); n (%)

² Welch Two Sample t-test

³ Pearson's Chi-Squared test

⁴ Fisher's exact test

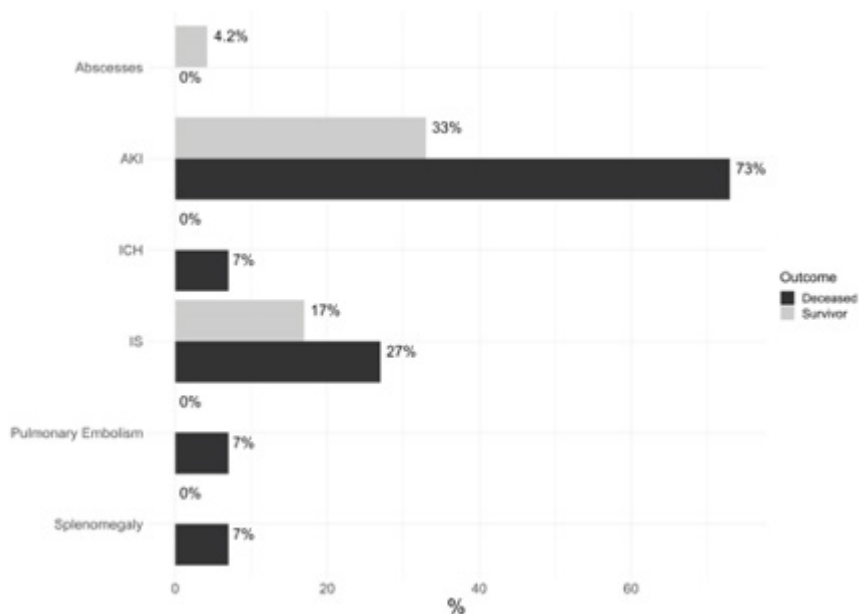


Figure 2. Comorbidities and clinical findings in patients with IE according to outcome

Clinical and Echocardiographic Manifestations

Table 3 presents a summary of the primary clinical and echocardiographic findings in patients with infective endocarditis, categorized by the outcome. In terms of clinical manifestations, a notably higher proportion of deceased patients exhibited fatigue (71 % vs. 100 %, p = 0.03) and lower limb edema (60 % vs. 21 %, p = 0.01) compared to survivors. However, no significant differences were detected in left ventricular ejection fraction between survivors and deceased patients (53.2 ± 10.3 vs. 52.1 ± 15.2, p = 0.8) (Figure 3). Similarly, there were no significant disparities in the affected heart valves, as the mitral, aortic, mitral, and tricuspid valves displayed similar frequencies across both groups (p > 0.05) (Table 2).

Microbiological Profile and Bacterial Resistance

Microbiological characterization of patients with IE is summarized in Table 4. There were no significant differences observed in culture positivity between survivors and deceased individuals (29 % vs. 53 %, p = 0.18) (Table 3) (Figure 4). *Staphylococcus aureus* (13 %) was the most frequently isolated microorganism in both groups. No significant differences were found in the distribution of isolated microorganisms between the groups. Regarding the resistance profile, there were no significant differences observed in sensitivity or resistance to antimicrobials (p > 0.05). Specifically for resistance, two cases of *methicillin-resistant Staphylococcus aureus* (MRSA) were identified in each group for MDR (Multidrug Resistance), along with one case of *methicillin-resistant Staphylococcus aureus* (MRSA) with the *mecA* gene in the deceased group. Furthermore, one case of extensively drug-resistant (XDR) bacteria was identified in the deceased group (Table 3).

Table 2
Clinical and Echocardiographic Manifestations in Surviving vs. Deceased Patients with Infective Endocarditis

	Characteristic	Overall (n=39) ¹	Deceased (n=15) ¹	Survivor (n=24) ¹	p-value
Clinical Manifestations	Arthralgia	8 (21 %)	4 (27 %)	4 (17 %)	0.7 ²
	Myalgia	4 (10 %)	2 (13 %)	2 (8.3 %)	0.6 ²
	Dyspnea	24 (62 %)	11 (73 %)	13 (54 %)	0.2 ³
	Fatigue	32 (82 %)	15 (100 %)	17 (71 %)	0.031 ²
	Edema	14 (36 %)	9 (60 %)	5 (21 %)	0.013 ³
	ACS	9 (23 %)	2 (13 %)	7 (29 %)	0.4 ²
	Chills	10 (26 %)	3 (20 %)	7 (29 %)	0.72
Echocardiography	EF	52 ± 12	52.1 ± 15.2	53.2 ± 10.3	0.8 ⁴
	EF Categories				0.9 ³
	HFpEF	24 (62 %)	9 (60 %)	15 (63 %)	
	HFrEF	15 (38 %)	6 (40 %)	9 (38 %)	
	Affected Heart Valve				>0.9 ²
	Aortic	3 (18 %)	1 (14 %)	2 (20 %)	
	Mitral	7 (41 %)	3 (43 %)	4 (40 %)	
	Mitral y Aortic	5 (29 %)	2 (29 %)	3 (30 %)	
Tricuspid	2 (12 %)	1 (14 %)	1 (10 %)		

EF: Ejection Fraction, HFpEF: Heart failure with preserved ejection fraction, HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction

¹ n (%); Mean ± SD

² Fisher’s exact test

³ Pearson’s Chi-Square test

⁴ Welch Two Sample t-test

Table 3

Microbiological Characterization in Surviving vs. Deceased Patients with Bacterial Endocarditis

Characteristic	Overall (n=39) ¹	Deceased (n=15) ¹	Survivor (n=24) ¹	p-value
Culture				0.13 ²
Negative	24 (62 %)	7 (47 %)	17 (71 %)	
Positive	15 (38 %)	8 (53 %)	7 (29 %)	
Microbial Profile				0.06 ³
<i>Enterobacter cloacae</i>	1 (2.6 %)	1 (6.7 %)	0 (0 %)	
<i>Enterococos faecalis</i>	3 (7.7 %)	3 (20 %)	0 (0 %)	
<i>Klebsiella pneumoniae</i>	1 (2.6 %)	1 (6.7 %)	0 (0 %)	
<i>Pseudomonas aeruginosa</i>	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
<i>Staphylococcus aureus</i>	5 (13 %)	2 (13 %)	3 (13 %)	
<i>Staphylococcus lentus</i>	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
<i>Staphylococcus saprophyticus</i>	1 (2.6 %)	1 (6.7 %)	0 (0 %)	
<i>Stenotrophomona maltophila</i>	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
<i>Streptococcus bovis</i>	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
AMR				0.4 ³
MDR	6 (15 %)	3 (20 %)	3 (13 %)	
XDR	1 (2.6 %)	1 (6.7 %)	0 (0 %)	

AMR: Antimicrobial Resistance, MDR: Multi-Drug Resistant, XDR: Extensively Drug-Resistant

¹ n (%)

² Pearson's Chi-Square test

³ Fisher's exact test

Risk Factors for Mortality

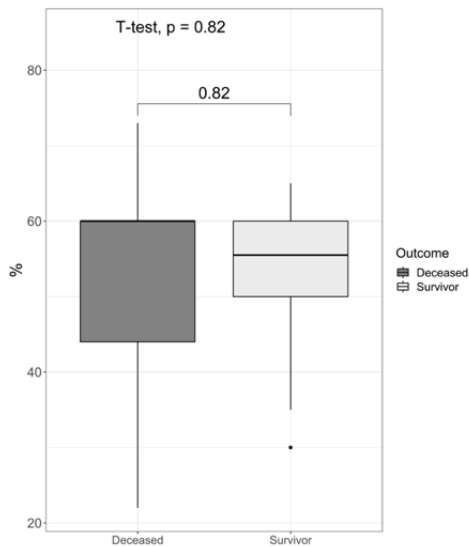


Figure 3. Left ventricular ejection fraction.

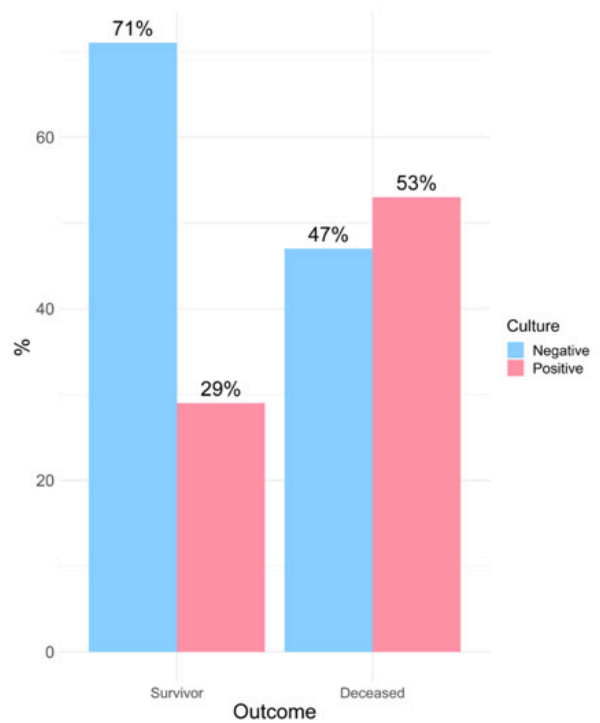


Figure 4. Culture positivity and negativity in survivors and deceased IE patients.

INFECTIVE ENDOCARDITIS IN THE COLOMBIAN CARIBBEAN REGION

In the multivariate logistic regression analysis, we assessed several factors with mortality outcomes in patients with IE. Following model adjustments, our results revealed that edema (OR 8.6, 95 % CI 1.5 – 49, $p = 0.01$) and AKI (OR 7.8, 95 % CI 1.65 – 37.2, $p = 0.01$)

significantly elevated the risk of mortality among IE patients (Table 4). No statistically significant associations were identified in variables related to microbiological, echocardiographic, or antimicrobial resistance factors.

Table 4
Results of the logistic regression multivariable model

Characteristic	n	OR1	95% CI1	p-value	Adjusted OR1*	95% CI1	p-value
Age	39	1.01	0.98, 1.05	0.5			
Sex	39						
Male		0.97	0.26, 3.59	>0.9			
Age Group	39						
Elderly		1.11	0.28, 4.50	0.9			
Youth		0.29	0.01, 2.32	0.3			
Edema	39						
Yes		5.70	1.43, 25.8	0.017	8.6	1.5, 49	0.01
AKI	39						
Yes		5.50	1.41, 25.4	0.019	7.8	1.65, 37.2	0.01
HF	39						
Yes		1.90	0.43, 8.44	0.4			
EF Category	39						
HFrEF		1.11	0.29, 4.19	0.9			
Affect Heart Valve	17						
Mitral		1.50	0.09, 42.1	0.8			
Mitral y Aortic		1.33	0.07, 41.6	0.9			
Tricuspid		2.00	0.04, 120	0.7			
Culture	39						
Positive		2.78	0.74, 11.1	0.14			

AKI: Acute kidney injury, EF: Ejection fraction, HF: Heart failure, HFrEF: Heart failure with reduced ejection fraction

* Adjusted by Backward method

1 OR = Odds Ratio, CI = Confidence Interval

DISCUSSION

Staphylococcus aureus was the most frequently isolated microorganism, and no differences were observed in culture positivity or the distribution of isolated microorganisms between the groups. Cases of methicillin resistance and MRSA were identified in the deceased group. Finally, in the multivariate logistic regression model, the presence of lower limb edema was found to increase the likelihood of mortality in patients with Bacterial Endocarditis. These findings underscore the significance of edema and AKI

as risk factors in the outcome and mortality of patients with IE.

One of the key findings of this study is the sociodemographic and clinical profile of patients with infective endocarditis. With a sample of 39 patients, an average age of 51 years was identified, with the adult patient group (44 %) being the most frequent. These results support the notion that IE can affect a wide range of ages, although it appears to be more common in adults. The absence of significant differences in patient gender suggests that this disease does not exhibit a marked gender preference (12,13).

The comorbidities identified in the study population shed light on concurrent medical conditions in patients with IE. The most prevalent comorbidities included AKI, heart failure, and ischemic stroke. These findings are consistent with existing medical literature, highlighting how preexisting medical conditions can increase susceptibility to developing infective endocarditis and complicate its clinical management (14,15).

The results showed that there were no significant differences in the frequency of comorbidities between survivors and deceased individuals, except in the case of AKI. This suggests that the presence of AKI could serve as a predictive indicator of a worse prognosis in IE patients. This could have significant implications in the assessment and management of patients with this disease, allowing for early identification of cases at higher risk and more intensive medical care (9,16).

The significant association between lower limb edema and mortality is another notable finding. This observation underscores the existence of serious complications related to the cardiovascular or renal system in patients with IE who present lower limb edema. It indicates that the presence of lower limb edema could be linked to the progression of the disease or the development of severe complications, which could explain its association with mortality (9).

It is noteworthy that no significant differences were found in most clinical and echocardiographic manifestations between surviving and deceased patients. This finding might suggest that, in general, clinical, and echocardiographic features are not definitive predictors of mortality risk in patients with IE. However, one aspect to highlight is the identification of significant associations between specific symptoms and the fatal outcome. In particular, the significant relationship between fatigue and mortality raises the possibility that other factors may influence the deterioration of patients' conditions and their lack of response to treatment in these cases (14,15).

The predominant presence of *Staphylococcus aureus* as the most frequently isolated microorganism in both groups, survivors, and deceased, highlights the importance of this pathogen in the etiology of IE in the region. This finding supports existing literature,

which also emphasizes the relevance of *Staphylococcus aureus* in cardiac infections (17-19). No significant differences were observed in culture positivity or the distribution of isolated microorganisms between the groups of survivors and deceased individuals, this could indicate that the presence of certain pathogens may not be a determining factor in the mortality associated with infective endocarditis. This raises the possibility that other clinical factors, such as the severity of the infection, the patient's immune response, and the effectiveness of treatment, may have a more direct impact on clinical outcomes (20).

The identification of cases of antibiotic resistance in the deceased patient group underscores a concerning trend in bacterial resistance and its association with worse clinical outcomes. These results suggest that antibiotic resistance could play a relevant role in the disease's progression and possibly in the mortality of patients with infective endocarditis. This highlights the ongoing need for monitoring and proper management of bacterial resistance in the clinical context to ensure that treatments are effective and can adequately control infections (21).

The fact that no significant differences were found in the sensitivity or resistance to antimicrobials based on the outcome is an important consideration. This could suggest that, in the context of this research, bacterial resistance was not directly related to the patient's outcomes. However, it is crucial to consider that clinical and therapeutic factors may be interrelated and may have influenced the observed relationship. It is possible that other elements, such as timely antimicrobial therapy and proper disease management, may have mitigated the impact of bacterial resistance in this population (1,22).

Risk factors for mortality in patients with IE are of great interest as they allow for the identification of critical elements that influence clinical outcomes. In this study, a significant result is highlighted through a multivariate logistic regression model: the presence of lower limb edema and AKI are significantly associated with an increased likelihood of mortality in patients with IE. This finding has important implications for clinical practice and the management of patients with infective endocarditis (23). It is

plausible that this clinical manifestation is related to the spread of the infection or the involvement of the cardiovascular system that leads to kidney injury, which could explain its association with increased mortality. These results underscore the need for a comprehensive and vigilant evaluation of patients with endocarditis, especially those presenting clinical signs such as lower limb edema (23,24).

This study highlights the clinical significance of lower limb edema and AKI as critical markers in the progression and resolution of IE. These findings underscore the importance of early detection and intervention in patients presenting with these symptoms, as they are associated with an increased risk of mortality. Additionally, the prevalence of *Staphylococcus aureus*, including multi-drug-resistant and extensively drug-resistant strains, emphasizes the need for vigilant monitoring of bacterial resistance in IE cases. Further research is warranted to explore additional variables and risk factors that may influence the mortality of IE patients, ultimately enhancing our ability to predict and manage adverse outcomes in this population.

Ethics approval and consent to participate

This study was approved by the ethics committee of the clinic where the research was conducted. All procedures were performed under the relevant guidelines and regulations. Written informed consent was obtained from the patients for their participation in this study.

Consent for publication

Written informed consent was obtained from the patients for publication. There are no identifying images or other personal or clinical details of the patient that compromise their anonymity in this manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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REFERENCES

1. Wang A, Gaca JG, Chu VH. Management Considerations in Infective Endocarditis: A Review. *JAMA*. 2018;320(1):72-83.
2. Bussani R, DE-Giorgio F, Pesel G, Zandonà L, Sinagra G, Grassi S, et al. Overview and Comparison of Infectious Endocarditis and Non-infectious Endocarditis: A Review of 814 Autoptic Cases. *In Vivo*. 2019;33(5):1565-1572.
3. Chomette G, Auriol M, Baubion D, de Frejacques C. Non-bacterial thrombotic endocarditis. Autopsy study, clinicopathological correlations (author's transl). *Ann Med Interne (Paris)*. 1980;131(7):443-447.
4. Yallowitz AW, Decker LC. Infectious Endocarditis. *StatPearls*. 2023.
5. Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burri H, et al. 2023 ESC Guidelines for the management of endocarditis. *Eur Heart J*. 2023.
6. Ojha N, Dharmoon AS. Fungal Endocarditis. *StatPearls*. 2023.
7. Nakagawa N. Infective Endocarditis in Congenital Heart Disease. In: *Endocarditis - Diagnosis and Treatment*. IntechOpen; 2022.
8. Moreno AR, Sánchez MA, Domínguez JCC, Rubio JRS, Vallés Belsué F, Calvo FT. Endocarditis por hongos en pacientes no adictos a drogas por vía parenteral. Nuestra experiencia en 10 años. *Rev Española Cardiol*. 2000;53(4):507-510.
9. Keynan Y, Rubinstein E. Pathophysiology of infective endocarditis. *Curr Infect Dis Rep*. 2013;15(4):342-346.
10. Alvarado Rubio E, Brugada Molina R, Alvarado Ávila E, González Mora A, González López A. Infective Endocarditis: Inflammatory Response, Genetic Susceptibility, Oxidative Stress, and Multiple Organ Failure. In: *Infective Endocarditis*. IntechOpen. 2019.

11. R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.
12. ten Hove D, Slart RHJA, Sinha B, Glaudemans AWJM, Budde RPJ. 18F-FDG PET/CT in Infective Endocarditis: Indications and Approaches for Standardization. *Curr Cardiol Rep.* 2021;23(9):130.
13. Gupta R, Kaushal V, Goyal A, Kumar P, Gupta D, Tandon R, et al. Changing microbiological profile and antimicrobial susceptibility of the isolates obtained from patients with infective endocarditis – The time to relook into the therapeutic guidelines. *Indian Heart J.* 2021;73(6):704-710.
14. Perek S, Nussinovitch U, Sagi N, Gidron Y, Raz-Pasteur A. Prognostic implications of ultra-short heart rate variability indices in hospitalized patients with infective endocarditis. Tekleab AM, editor. *PLoS One.* 2023;18(6):e0287607.
15. Liesman RM, Pritt BS, Maleszewski JJ, Patel R. Laboratory Diagnosis of Infective Endocarditis. Kraft CS, editor. *J Clin Microbiol.* 2017;55(9):2599-2608.
16. McDonald JR. Acute Infective Endocarditis. *Infect Dis Clin North Am.* 2009;23(3):643-664.
17. Lagier J-C, Létranchant L, Selton-Suty C, Nloga J, Aissa N, Alauzet C, et al. *Staphylococcus aureus* bacteremia and endocarditis. *Ann Cardiol Angeiol (Paris).* 2008;57(2):71-77.
18. Petti CA, Fowler VG. *Staphylococcus aureus* bacteremia and endocarditis. *Cardiol Clin.* 2003;21(2):219-233, vii.
19. Khalid N, Shlofmitz E, Ahmad SA. Aortic Valve Endocarditis. *StatPearls.* 2023. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26341945>
20. Murray RJ. *Staphylococcus aureus* infective endocarditis: Diagnosis and management guidelines. *Intern Med J.* 2005;35(Suppl 2):S25-S44.
21. Correction to Comparative effectiveness of β -lactams for empirical treatment of methicillin-susceptible *Staphylococcus aureus* bacteremia: a prospective cohort study. *J Antimicrob Chemother.* 2023;78(7):1811.
22. Chopra T, Kaatz GW. Treatment strategies for infective endocarditis. *Expert Opin Pharmacother.* 2010;11(3):345-360.
23. Ioannou P. Special Issue “Infective Endocarditis: What Is New in the Clinical Research?”. *J Clin Med.* 2023;12(15).
24. Keynan Y, Singal R, Kumar K, Arora RC, Rubinstein E. Infective endocarditis in the intensive care unit. *Crit Care Clin.* 2013;29(4):923-951.

Trazando el Rumbo hacia la Inmunización: Explorando las Creencias, Actitudes, Desafíos y Estrategias de Vacunación en Estudiantes Universitarios ante la COVID-19

Paving the Way to Immunization: Exploring Beliefs, Attitudes, Challenges, and Vaccination Strategies Among University Students in the Face of COVID-19

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RESUMEN

La pandemia de la COVID-19 ha tenido un profundo impacto en la sociedad y en los estudiantes universitarios con la vacunación emergiendo como una herramienta esencial para enfrentarla. No obstante, la aceptación y participación en los programas de vacunación entre estudiantes varía ampliamente debido a creencias, actitudes y obstáculos diversos. Las creencias y percepciones estudiantiles están influenciadas por la percepción del riesgo, la confianza en las autoridades

*de salud y la desinformación. Las actitudes positivas hacia la vacunación se basan en la confianza en la ciencia y la responsabilidad comunitaria, mientras que actitudes negativas reflejan temores a los efectos secundarios y, por ende, a la desconfianza. Factores como el acceso limitado, barreras económicas y la influencia de las redes sociales impactan en los comportamientos de vacunación. **Objetivo:** Analizar de manera exhaustiva y sistemática la literatura científica disponible acerca de las creencias, actitudes y barreras relacionadas con la inmunización contra la COVID-19 entre estudiantes universitarios. Para abordar estas cuestiones, estrategias efectivas incluyen campañas educativas que brinden información precisa, colaboración con figuras influyentes y autoridades de salud, así como recompensas y mensajes emocionales. Comprender estas creencias, actitudes y barreras es esencial para diseñar estrategias que promuevan la aceptación de la vacunación. La colaboración entre instituciones educativas y autoridades de salud es fundamental para lograr una inmunización exitosa y proteger la salud de la comunidad universitaria y la sociedad en general. **Conclusión:** La vacunación contra la COVID-19 en estudiantes universitarios se ve influenciada por una variedad de factores cognitivos, emocionales y sociales. Abordar estas influencias de manera efectiva es crucial para fomentar la aceptación de la vacunación y contribuir a una respuesta más sólida ante la pandemia.*

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Palabras clave: Vacunación; COVID-19, estudiantes, universitarios, creencia, percepción, actitud, estrategias de vacunación.

SUMMARY

*The COVID-19 pandemic has had a profound impact on society and college students with vaccination emerging as an essential tool to address it. However, acceptance and participation in vaccination programs among students vary widely due to diverse beliefs, attitudes, and barriers. Risk perception, trust in health authorities, and misinformation influence student beliefs and perceptions. Positive attitudes towards vaccination are based on trust in science and community responsibility, while negative attitudes reflect fears of side effects and thus mistrust. Factors such as limited access, economic barriers, and the influence of social media impact vaccination behaviors. The objective was to analyze the available scientific literature comprehensively and systematically about beliefs, attitudes, and barriers related to COVID-19 immunization among university students. To address these issues, effective strategies include educational campaigns that provide accurate information, collaboration with influential figures and health authorities, as well as rewards and emotional messages. Understanding these beliefs, attitudes, and barriers is essential to designing strategies that promote vaccination uptake. Collaboration between educational institutions and health authorities is essential to achieve successful immunization and protect the health of the university community and society in general. **Conclusion.** COVID-19 vaccination in college students is influenced by a variety of cognitive, emotional, and social factors. Addressing these influences effectively is crucial to fostering vaccination uptake and contributing to a stronger response to the pandemic.*

Keywords: Vaccination, COVID-19, students, beliefs, perceptions, attitudes, vaccination strategies.

INTRODUCCIÓN

La pandemia de COVID-19 generó un impacto global sin precedentes, afectando diversos aspectos de la sociedad, incluida no solamente la salud pública, sino también la educación. Entre los grupos afectados se encuentran los estudiantes universitarios, quienes desempeñan un papel fundamental en la dinámica social y económica. En este contexto, la inmunización a través de las vacunas contra la COVID-19 se ha establecido como una estrategia crucial para controlar la propagación del virus y mitigar los efectos de la enfermedad. Sin embargo, la aceptación y participación en los programas de vacunación

contra la COVID-19 entre los estudiantes universitarios varía significativamente. Se ha observado una diversidad de creencias, actitudes y prácticas en torno a la vacunación, lo que plantea interrogantes sobre los factores que influyen en estas variaciones y las posibles implicaciones para la salud pública. A pesar de la relevancia de comprender estos aspectos, existe una necesidad de sintetizar y analizar de manera sistemática la información disponible en la literatura científica.

Recientemente, se publicaron varios estudios que investigan las actitudes y la voluntad de los estudiantes universitarios de vacunarse contra la COVID-19. Dos estudios de Italia mostraron que una alta proporción de estudiantes universitarios expresó su disposición a ser vacunados (1). En Estados Unidos, múltiples estudios han examinado la renuencia e intenciones de los estudiantes hacia la atención médica, donde profesores y estudiantes de enfermería solo el 45 % planeaban vacunarse (2). De igual manera, otro estudio de estudiantes de medicina encontró que el 23 % no estaba dispuesto a recibir una vacuna contra la COVID-19 tan pronto como fuera aprobada por la Administración de Alimentos y Medicamentos (FDA) (3). Algunos estudios también han encuestado las intenciones y actitudes de los estudiantes hacia la vacunación contra la COVID-19 antes de que comience la distribución de la vacuna (4,5), donde los niveles más altos de actitudes negativas hacia la vacunación generalmente se asociaron con una menor aceptación de la vacunación (4,5). Otro estudio en una importante universidad pública en el noroeste encontró que los estudiantes calificaron la obtención de la vacuna contra la COVID-19 como más importante que recibir la vacuna contra la gripe (6). Es decir, que los factores relacionados con las posibles intenciones de vacunación en los estudiantes universitarios contra la COVID-19 merecen mucha atención. En este sentido, la evidencia arroja resultados mixtos y faltan estudios que aborden las interacciones entre los diferentes factores y el comportamiento de vacunación entre los estudiantes universitarios (7,8).

Es claro, que solamente la intención informada no siempre conduce a la aceptación de la vacunación por parte de los estudiantes universitarios (3,9,10). Sin embargo, una mejor comprensión del tema es importante para

lograr una inmunización más amplia entre los grupos objetivos, mediante el desarrollo y la implementación de medidas adecuadamente adaptadas a las particularidades culturales de los universitarios. En los últimos meses, la vacunación de los estudiantes ha demostrado ser una clave importante para la vida universitaria normal y saludable, ya que mantener la presencia normal en muchas universidades durante la pandemia de COVID-19 resultó difícil sin vacunas. Un estudio en una universidad alemana encontró que los aspectos sociodemográficos estaban relacionados con el aprendizaje y la salud en los universitarios. Se encontró que los factores psicológicos y la comunicación se relacionan con: (a) la probabilidad de vacunación contra la COVID-19 entre los estudiantes universitarios y (b) la voluntad de vacunarse entre los no vacunados. Los hallazgos contribuyeron a una mejor comprensión sobre el comportamiento de la vacunación, y en el diseño e implementación de estrategias personalizadas para los estudiantes, contribuyendo a la reducción de la vacilación a la vacunación (1).

METODOLOGÍA

El objetivo del presente estudio fue analizar de manera exhaustiva y sistemática la literatura científica disponible acerca de las creencias, actitudes y barreras relacionadas con la inmunización contra la COVID-19 entre estudiantes universitarios, con el fin de identificar patrones, factores influyentes y posibles estrategias para fomentar la aceptación y participación en los programas de vacunación. Se realizó una búsqueda exhaustiva de la literatura científica en las siguientes bases de datos: PubMed, Scopus, Web of Science, utilizando términos de búsqueda específicos relacionados con la vacunación contra la COVID-19 y estudiantes universitarios. La búsqueda se realizó con las siguientes palabras clave tanto en inglés como en español: COVID-19, SARS-CoV-2, vacunación, inmunización, estudiantes universitarios, comportamientos, actitudes, perspectivas, aceptación de la vacuna, creencias, adherencia a la vacuna, programas de vacunación, factores de influencia, pandemia, vacuna contra el COVID-19, percepción de riesgo. Para la selección de los artículos se aplicaron criterios:

calidad metodológica, el alcance temático y la fecha de publicación, para un total de 52 artículos publicados entre 2021 al 2023, con un factor de impacto entre todos los artículos de aproximadamente 4.35.

Creencias y Percepciones sobre la Vacunación del COVID-19 en Estudiantes Universitarios

Las creencias y percepciones de los estudiantes universitarios sobre la vacunación contra la COVID-19 desempeñan un papel fundamental en su decisión de aceptar o rechazar la vacunación.

Estas creencias y percepciones están influenciadas por una variedad de factores, incluyendo la información que reciben, sus experiencias personales, la confianza en las autoridades de salud y la comunicación pública sobre las vacunas (1,4,6). Comprender estas creencias y percepciones es esencial para diseñar estrategias efectivas de promoción de la vacunación, entre las cuales se encuentran:

La Percepción de Riesgo: La percepción de riesgo es un componente clave en las creencias de los estudiantes sobre la vacunación contra la COVID-19. Algunos estudiantes pueden sentir que el virus no representa un riesgo significativo para su grupo demográfico, lo que podría influir en su decisión de no vacunarse. Otros pueden considerar que la gravedad de la enfermedad es suficiente para justificar la vacunación (3,11).

Confianza en la Vacuna y en las Autoridades de Salud: La confianza en la seguridad y eficacia de la vacuna es un factor esencial en las creencias de los estudiantes. La desconfianza en la ciencia detrás de la vacuna, los temores sobre los efectos secundarios y la percepción de que las autoridades de salud pueden no estar brindando información transparente, pueden influir en la decisión de no vacunarse (10,12,13).

Influencia de la Desinformación: La desinformación y los mitos sobre las vacunas contra la COVID-19 pueden afectar las creencias de los estudiantes. La exposición a información errónea en línea y en redes sociales puede llevar a una percepción distorsionada de los riesgos y beneficios de la vacunación (4,7).

Percepciones Sociales y Normas Culturales: Las percepciones sociales y las normas culturales

también influyen en las creencias de los estudiantes. La opinión de amigos, familiares y figuras de autoridad en sus círculos sociales puede desempeñar un papel importante en su decisión de vacunarse o no (12,14–16).

Mitos y Creencias sobre la Vacunación: Las creencias sobre las vacunas en general también pueden influir en las percepciones de los estudiantes sobre la vacunación contra la COVID-19. Algunos estudiantes pueden tener preocupaciones basadas en mitos y falsas creencias sobre vacunas en general (14,17-20).

Es claro, que las creencias y percepciones de los estudiantes universitarios sobre la vacunación del COVID-19 son multifacéticas y pueden variar ampliamente según la cultura (12,19,21,22). Abordar estas creencias de manera efectiva requiere una comunicación clara y basada en evidencia científica, así como la consideración de los factores sociales, culturales y psicológicos que influyen en sus perspectivas. Las estrategias de promoción de la vacunación deben abordar estos factores para fomentar una comprensión precisa de los riesgos y beneficios de la vacunación contra la COVID-19.

Actitudes y Barreras hacia la Inmunización en Estudiantes Universitarios

Las actitudes de los estudiantes universitarios hacia la vacunación contra la COVID-19 y las posibles barreras que enfrentan, como la falta de acceso, el miedo a los efectos secundarios y las preocupaciones éticas son un factor determinante para las actitudes frente a la inmunización de manera general y más con el COVID-19, donde al inicio de la pandemia se sabía poco o nada acerca de la enfermedad (6,23-26). Entre los factores más importantes tenemos disposiciones mentales y emocionales como los desafíos propios propuesto por la vacuna. La comprensión de las actitudes y barreras son esenciales para diseñar intervenciones que promuevan la aceptación de la vacunación, entre las cuales tenemos:

1. **Actitudes Positivas:** Algunos estudiantes pueden tener actitudes positivas hacia la vacunación contra la COVID-19 debido a su confianza en la ciencia, la protección personal que creen que la vacuna brindará y su deseo de contribuir a la contención
- de la pandemia, la cual es una percepción compartida independientemente del país analizado (27). Estas actitudes positivas pueden ser impulsadas por la percepción de que la vacunación es un deber cívico y un acto de solidaridad hacia la comunidad (28). Sin embargo, se muestra que las palabras "muerte", "morir" y "matar", están relacionadas con no recibir la vacuna en lugar de temer por los efectos secundarios (27).
2. **Actitudes Negativas:** Por otro lado, algunos estudiantes pueden tener actitudes negativas debido a preocupaciones sobre los efectos secundarios de la vacuna, la rapidez con la que se desarrollaron las vacunas o la falta de confianza en las autoridades de salud (23,29,30). Estas actitudes pueden estar influidas por la desinformación y los mitos en torno a las vacunas (22).
3. **Barreras de Acceso:** Las barreras de acceso pueden dificultar la vacunación para algunos estudiantes universitarios. Estas barreras pueden incluir la falta de disponibilidad de la vacuna en su área geográfica, la dificultad para programar citas de vacunación, la falta de información sobre los lugares y horarios de vacunación, y las limitaciones de transporte (15,18,27,31-33).
4. **Barreras Económicas:** La falta de recursos económicos puede ser una barrera significativa para algunos estudiantes. Los costos asociados con la vacunación, como el transporte hacia los lugares de vacunación o la pérdida de ingresos debido a la necesidad de ausentarse del trabajo para recibir la vacuna, pueden desalentar la inmunización (34-39).
5. **Influencia de las Redes Sociales:** Las redes sociales y las interacciones personales pueden influir en las actitudes y barreras hacia la inmunización. Los estudiantes pueden verse influenciados por las opiniones de amigos, familiares o figuras influyentes en línea, lo que puede afectar su decisión de vacunarse (5,9,15,16,29,38).
6. **Barreras Culturales y Lingüísticas:** Las diferencias culturales y lingüísticas pueden actuar como barreras para algunos estudiantes. La falta de información en su idioma nativo o la falta de comprensión culturalmente sensible

sobre la importancia de la vacunación puede considerarse también como un obstáculo (4,14,15,19,22,23,26,31).

En Conclusión, las actitudes y barreras que los estudiantes universitarios enfrentan en relación con la inmunización contra la COVID-19 son diversas y pueden influir en su decisión de vacunarse. Abordar estas actitudes y barreras requiere estrategias que aborden preocupaciones específicas, mejoren el acceso y la información, y promuevan una comprensión precisa de los beneficios de la vacunación.

Comportamientos de Vacunación y Participación en Programas de Inmunización

Los comportamientos de vacunación y la participación en programas de inmunización son indicadores clave de cómo los estudiantes universitarios están respondiendo a las oportunidades de recibir la vacuna contra la COVID-19. Estos comportamientos reflejan la decisión final de los estudiantes de aceptar o rechazar la vacunación, donde su falta de participación en los programas de inmunización puede tener un impacto directo en la propagación del virus dentro de la comunidad estudiantil y más allá.

1. **Adhesión a los Programas de Inmunización:** La adhesión a los programas de inmunización se refiere a la medida en que los estudiantes universitarios siguen las recomendaciones de salud pública y se vacunan de acuerdo con el calendario y las pautas establecidas. Algunos estudiantes pueden estar dispuestos a recibir la vacuna tan pronto como esté disponible, mientras que otros pueden retrasar o evitar la vacunación por diversas razones (40-43).
2. **Comportamientos de Recomendación:** Los estudiantes universitarios también pueden influir en los comportamientos de sus pares al recomendar la vacunación o compartir sus propias experiencias. Aquellos que han recibido la vacuna y tienen una experiencia positiva pueden desempeñar un papel importante al promover la aceptación de la vacunación entre sus compañeros (31,44-47).
3. **Desafíos de Recordatorios y Segundas Dosis:** El seguimiento de las segundas dosis y la

necesidad de recordatorios para completar el proceso de vacunación pueden ser desafíos. Algunos estudiantes pueden olvidar o tener dificultades para coordinar sus horarios para la segunda dosis, lo que puede afectar la efectividad de la inmunización (48).

4. **Influencia de la Desinformación Persistente:** A pesar de la disponibilidad de información precisa sobre la seguridad y eficacia de las vacunas contra la COVID-19, la persistencia de la desinformación puede llevar a algunos estudiantes a dudar en completar su proceso de vacunación. Esta desinformación puede afectar la percepción de la necesidad de la segunda dosis o generar miedo a los efectos secundarios (4,16,34,47).
5. **Efectos de la Opinión Pública y Medios de Comunicación:** La opinión pública y la cobertura mediática pueden influir en los comportamientos de los estudiantes hacia la vacunación. Si los medios de comunicación resaltan eventos negativos relacionados con la vacuna o si la opinión pública está dividida, esto puede afectar la decisión de algunos estudiantes de recibir la vacuna (4,15,34).
6. **Responsabilidad Personal y Colectiva:** La vacunación del COVID-19 no solo es una decisión individual, sino que también tiene implicaciones colectivas para la salud de la comunidad estudiantil y más amplia. Los comportamientos de vacunación pueden reflejar la percepción de los estudiantes sobre su responsabilidad hacia los demás y su contribución a la inmunidad colectiva (27,35,49).

Estrategias para Fomentar la Aceptación de la Vacunación

En este apartado se presentarán las estrategias efectivas para promover la aceptación de la vacunación contra la COVID-19 entre los estudiantes universitarios, como campañas de información, educación y sensibilización.

Para promover la aceptación de la vacunación contra la COVID-19 entre los estudiantes universitarios, es esencial implementar estrategias efectivas que aborden las barreras y preocupaciones específicas que puedan tener. Estas estrategias deben estar respaldadas por

comunicación clara, información precisa y enfoques que fomenten la confianza en las vacunas y en las autoridades de salud.

Desarrollar campañas educativas y de concienciación que proporcionen información precisa y basada en evidencia sobre la seguridad, eficacia y beneficios de la vacunación. Estas campañas pueden utilizar múltiples canales, incluyendo redes sociales, plataformas en línea, carteles en el campus y sesiones informativas presenciales (7,29,32,34,42). Los mensajes deben implementarse teniendo presente las principales creencias tanto individuales como grupales, además del factor sociodemográfico de los estudiantes. Por otro lado, la cooperación de los influencers como también las figuras de autoridad dentro de la comunidad estudiantil para promover la vacunación (4,50,51). Es decir, estudiantes influyentes y profesores respetados pueden tener un impacto significativo al compartir sus experiencias positivas y fomentar la aceptación entre sus pares. Todo esto, sumado al hecho de asegurarse que la vacuna esté fácilmente accesible en el campus o en lugares cercanos, así como también organizar campañas de vacunación en el campus o establecer acuerdos con centros de salud locales, esto puede facilitar que los estudiantes se vacunen sin enfrentar barreras logísticas.

Además, instalar proyectos como, por ejemplo: descuentos en comidas, certificados de participación o recompensas simbólicas, para motivar a los estudiantes a recibir la vacuna. Estas recompensas pueden servir como refuerzos positivos para la toma de decisiones de salud, contribuyendo a la vacunación exitosa con mensajes emotivos que generen empatía y, por ende, conexión emocional que fomente la aceptación de la vacunación (4,10,26,49,52).

Los estudiantes pueden desempeñar un papel vital en la prevención de la propagación del virus sobre todo contrarrestando los rumores y afirmaciones infundadas, es decir, verdaderos evaluadores de riesgos para la toma de decisión positiva de vacunarse.

En resumen, la pandemia del COVID-19 ha tenido un impacto significativo en la sociedad y en la vida de los estudiantes universitarios. La inmunización a través de la vacunación se ha convertido en una herramienta esencial para controlar la propagación del virus y mitigar

los efectos de la enfermedad. Sin embargo, la aceptación y participación en los programas de vacunación entre los estudiantes varía ampliamente debido a sus creencias, actitudes y barreras diversas.

CONCLUSIÓN

Las creencias, percepciones y prácticas de los estudiantes sobre la vacunación están influenciadas por la percepción de riesgo, la confianza en la vacuna y en las autoridades de salud, la influencia de la desinformación y las normas culturales. Abordar estas creencias requiere estrategias de comunicación claras y basadas en evidencia que fomenten una comprensión precisa de los beneficios de la vacunación.

Las actitudes de los estudiantes universitarios hacia la vacunación también son variadas, con algunas actitudes positivas motivadas por la confianza en la ciencia y el deseo de proteger a la comunidad; y otras actitudes negativas debido a preocupaciones sobre los efectos secundarios y la falta de confianza. Además, las barreras como el acceso limitado, barreras económicas y la influencia de las redes sociales pueden impactar las actitudes y comportamientos de vacunación. Los comportamientos de vacunación y la participación en programas de inmunización son cruciales para la contención de la pandemia. Estrategias como campañas educativas, influencia de figuras de autoridad, recompensas y mensajes emotivos pueden fomentar la aceptación de la vacunación y mejorar la participación en los programas de inmunización.

En última instancia, comprender las creencias, actitudes y comportamientos de los estudiantes universitarios hacia la vacunación contra la COVID-19 es fundamental para diseñar estrategias efectivas que promuevan la aceptación y participación en los programas de vacunación. La colaboración entre las instituciones educativas, autoridades de salud y comunicadores, es esencial para abordar los desafíos y trabajar juntos para lograr una inmunización exitosa y proteger la salud de la comunidad estudiantil y de la sociedad en general.

REFERENCIAS

1. Schäfer M, Stark B, Werner AM, Mülder LM, Heller S, Reichel JL, et al. Determinants of university students' COVID-19 vaccination intentions and behavior. *Sci Rep.* 2022;12(1):18067.
2. Kecojevic A, Basch CH, Sullivan M, Chen YT, Davi NK. COVID-19 vaccination and intention to vaccinate among a sample of college students in New Jersey. *J Community Health.* 2021;46(6):1059-1068.
3. Kelekar AK, Lucia VC, Afonso NM, Mascarenhas AK. COVID-19 vaccine acceptance and hesitancy among dental and medical students. *J Am Dent Assoc.* 2021;152(8):596-603.
4. Niu Q, Liu J, Kato M, Shinohara Y, Matsumura N, Aoyama T, et al. Public opinion and sentiment before and at the beginning of COVID-19 vaccinations in Japan: Twitter analysis. *JMIR Infodemiology.* 2022;2(1):e32335.
5. Mascarenhas AK, Lucia VC, Kelekar A, Afonso NM. Dental students' attitudes and hesitancy toward COVID-19 vaccine. *J Dent Educ.* 2021;85(9):1504-1510.
6. Abdallah DA, Lee CM. Social norms and vaccine uptake: College students' COVID-19 vaccination intentions, attitudes, and estimated peer norms and comparisons with influenza vaccine. *Vaccine.* 2021;39(15):2060-2067.
7. Shmueli L. Predicting intention to receive COVID-19 vaccine among the general population using the health belief model and the theory of planned behavior model. *BMC Public Health.* 2021;21(1):1-13.
8. Simone L, Vagni M, Gnagnarella C, Bersani G, Pajardi D. Mistrust and beliefs in conspiracy theories differently mediate the effects of psychological factors on propensity for COVID-19 vaccine. *Front Psychol.* 2021;12:683684.
9. Lehmann BA, de Melker HE, Timmermans DR, Mollema L. Informed decision making in the context of childhood immunization. *Patient Educ Couns.* 2017;100(12):2339-2345.
10. Troiano G, Nardi A. Vaccine hesitancy in the era of COVID-19. *Public Health.* 2021;194:245-251.
11. Sherman SM, Smith LE, Sim J, Amlôt R, Cutts M, Dasch H, et al. COVID-19 vaccination intention in the UK: results from the COVID-19 vaccination acceptability study (CoVAccS), a nationally representative cross-sectional survey. *Hum Vaccines Immunother.* 2021;17(6):1612-1621.
12. Latkin CA, Dayton L, Yi G, Konstantopoulos A, Boodram B. Trust in a COVID-19 vaccine in the US: A social-ecological perspective. *Soc Sci Med.* 2021;270:113684.
13. Gabay G, Tarabieh M. Science and behavioral intentions among Israeli Jewish ultra-Orthodox males: death from COVID-19 or from the COVID-19 vaccine? A thematic study. *Public Underst Sci.* 2022;31(4):410-427.
14. Yaqub O, Castle-Clarke S, Sevdalis N, Chataway J. Attitudes to vaccination: a critical review. *Soc Sci Med.* 2014;112:1-11.
15. Larson HJ, Clarke RM, Jarrett C, Eckersberger E, Levine Z, Schulz WS, et al. Measuring trust in vaccination: A systematic review. *Hum Vaccines Immunother.* 2018;14(7):1599-1609.
16. Brunson EK. The impact of social networks on parents' vaccination decisions. *Pediatrics.* 2013;131(5):e1397-1404.
17. Magadmi RM, Kamel FO. Beliefs and barriers associated with COVID-19 vaccination among the general population in Saudi Arabia. *BMC Public Health.* 2021;21(1):1-8.
18. Mahmud S, Mohsin M, Khan IA, Mian AU, Zaman MA. Knowledge, beliefs, attitudes and perceived risk about COVID-19 vaccine and determinants of COVID-19 vaccine acceptance in Bangladesh. *PloS One.* 2021;16(9):e0257096.
19. Jennings W, Stoker G, Bunting H, Valgarðsson VO, Gaskell J, Devine D, et al. Lack of trust, conspiracy beliefs, and social media use predict COVID-19 vaccine hesitancy. *Vaccines.* 2021;9(6):593.
20. Saied SM, Saied EM, Kabbash IA, Abdo SAEF. Vaccine hesitancy: Beliefs and barriers associated with COVID-19 vaccination among Egyptian medical students. *J Med Virol.* 2021;93(7):4280-4291.
21. Urrunaga-Pastor D, Bendezu-Quispe G, Herrera-Añazco P, Uyen-Cateriano A, Toro-Huamanchumo CJ, Rodríguez-Morales AJ, et al. Cross-sectional analysis of COVID-19 vaccine intention, perceptions and hesitancy across Latin America and the Caribbean. *Travel Med Infect Dis.* 2021;41:102059.
22. Caycho-Rodríguez T, Ventura-León J, Valencia PD, Vilca LW, Carbajal-León C, Reyes-Bossio M, et al. What is the support for conspiracy beliefs about COVID-19 vaccines in Latin America? A prospective exploratory study in 13 countries. *Front Psychol.* 2022;13:1885.
23. Al-Mugheed K, Al Rawajfah O, Bani-Issa W, Rababa M. Acceptance, attitudes, and barriers of vaccine booster dose among nursing students: A multicounty survey. *J Nurs Manag.* 2022;30(7):3360-7.
24. Gallant AJ, Harding A, Johnson C, Steenbeek A, Curran JA. Identifying H1N1 and COVID-19 vaccine hesitancy or refusal among health care providers: a

- scoping review. *JBIEvid Synth.* 2023;21(5):913.
25. Ruiz JB, Bell RA. Predictors of intention to vaccinate against COVID-19: Results of a nationwide survey. *Vaccine.* 2021;39(7):1080-1086.
 26. Goldenberg MJ. *Vaccine hesitancy: public trust, expertise, and the war on science.* University of Pittsburgh Press; 2021.
 27. Greyling T, Rossouw S. Positive attitudes towards COVID-19 vaccines: A cross-country analysis. *PLoS One.* 2022;17(3):e0264994.
 28. Bai W, Cai H, Liu S, Liu H, Qi H, Chen X, et al. Attitudes toward COVID-19 vaccines in Chinese college students. *Int J Biol Sci.* 2021;17(6):1469.
 29. Qiao S, Tam CC, Li X. Risk exposures, risk perceptions, negative attitudes toward general vaccination, and COVID-19 vaccine acceptance among college students in South Carolina. *Am J Health Promot.* 2022;36(1):175-179.
 30. Campo-Arias A, Pedrozo-Pupo JC. Attitude towards COVID-19 vaccines in Colombian university students: Frequency and associated variables. *Acta Bio Medica Atenei Parm.* 2021;92(6).
 31. Lee D, Rundle-Thiele S, Wut TM, Li G. Increasing seasonal influenza vaccination among university students: A systematic review of programs using a social marketing perspective. *Int J Environ Res Public Health.* 2022;19(12):7138.
 32. Ball H, Wozniak TR, Kuchenbecker CM. Shot talk: Development and pilot test of a theory of planned behavior campaign to combat college student COVID-19 vaccine hesitancy. *J Health Commun.* 2023;28(2):82-90.
 33. Umucu E, Lee B, Bezyak J. Measuring COVID-19 vaccine hesitancy among college students with disabilities: Sociodemographic and psychological correlates of COVID-19 vaccine hesitancy. *J Am Coll Health.* 2022;1-7.
 34. Gunawardena M, Dhanapala KV. Barriers to Removing Barriers of Online Learning. *Commun Assoc Inf Syst.* 2023;52(1):17.
 35. Elbarazi I, Yacoub M, Reyad OA, Abdou MS, Elhadi YAM, Kheirallah KA, et al. Exploring enablers and barriers toward COVID-19 vaccine acceptance among Arabs: A qualitative study. *Int J Disaster Risk Reduct.* 2022;82:103304.
 36. Khowa T, Cimi A, Mukasi T. Socio-economic impact of COVID-19 on rural livelihoods in Mbashe Municipality. *Jamba J Disaster Risk Stud.* 2022;14(1):1-8.
 37. Savina K, Sreekumar R, Soonu VK, Variyar EJ. Various vaccine platforms in the field of COVID-19. *Beni-Suef Univ J Basic Appl Sci.* 2022;11(1):35.
 38. Akhter H, Abdul Rahman AA, Jafrin N, Mohammad Saif AN, Esha BH, Mostafa R. Investigating the barriers that intensify undergraduates' unwillingness to online learning during COVID-19: A study on public universities in a developing country. *Cogent Educ.* 2022;9(1):2028342.
 39. Ali S, Faizi B, Waqas H, Ahmed W, Shah S AA. Analysis of the socioeconomic barriers in implementing public health measures to contain COVID-19 transmission in Pakistan: A DELPHI-DEMATEL-based approach. *Kybernetes.* 2023;52(3):1149-1170.
 40. Corea F, Folcarelli L, Napoli A, Del Giudice GM, Angelillo IF. The impact of COVID-19 vaccination in changing the adherence to preventive measures: evidence from Italy. *Vaccines.* 2022;10(5):777.
 41. Efendi D, Rifani SR, Milanti A, Efendi F, Wong CL, Rustina Y, et al. The role of knowledge, attitude, confidence, and sociodemographic factors in COVID-19 vaccination adherence among adolescents in Indonesia: A nationwide survey. *Vaccines.* 2022;10(9):1489.
 42. Salazar-Fernández C, Baeza-Rivera MJ, Villanueva M, Bautista JAP, Navarro RM, Pino M. Predictors of COVID-19 Vaccine Intention: Evidence from Chile, Mexico, and Colombia. *Vaccines.* 2022;10(7):1129.
 43. LaRotta J, Escobar O, Ávila-Aguero ML, Torres JP, Sini de Almeida R, Morales G del C, et al. COVID-19 in Latin America: A Snapshot in Time and the Road Ahead. *Infect Dis Ther.* 2023;12(2):389-410.
 44. Jaffe AE, Graupensperger S, Blayney JA, Duckworth JC, Stappenbeck CA. The role of perceived social norms in college student vaccine hesitancy: Implications for COVID-19 prevention strategies. *Vaccine.* 2022;40(12):1888-1895.
 45. Bradshaw AS. To share or not to share: A framing analysis of paid vaccine advertisements on Facebook during COVID-19 and Pro-Vaccine mothers' willingness to promote vaccines within their peer networks. *J Curr Issues Res Advert.* 2023;44(2):142-168.
 46. Lin C, Parker T, Pejavarra K, Smith D, Tu R, Tu P. I Would Never Push a Vaccine on You: A Qualitative Study of Social Norms and Pressure in Vaccine Behavior in the US. *Vaccines.* 2022;10(9):1402.
 47. Berry CN, Walker K, Baker N, Trevor-Wright C. I See a Lot of Crazy Things and I Don't Know What to Believe: Lessons Learned about Health Literacy and Strategies for Communicating with Vaccine-Hesitant College Students. *Healthcare.* 2023;11(15):2212.
 48. Sartorão-Filho CI, Zoqui MC, Duarte DO, Ribeiro EA, Bisetto VCQ, Cachoni LEG, et al. Prediction and reasons for COVID-19 second dose vaccine hesitation: A cross-sectional study in a municipality of Brazil. *Sao Paulo Med J.* 2022;141:e202295.
 49. Patwary MM, Bardhan M, Haque MZ, Sultana R, Alam MA, Browning MH. COVID-19 vaccine acceptance rate and its factors among healthcare students: A

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- systematic review with meta-analysis. *Vaccines*. 2022;10(5):806.
50. Abidin C, Lee J, Barbeta T, Miao WS. Influencers and COVID-19: Reviewing key issues in press coverage across Australia, China, Japan, and South Korea. *Media Int Aust*. 2021;178(1):114-135.
51. Femenia-Serra F, Gretzel U, Alzua-Sorzabal A. Instagram travel influencers in # quarantine: Communicative practices and roles during COVID-19. *Tour Manag*. 2022;89:104454.
52. DeRoo SS, Pudalov NJ, Fu LY. Planning for a COVID-19 vaccination program. *JAMA*. 2020;323(24):2458-2459.

Diseción Coronaria Espontánea, Causa Común de Síndrome Coronario Agudo en Mujeres. Presentación de un Caso y Revisión

Spontaneous Coronary Dissection a Common Cause of Acute Coronary Syndrome in Women. Presentation of a Case and Review

Hildelia Hernández¹, Carlos Ascanio², Luisa Vera³

RESUMEN

La Diseción Coronaria Espontánea (DCE) es una causa rara de síndrome coronario agudo (SCA), pero es común en mujeres jóvenes y de edad media, sin factores de riesgo cardiovasculares. Presentamos un caso típico, que nos permite hacer una revisión del tema. Se trata de una mujer de 53 años, sin factores de riesgo cardiovasculares, que posterior a levantamiento de peso y crisis asmática severa, presenta Infarto del Miocardio, causado por diseción de arteria coronaria derecha (ACD), tratada de manera conservadora y con evolución satisfactoria.

Palabras claves: *Diseción coronaria espontánea, síndrome coronario en mujeres, infarto del miocardio, displasia fibromuscular.*

SUMMARY

Spontaneous Coronary Dissection (SCAD) is a rare cause of acute coronary syndrome (ACS), but it is common in young and middle-aged women without cardiovascular risk factors. We present a typical case, which allows us to review the topic. This is a 53-year-old woman, without cardiovascular risk factors, who after weightlifting and severe asthmatic crisis, presented a myocardial infarction caused by right coronary artery (RCA) dissection, treated conservatively and with satisfactory evolution.

Keywords: *Spontaneous coronary dissection, coronary syndrome in women, myocardial infarction, fibromuscular dysplasia.*

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INTRODUCCIÓN

La DCE, es un desgarro agudo no iatrogénico en la pared de la arteria coronaria, que conduce a la interrupción del flujo sanguíneo coronario y al SCA. Se produce un hematoma dentro de la túnica media que conduce a la separación de la íntima o del complejo íntima-media del vaso y comprime la luz verdadera causando isquemia e infarto. Ocurre predominantemente en mujeres jóvenes y de mediana edad sin factores de riesgo convencionales para la enfermedad arterial coronaria aterosclerótica.

Se ha estimado una prevalencia de DCE de hasta el 4 % de los pacientes que presentan SCA (1,2). Actualmente se reconoce como una causa común de SCA, particularmente en mujeres jóvenes (3) y es la causa más común de infarto agudo de miocardio (IAM) asociado al embarazo (43 %) (4).

Es la causa de hasta 35 % de todos los casos de SCA en mujeres de 50 años de edad o menos (5,6). El 87 % al 95 % de las disecciones coronarias espontáneas ocurren en mujeres, con una edad promedio entre 44 y 53 años (7,8). En los hombres se estima que ocurre en aproximadamente 10 %, después de un factor estresante o del levantamiento de objetos pesados (9).

PRESENTACIÓN DEL CASO

Paciente femenina de 53 años, asmática conocida y entrenadora de halterofilia, quien posterior a levantamiento de pesas (15 kg), presenta de manera abrupta dificultad para respirar, por lo que se automedica con broncodilatador, sin mejoría, por lo cual, acude a centro clínico donde se diagnostica

asma en crisis y se mantienen tratamiento con broncodilatadores. Mientras recibe tratamiento presenta síncope, de pocos minutos de duración y al recuperar la consciencia, refiere opresión retroesternal de fuerte intensidad. Posterior a la evidencia de enzimas cardíacas elevadas y electrocardiograma (ECG) alterado, se solicita evaluación por cardiología, 2 horas después del ingreso. Niega hipertensión arterial, diabetes, cardiopatía y nefropatía. Niega antecedentes familiares de enfermedad cardiovascular. Niega angina previa, palpitaciones, síncope previo, mareos. Antecedentes quirúrgicos: Mamoplastia de aumento.

Niega aabaquismo, drogas, alcohol. Niega tratamiento hormonal, suplementos proteicos, esteroides y drogas y sus menstruaciones son normales. Al examen físico de ingreso se encuentra taquipneica, con presión arterial, frecuencia cardíaca y saturación de oxígeno normales y tiene índice de masa corporal normal.

EL ECG de ingreso y el del día siguiente se muestran en Figura 1 y 2, respectivamente. Presenta aumento discreto de troponina con normalización en 48 horas y el colesterol y los triglicéridos son normales.



Figura 1. ECG de ingreso muestra, ritmo sinusal, supradesnivel leve del ST y rS en D2, D3 y aVF, falta de progresión de R de V1 a V4, T negativa en D2, D3, aVF y aVL y QTc 498 ms.

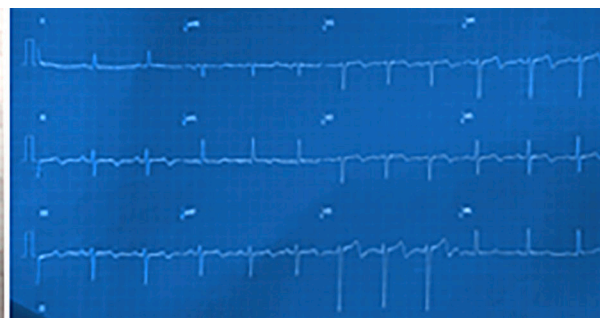


Figura 2. ECG del segundo día donde se agrega T negativas de V1 a V5.

En el ecocardiograma, se evidencia un ventrículo izquierdo de grosor, diámetros y función sistólica normales con Acinesia Inferior e Infero-lateral media y apical e Infero-septal

media. Válvulas estructural y funcionalmente normales, cavidades derechas normales y pericardio normal, sin derrame. La angiografía coronaria, realizada después de compensar la crisis asmática, se muestra en Figura 3.



Figura 3. Angiografía donde se observa flap de disección en Arteria coronaria derecha, desde tercio proximal al tercio distal, antes de la bifurcación. No se observan tortuosidades en coronarias.

En la Angiotomografía coronaria (ATC), realizada 3 días después, se evidencia estenosis de la ACD distal, siendo más evidente en diástole final, con engrosamiento de la pared, extendiéndose desde la rama marginal aguda hasta la arteria descendente posterior, sin evidencia de hiperdensidad de la pared, previo a la administración de contraste, que sugiriera hematoma, ni trombo y al observar el lumen, se evidencia doble luz en parte del trayecto. La ACD proximal mostró un realce normal durante la administración de contraste endovenoso, indicando patencia. No se observó aterosclerosis en las arterias coronarias (Figura 4).

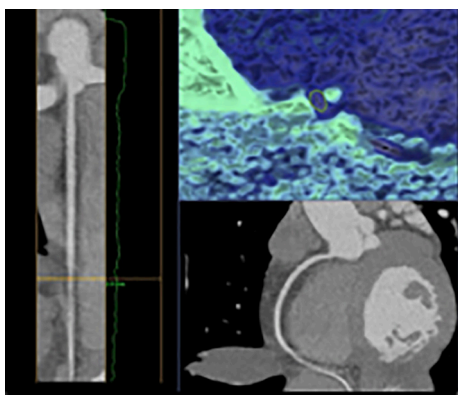


Figura 4. Angiotomografía coronaria con estenosis de ACD e imagen de doble luz distal.

La paciente presenta mejoría de la crisis asmática y se decide manejo médico de la DCE, por evolución satisfactoria, con desaparición del dolor a las 12 horas, mejoría de sinergia en tercios medios de las regiones afectadas en 24 horas y descenso de troponina en 48 horas. Egresa 4 días después, en buenas condiciones.

DISCUSIÓN

En la DCE, se desarrolla un hematoma dentro de la capa media que ocasiona la separación de la íntima o del complejo íntima-media del vaso y comprime la luz verdadera causando isquemia e infarto. Se han propuesto dos hipótesis para explicar el proceso fisiopatológico: la hipótesis “de adentro hacia afuera” sugiere que la sangre ingresa al espacio subintimal desde la luz verdadera después del desarrollo de una disrupción o “colgajo” íntima endotelial; y la hipótesis de “afuera hacia adentro”, el hematoma surge *de novo* en la capa media, posiblemente debido a la disrupción de los microvasos que atraviesa (10,11).

En la patogenia de la DCE no aterosclerótica, están involucrados, múltiples mecanismos. Existen factores predisponentes y factores desencadenantes y su combinación; que incluyen sexo, fluctuaciones hormonales, arteriopatías subyacentes, enfermedades inflamatorias, genética y precipitantes ambientales, físicos y emocionales (12). Dentro de los predisponentes se describen: Arteriopatías como la displasia Fibromuscular (DFM), los trastornos del tejido conectivo (Síndrome de Marfan, Síndrome de Ehler Danlos, Enfermedad renal poliquística autosómica dominante y síndrome de Loey-Dietz), las enfermedades inflamatorias sistémicas (Lupus eritematoso sistémico, Enfermedad de Crohn, Poliarteritis Nodosa y Sarcoidosis), embarazo, terapia hormonal y espasmo coronario.

Dentro de los eventos de estrés que la desencadenan están: el ejercicio intenso (aeróbico o isométrico), estrés emocional intenso, trabajo de parto y parto, actividades intensas tipo Valsalva (tos repetitiva intensa, arcadas/vómitos, evacuaciones intestinales) y drogas (cocaína, anfetaminas, metanfetaminas, beta-gonadotropina coriónica humana).

En vista de la alta prevalencia en mujeres, la hipótesis hormonal, cobra un papel preponderante. La disección espontánea de la arteria coronaria puede ocurrir en edad fértil y posmenopáusica, tanto en mujeres multíparas, como nulíparas, en embarazos sin complicaciones (70 % en el posparto temprano) así como en embarazos complicados (eclampsia y preeclampsia) (4,13,14).

En estudios realizados hasta la fecha, el dolor torácico fue el síntoma de presentación más frecuente (96 % de los casos). Los síntomas menos comunes incluyen dolor en el brazo, dolor en el cuello, náuseas o vómitos, diaforesis, disnea y dolor de espalda. (15-17). También puede presentarse con arritmias ventriculares, shock cardiogénico o paro cardíaco repentino (18).

El IM con elevación del ST, estuvo presente en 25 a 50 % de los pacientes, y el resto presentó IM sin elevación del ST.

Las características (12) que nos deben hacer sospechar de una DCE son las siguientes: infarto del miocardio en mujeres jóvenes (de 50 años o menos), ausencia de factores de riesgos cardiovasculares tradicionales, poca o ninguna evidencia de lesiones ateroscleróticas típicas en las arterias coronarias, estado periparto, antecedentes de DFM o enfermedades del tejido conectivo e inflamatorias sistémicas antes nombradas y eventos precipitantes emocionales o físicos intensos.

Los niveles de troponina generalmente aumentan, pero pueden ser normales (18).

La angiografía coronaria se considera el estándar de oro para confirmar la presencia de DCE. Las características angiográficas que orientan al diagnóstico son: falta de cambios ateroscleróticos en otras arterias coronarias; lesiones largas (11-20 mm), estenosis borrosa; y estenosis lineal (12). Angiográficamente (19) se describen 3 tipos: La DCE tipo 1 se caracteriza por la entrada de contraste en la luz falsa, que se observa en menos de un tercio de los pacientes. La DCE tipo 2 es la más común, se observa hasta en dos tercios de los pacientes, y tiene la apariencia de un largo, suave y segmento estrechado difusamente con un hematoma intramural. Este tipo conlleva el mayor riesgo de no ser detectado en angiografía. La DCE tipo

3 es la menos frecuente y puede simular lesiones ateroscleróticas dada su apariencia focal. La confirmación diagnóstica de los tipos 2 y 3 de DCE puede requerir imagenología intracoronaria, incluida la tomografía de coherencia óptica (OCT) y el ultrasonido intravascular (IVUS) (20). El IVUS y la OCT son herramientas que permiten visualizar mejor la estructura y composición de la pared arterial, especialmente identificar desgarros y colgajos de la íntima.

El papel de la ATC no ha sido establecido completamente. Un beneficio adicional de la ATC es la evaluación de la pared, para visualizar hematoma intramural, lo cual es mejor evaluado en vistas con cortes ortogonales, sin y con contraste (21).

En pacientes estables el manejo de la DCE es principalmente médico y las pautas de manejo siguen estando basadas en gran medida en el consenso de expertos (9).

Algunos estudios han demostrado consistentemente que la intervención coronaria percutánea (ICP) en el contexto de DCE se asocia con peores resultados y altas tasas de complicaciones (15).

Los vasos disecados tienden a curarse con el tiempo; la evolución natural de la DCE parece ser la curación gradual espontánea de la pared del vaso, con una resolución de la lesión dentro de los 30 días, por lo que la mayoría de los intervencionistas prefieren un enfoque conservador (22,23).

La ICP en DCE con frecuencia, es técnicamente desafiante, debido a la fragilidad de la pared del vaso. Hacer avanzar las guías coronarias dentro de la luz verdadera es un desafío. Cualquier instrumentación (guía, angioplastia o colocación de stent) puede propagar la disección y ocluir las ramas laterales. Además, las disecciones suelen afectar vasos distales de pequeño calibre y son extensas, requiriendo largos stents con alta probabilidad de reestenosis interna del stent y la resolución temporal de hematoma intramural en segmentos con stent previos, puede aumentar el riesgo de malformaciones tardías del stent, aposición y trombosis del stent, por esa razón, la ICP en DCE, se reserva solo para pacientes con oclusiones coronarias proximales, con inestabilidad hemodinámica, arritmia refractaria,

isquemia en curso y en aquellos que progresan a la oclusión después del tratamiento conservador inicial (22,23).

La cirugía de bypass de arteria coronaria con injerto (CABG, por sus siglas en inglés) generalmente se reserva para situaciones en las que la ICP ha fracasado o se considera de riesgo extremadamente alto, por ejemplo, disecciones del tronco principal con isquemia/infarto en curso (22).

El tratamiento médico de inicio se basa en antiagregación dual y betabloqueantes (23).

Los betabloqueantes son fundamentales porque reducen la tensión de cizallamiento en la pared del vaso y minimizan el riesgo de propagación, al disminuir la presión arterial y la frecuencia cardíaca. La antiagregación dual tiene el objetivo de minimizar la carga del trombo y mantener la permeabilidad de la luz verdadera. La anticoagulación y la trombólisis están contraindicada y los hipolipemiantes se usan solo en caso de dislipidemia asociada.

El manejo a largo plazo de la DCE se basa en la detección de DFM, el control del dolor torácico y la recurrencia y la rehabilitación cardíaca (22,23).

La DFM, es una enfermedad segmentaria idiopática, no aterosclerótica y no inflamatoria de las arterias musculares de tamaño mediano, que produce su estenosis. La DFM coronaria debería considerarse en presencia de marcada tortuosidad coronaria; generalmente definido como ≥ 3 curvas (definido como un cambio de $\geq 45^\circ$ en la dirección del vaso) (24).

Aunque se conocen algunos factores de riesgo y desencadenantes, la DCE es un evento coronario agudo, que todavía no se conoce la manera de prevenirlo, diagnosticarlo y tratarlo, convirtiéndolo en una necesidad clínica importante e insatisfecha (25).

CONCLUSIONES

La DEC forma parte de las causas atípicas de SCA, sin embargo, es una causa común de IM en mujeres jóvenes y de mediana edad, sin factores de riesgo y en embarazadas. La inusual presentación en mujeres jóvenes, pre-menopáusicas, o en mujeres menores de 60 años; su clínica en

ocasiones atípica y los hallazgos angiográficos confusos, contribuyen al infradiagnóstico y al tratamiento tardío e inapropiado en detrimento de las pacientes. Conociendo el fenotipo característico de estas pacientes y entendiendo que no debemos desestimar el dolor torácico en mujeres jóvenes, que llegan a nuestras salas de urgencia, podemos aproximarnos al diagnóstico y a su manejo adecuado y oportuno.

REFERENCIAS

1. Nishiguchi T, Tanaka A, Ozaki Y, Taruya A, Fukuda S, Taguchi H, et al. Prevalence of spontaneous coronary artery dissection in young patients with acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care*. 2016;5:263-270.
2. Gad MM, Mahmoud AN, Saad AM, Bazarbashi N, Ahuja KR, Karrthik AK, et al. Incidence, clinical presentation, and causes of 30-day readmission following hospitalization with spontaneous coronary artery dissection. *JACC Cardiovasc Interv*. 2020;13(8):921-932.
3. Lebrun S, Bond RM. Spontaneous coronary artery dissection: the underdiagnosed cardiac condition that plagues women. *Trends Cardiovasc Med*. 2018;28(5):340-345.
4. Elkayam U, Jalnapurkar S, Barakkat MN, Khatri N, Kealey AJ, Mehra A, et al. Pregnancy-associated acute myocardial infarction: A review of contemporary experience in 150 cases between 2006 and 2011. *Circulation*. 2014;129:1695-1702.
5. Nakashima T, Noguchi T, Haruta S, Yamamoto Y, Oshima S, Nakao K, et al. Prognostic impact of spontaneous coronary artery dissection in young female patients with acute myocardial infarction: A report from the Angina Pectoris-Myocardial Infarction Multicenter Investigators in Japan. *Int J Cardiol*. 2016;207:341-348.
6. Meng PN, Xu C, You W, Wu ZM, Xie DJ, Zhang H, et al. Spontaneous coronary artery dissection as a cause of acute myocardial infarction in young female population: A single-center study. *Chin Med J (Engl)*. 2017;130:1534-1539.
7. Kok SN, Hayes SN, Cutrer FM, Raphael CE, Gulati R, Best PJM, et al. Prevalence and clinical factors of migraine in patients with spontaneous coronary artery dissection. *J Am Heart Assoc*. 2018;7:e010140.
8. Saw J, Starovoytov A, Humphries K, Sheth T, So D, Minhas K, et al. Canadian spontaneous coronary artery dissection cohort study: In-hospital and 30-day outcomes. *Eur Heart J*. 2019;40:1188-1197.

DISECCIÓN CORONARIA ESPONTÁNEA

9. Kim ESH. Spontaneous coronary artery dissection. *N Engl J Med.* 2020;383(24):2358-2370.
10. Waterbury TM, Tweet MS, Hayes SN, Eleid MF, Bell MR, Lerman A, et al. Early natural history of spontaneous coronary artery dissection. *Circ Cardiovasc Interv.* 2018;11: e006772.
11. Waterbury TM, Tarantini G, Vogel B, Mehran R, Gersh BJ, Gulati R. Non-atherosclerotic causes of acute coronary syndromes. *Nat Rev Cardiol.* 2020;17:229-241.
12. Yip A, Saw J. Spontaneous coronary artery dissection—A review. *Cardiovasc Diagn Ther.* 2015;5(1):37-48.
13. Tweet MS, Hayes SN, Codsí E, Gulati R, Rose CH, Best PJM. Spontaneous coronary artery dissection associated with pregnancy. *J Am Coll Cardiol.* 2017;70:426-435.
14. Keepanasseril A, Pfaller B, Metcalfe A, Siu SC, Davis MB, Silversides CK. Cardiovascular deaths in pregnancy: Growing concerns and preventive strategies. *Can J Cardiol.* 2021;37:1969-1978.
15. Tweet MS, Hayes SN, Pitta SR, Simari RD, Lerman A, Lennon RJ, et al. Clinical features, management, and prognosis of spontaneous coronary artery dissection. *Circulation.* 2012;126:579-588.
16. Mortensen KH, Thuesen L, Kristensen IB, Christiansen EH. Spontaneous coronary artery dissection: A Western Denmark Heart Registry study. *Catheter Cardiovasc Interv.* 2009;74(5):710-717.
17. Luong C, Starovoytov A, Heydari M, Sedlak T, Aymong E, Saw J. Clinical presentation of patients with spontaneous coronary artery dissection. *Catheter Cardiovasc Interv.* 2017;89:1149.
18. Lindor RA, Tweet MS, Goyal KA, Lohse CM, Gulati R, Hayes SN, et al. Emergency department presentation of patients with spontaneous coronary artery dissection. *J Emerg Med.* 2017;52:286-291.
19. Saw J. Coronary angiogram classification of spontaneous coronary artery dissection. *Catheter Cardiovasc Interv.* 2014;84:1115-1122.
20. Tweet MS, Gulati R, Williamson EE, Vrtiska TJ, Hayes SN. Multimodality imaging for spontaneous coronary artery dissection in women. *JACC Cardiovasc Imaging.* 2016;9:436-450.
21. Aslam A, Stojanovska J, Khokhar US, Weinberg RL, Ganesh SK, Labounty T, et al. Spontaneous Coronary Artery dissection: An Underdiagnosis clinical entity- A primer for cardiac imagers. *Radiographics.* 2021;41(7):1897-1915.
22. Hayes SN, Tweet MS, Adlam D, Kim ESH, Gulati R, Price JE, Rose CH. Spontaneous Coronary Artery Dissection: JACC State-of-the-Art Review. *J Am Coll Cardiol.* 2020;76(8):961-984.
23. Pristera N, Chaudhury P, Van Iterson EH, Cho LS. Spontaneous coronary artery dissection: Principles of management. *Cleve Clin J Med.* 2021;88(11):623-630.
24. Van der Niepen P, Robberechts T, Devos H, Van Tussenbroek F, Januszewicz A, Persu A. Fibromuscular dysplasia: its various phenotypes in everyday practice in 2021. *Kardiol Pol.* 2021;79(7-8):733-744.
25. Smirnova A, Aliberti F, Cavaliere C, Gatti I, Vilardo V, Giorgianni C, et al. Spontaneous coronary artery dissection: An unpredictable event. *Eur Heart J.* 2023;25(Suppl B):B7-B11.

Importancia de la Nueva Clasificación OMS para la Caracterización Molecular de Oligodendrogliomas: A Propósito de un Caso Clínico

Importance of the New WHO Classification for the Molecular Characterization of Oligodendrogliomas: About a Clinical Case

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RESUMEN

En 2021, la Organización Mundial de la Salud (OMS) emitió la nueva clasificación de tumores del sistema nervioso central destacando el diagnóstico molecular, histológico e inmunohistoquímico. Se presenta el caso clínico de una paciente femenina de 22 años quien durante 5 años tuvo movimientos anormales e involuntarios y un único episodio de alteración del estado de consciencia. Mediante estudios imagenológicos, histopatológicos e hibridación fluorescente in situ (FISH) se diagnostica oligodendroglioma con mutación de isocitrato deshidrogenasa (IDH) y co-delección 1p19q. Se realizó craneotomía parcial y radioterapia adyuvante. La

nueva clasificación de la OMS permite una terapia orientada y resultados clínicos favorables.

Palabras clave: *Tumores cerebrales, oligodendroglioma, co-delección 1p19q, hibridación fluorescente in situ (FISH), reporte de caso.*

SUMMARY

In 2021, the World Health Organization (WHO) issued a new classification of central nervous system tumors, emphasizing molecular, histological, and immunohistochemical diagnosis. We present the clinical case of a 22-year-old female patient who experienced abnormal and involuntary movements for 5 years, along with a single episode of altered consciousness. Through imaging studies, histopathology, and fluorescence in situ hybridization (FISH) analysis, she was diagnosed with oligodendroglioma with isocitrate dehydrogenase (IDH) mutation and 1p19q codeletion.

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A partial craniotomy and adjuvant radiotherapy were performed. The new WHO classification allows for targeted therapy and favorable clinical outcomes.

Keywords: *Brain tumors, oligodendroglioma, 1p19q codeletion, fluorescence in situ hybridization (FISH), case report.*

INTRODUCCIÓN

Los oligodendrogliomas, también llamados tumores oligodendrogliales, forman parte del grupo de los gliomas, descritos como neoplasias poco frecuentes y de crecimiento lento que se originan a partir de células gliales ubicadas exclusivamente en el sistema nervioso central (1).

Dentro de los tumores intracraneales, los oligodendrogliomas representan el 2-5 % de todas las neoplasias intracraneales primarias. El 85 % de estos se localizan en los hemisferios cerebrales, especialmente en los lóbulos frontales, por lo que se pueden caracterizar clínicamente por convulsiones. En cuanto a su incidencia, se observan entre la cuarta y quinta década de la vida, siendo menos frecuentes en la niñez y la adolescencia. El tratamiento consiste principalmente en la resección quirúrgica con radioterapia y quimioterapia adyuvante (2).

Recientemente, en 2021 se emitió la quinta edición de la clasificación de tumores del sistema nervioso central de la OMS (WHO CNS5) en la cual se presenta la importancia del diagnóstico molecular para la caracterización de tumores, incluida la histología y la inmunohistoquímica. Dentro de esta clasificación se encuentran los oligodendrogliomas con mutación de la enzima isocitrato deshidrogenasa (IDH) y co-delección de 1p/19q. La mutación de la enzima IDH se ha vuelto clave en la definición de oligodendrogliomas infiltrantes en adultos, así como la co-delección 1p19q la cual determina aún más este tipo de tumor y lo diferencia de otros gliomas como el astrocitoma, en el cual la mutación de esta enzima está presente en ausencia de la co-delección cromosómica (3).

El objetivo del presente artículo es exponer el caso clínico de un oligodendroglioma por delección 1p/19q con estudios imagenológicos, histológicos, inmunohistoquímicos y cromosómicos para

así destacar la utilidad de la clasificación del 2021 de la OMS dado que hasta el momento no se han documentado reportes de caso de oligodendrogliomas en Colombia haciendo uso de esta caracterización molecular.

PRESENTACIÓN DEL CASO CLÍNICO

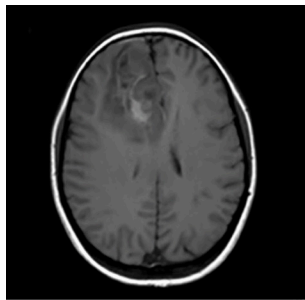
Paciente femenina de 22 años originaria de Popayán, Colombia, sin antecedentes patológicos de interés quien presenta cuadro clínico de 5 años evolución consistente en ligera bradipsiquia asociado a episodios ocasionales (mensuales) de movimientos anormales e involuntarios de la cabeza, mandíbula, y ojos. Adicionalmente, episodios de desviación de la mirada a la izquierda y visión borrosa de pocos segundos de duración sin alteración del estado de conciencia. Presentó un único episodio de mayor severidad; asociado a vómito, pérdida de la conciencia y caída desde su propia altura sin relajación de esfínteres, no presentó postura tónica ni movimientos clónicos, motivo por el cual consulta al servicio de urgencias.

Se realiza una resonancia magnética cerebral (RMC) contrastada con gadolinio cuyos hallazgos sugieren neoplasia cerebral primaria de origen glial de bajo grado, la cual infiltra el lóbulo frontal derecho, cuerpo caloso y núcleo caudado; así mismo, genera efecto de masa sobre el ventrículo derecho (Figura 1). No se realizan imágenes adicionales.

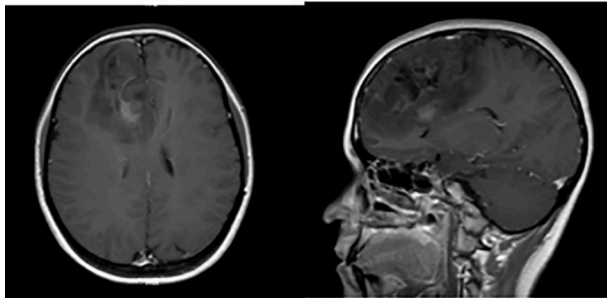
Dados los hallazgos imagenológicos, se decide manejo quirúrgico realizándose craneotomía frontoparietotemporal derecha, con amplia resección tumoral microquirúrgica, sin resección de las zonas más profundas como cuerpo caloso y núcleo caudado para evitar secuelas neurológicas permanentes. Procedimiento sin complicaciones. Durante el postoperatorio evoluciona de manera favorable con ligera hemiparesia de predominio crural con mejoría progresiva y recuperación completa al recibir fisioterapia.

Al ser una resección incompleta, se realiza terapia adyuvante con 27 sesiones de radioterapia. Se administra un total de 54 Gy con un fraccionamiento convencional de 2 Gy por sesión.

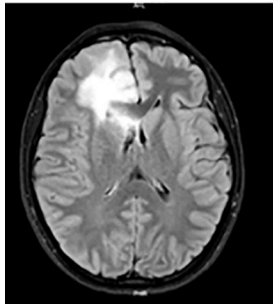
En el estudio histopatológico del bloque extraído se documentan células redondas con



A. T1 sin contraste



B, C. T1 con contraste corte transversal y sagital



D. FLAIR

Figura 1. **A.** Lesión infiltrativa de un volumen mayor de 80 mm x 48 mm x 51 mm de características heterogéneas con pequeñas calcificaciones que compromete la primera y segunda circunvolución frontal derecha, giro del cíngulo, porción anterior del cuerpo calloso con infiltración del esplenio y se observa compresión del cuerno frontal derecho y del caudado. **B y C.** Tras administración de gadolinio no se observa realce importante de la lesión. **D.** En el Flair, se observa lesión hiperintensa difusa rodeada de edema. Hallazgos sugestivos de oligodendroglioma.

citoplasma claro y núcleos redondos con pequeño nucléolo y con muy esporádicas mitosis; las cuales tienen apariencia de “huevo frito” (Figura 2). El estroma se visualiza fibroso, vascularizado, sin áreas de necrosis. Inmunohistoquímica

OLIG2 (71X) e IDH1(71X) evidencia intensa reactividad de las células neoplásicas (Figura 3). Neurofilamento con positividad focal. Reactividad nuclear para P53 en el 1 % de las células neoplásicas. Ki67, positivo nuclear del 12 % de las células tumorales. CD56, intensamente positivas. Reactividad negativa para CK20 y, por último, vimentina positiva, compatible con diagnóstico de oligodendroglioma tipo 2 según la anterior clasificación de la WHO 2016 según patología. En comparación con la clasificación de la WHO 2016, según la actual clasificación, el diagnóstico corresponde a un oligodendroglioma IDH- mutante y 1p/19q codificado, CNS WHO grado 2, dados los hallazgos a nivel imagenológico, puesto que este infiltra de forma difusa el parénquima cerebral, con calcificaciones sin áreas de necrosis, se encuentra la predilección por la ubicación en lóbulos frontales, no se observa realce en la resonancia T1 con la administración del medio de contraste, asimismo, a nivel histopatológico, las características de las células son núcleos redondos con aumento en densidad de la cromatina y citoplasma claro, compatible con apariencia de huevo frito sin otros fenotipos celulares y actividad mitótica baja, y por último, a nivel molecular, presencia de la mutación en la enzima IDH y co-delección de los brazos cromosómicos 1p y 19q (3).

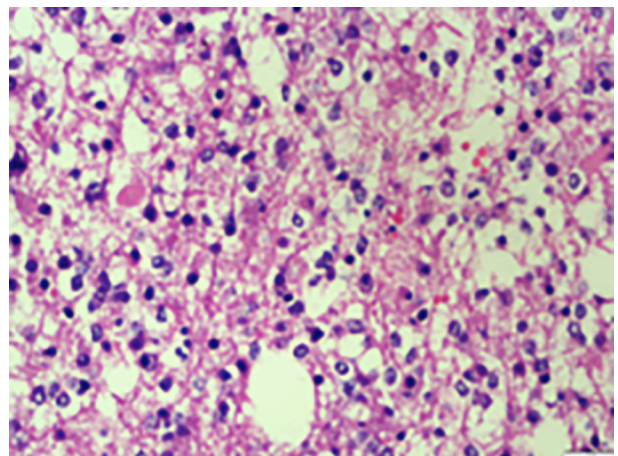


Figura 2. H/E (100X) Células redondas con citoplasma claro con aspecto de huevo frito, mitosis esporádicas.

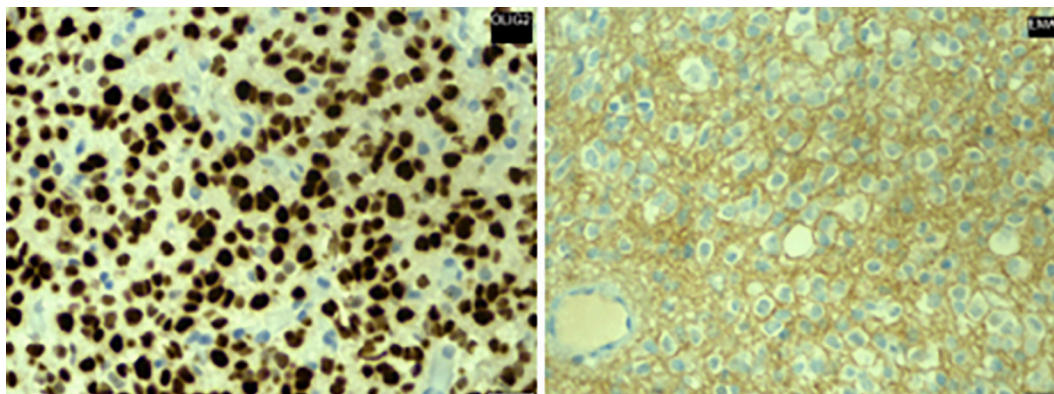


Figura 3. A. OLIG2 (71X) Positivo nuclear en células neoplásicas B. IDH (71X) Positivo nuclear en células neoplásicas

Teniendo en cuenta las características de esta neoplasia y la alta probabilidad de una mutación cromosómica responsable de la formación tumoral, se efectuó el protocolo de hibridación *in situ* con fluoresceína (FISH) para la determinación de la co-delección cromosómica. Se reporta el FISH positivo para la co-delección del 1p36 y del 19q13.

Se realiza control y seguimiento de la paciente mediante realización periódica de neuroimágenes (resonancia nuclear magnética contrastada cerebral) en las cuales se observan cambios postquirúrgicos en la región frontal derecha (área de encefalomalacia tabicada, restos hemáticos en diferentes estadios, realce dural y edema perilesional), sin hallazgos sugestivos de recidiva ni tumor residual basados en las secuencias de perfusión, difusión y contraste.

Consentimiento: Se obtuvo el consentimiento informado por escrito de la paciente para la publicación de este informe de caso y las imágenes que lo acompañan.

DISCUSIÓN

La actualización para las neoplasias del SNC OMS en 2021 incorporó la utilidad clinicopatológica de los parámetros histológicos y cambios moleculares para realizar una clasificación más precisa, que, además, aporta

información pronóstica. De esta forma, se ha adoptado un nuevo enfoque para clasificar los gliomas, los tumores glioneurales y los tumores neuronales dividiéndolos en 6 familias: gliomas difusos de tipo adulto, gliomas difusos de bajo y alto grado de tipo pediátrico, gliomas astrocíticos circunscritos, tumores glioneurales y neuronales y ependimomas. Entre los gliomas difusos de tipo adulto, se encuentran los oligodendrogliomas, IDH- mutado, y con co-delección de 1p/19q (3).

Desde el punto de vista histopatológico, los oligodendrogliomas se caracterizan por presentar cromatina delicada, nucleolos pequeños con núcleos generalmente redondos y uniformes recubiertos por membranas nucleares. La imagen típica de esta neoplasia es la presencia de un halo claro y perinuclear que da la apariencia de un “huevo frito” (4).

Para realizar el diagnóstico, es esencial tener características histológicas, así como pruebas genéticas y moleculares, que evidencien la mutación de la enzima IDH junto con la co-delección 1p/19q la cual corresponde a la translocación balanceada del brazo corto del cromosoma 1 y el brazo largo del cromosoma 19 (3). La detección de esta anomalía cromosómica se realiza por técnica de hibridación *in situ* (FISH), que detecta secuencias específicas de ácidos nucleicos a través de marcación con fluorescencia permitiendo visualizar el cromosoma. La pérdida de los alelos en los

cromosomas 1p y 19q representan un factor pronóstico marcador y predictor de supervivencia prolongada (5).

Por otro lado, los signos y síntomas que los pacientes pueden presentar están íntimamente relacionados con la ubicación, velocidad de crecimiento y tamaño de la lesión. La manifestación clínica más común son las convulsiones (3,6). Otros síntomas encontrados son cefalea y manifestaciones asociadas a déficit neurológico. Las lesiones con compromiso de lóbulos frontales están asociadas con movimientos involuntarios en extremidades, alteraciones cognitivas, en la personalidad, el lenguaje y cambios comportamentales (3,7).

Cuando la lesión compromete áreas como el cuerpo calloso y regiones interhemisféricas se produce una alteración en la transmisión de un hemisferio a otro, lo que conduce a un procesamiento de la información inadecuado, generando en el paciente dificultad en el aprendizaje y alteraciones en la percepción de estímulos somáticos (8).

Para el abordaje de este tumor y la intervención quirúrgica que requiere, es indispensable la realización de neuroimágenes. La resonancia magnética se considera el método imagenológico de elección ya que aporta información morfológica detallada sobre metabolismo y perfusión de la lesión. Los oligodendrogliomas se presentan como lesiones isointensas o hipointensas en la secuencia de T1 e hiperintensas en T2 (9).

El tratamiento quirúrgico se realiza comúnmente con fines diagnósticos y terapéuticos, idealmente se extirpa tanto tejido tumoral como sea posible para realizar estudios moleculares y a la vez reducir los síntomas generados por el efecto de masa del tumor sobre estructuras adyacentes sin comprometer la función neurológica (10). Sin embargo, es importante tener en cuenta que los cambios postquirúrgicos pueden generar una zona epileptógena por lo que se recomienda el uso de manejo antiepiléptico (4).

Se requiere, además, de terapias coadyuvantes, en estudios retrospectivos realizados sugieren beneficios de la radioterapia independiente frente a la quimioterapia agregada en este tipo de tumores (2). El objetivo de la radioterapia es mejorar el control local sin inducir neurotoxicidad,

así como retrasar el deterioro neurológico y aumentar la supervivencia. La radioterapia debe comenzar dentro de las 3 a 5 semanas posteriores a la cirugía y comúnmente se administra a 50 a 60 Gy en fracciones diarias de 1,8 a 2 Gy (10).

Finalmente, en estos tipos de tumores tienen una adecuada respuesta al manejo con un tiempo de sobrevida mayor a 10 años (3). Este caso en particular se acompaña de factores clínicos de buen pronóstico como lo son la edad joven de la paciente, las convulsiones como la clínica inicial sin embargo debido a la localización la resección no fue completa lo cual podría afectar en el desenlace general (3).

Por todo lo anterior, se destaca la importancia del diagnóstico molecular, incluida la histología y la inmunohistoquímica de los tumores del sistema nervioso central para orientar de manera temprana el tratamiento y así lograr desenlaces clínicos favorables. De igual manera, se recomienda un estudio prospectivo para realizar un análisis comparativo de la radioterapia y/o quimioterapia en este tipo de tumores y su impacto en el pronóstico del paciente.

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Conflicto de intereses

Los autores declaran no tener conflicto de intereses alguno.

REFERENCIAS

1. Aiman W, Gasalberti DP, Rayi A. Low-Grade Gliomas. En: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. Disponible en: <http://www.ncbi.nlm.nih.gov/books/NBK560668/>
2. Cao L, Rong P, Zhu G, Xu A, Chen S. Clinical Characteristics and Overall Survival Prognostic Nomogram for Oligodendroglioma: A Surveillance,

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- Epidemiology, and End Results Population-Based Analysis. *World Neurosurg.* 2021;151:e810-20.
3. WHO Classification of Tumours Editorial Board. *Central Nervous System Tumours*. 5th edition. 2021;6.
 4. Winn HR. *Youmans and Winn Neurological Surgery*. 8^a edition. Elsevier Health; 2022;4.
 5. Bhattacharya D, Sinha N, Saini J. Determining chromosomal arms 1p/19q co-deletion status in low graded glioma by cross correlation-periodogram pattern analysis. *Sci Rep.* 2021;(23866).
 6. Englot DJ, Chang EF, Vecht CJ. Epilepsy and brain tumors. En: *Handbook of Clinical Neurology*. Elsevier. 2016:267-285.
 7. Rees JH. Diagnosis and treatment in neuro-oncology: an oncological perspective. *Br J Radiol.* 2011;84(Spec Iss 2): S082-9.
 8. Zarranz JJ. Trastornos de las funciones cerebrales superiores. En: *Neurología*. 6^a edición. Elsevier; 2018;181-217.
 9. Diaz AI, Gallardo F, Orellana M, Chiarullo M, Caicedo D CA, Nuñez M. Guía para la resección de gliomas de bajo grado en relación a áreas elocuentes en el paciente despierto con mapeo cortical y subcortical. *Rev Argent Neurocir.* 2022;36(02).
 10. Weller M, van den Bent M, Preusser M, Le Rhun E, Tonn JC, Minniti G, et al. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. *Nat Rev Clin Oncol.* 2021;18(3):170-186.

Treatment of Skin Oncological Disease Using an Immunosuppressive Medication

Tratamiento de la Enfermedad Oncológica de la Piel Mediante Medicamentos Inmunosupresores

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SUMMARY

Introduction: Skin cancer or non-melanoma malignant formations, as well as melanomas, are recorded in more than 2-3 million people every year. The most important cause of the occurrence of this disease is the effect of UV radiation on damaged areas of the skin, birthmarks, or sensitive skin (light, capable of burning). Dermatoscopy is one of the most important methods for determining the stage of tumor development, and the simplest method of treatment in the initial stages is the use of immunosuppressive agents that reduce the work of the immune system by preventing the formation of antibodies.

Objectives: The study aims to investigate the correlation between immunosuppressive drug usage and susceptibility to skin oncological diseases. The study investigated the correlation between immunosuppressive drug usage and susceptibility to skin cancer, particularly melanoma. The specific objectives involve assessing the influence of these medications on melanoma risk, understanding their effects on skin cancer treatment outcomes, optimizing treatment approaches for reduced adverse effects, uncovering the intricate interplay between immune suppression and cancer management, contextualizing findings within the framework of cancer immunotherapy advancements, and revealing the impact of immunosuppressive drugs on susceptibility to rare cancers like Kaposi's sarcoma. **Methods:** For this study, it was taken a case of Kaposi's sarcoma from

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an 82-year-old man. The patient took 122 doses of the immunosuppressive drug Nivolumab for 2 weeks.

Results: After the end of the drug's intake, the parts of the gastrointestinal tract were examined, and as a result, it was found that the patient recovered. When compared with people who do not take immunosuppressive drugs, there is a high risk of melanoma development; moreover, the highest risk has been found in drugs used to prevent the rejection of transplanted organs. The negative effects of immunosuppressive drugs such as immunosuppression and skin photosensitivity may explain these results. These findings may help reduce the risk of skin oncological disease through increased surveillance and awareness and more careful sun exposure for doctors and users of these drugs.

Keywords: Pharmacokinetics, Kaposi's sarcoma, corticosteroids, lysine cell syndrome, dermatosis, adenocarcinoma.

RESUMEN

Introducción: El cáncer de piel o las formaciones malignas no melanoma, así como los melanomas, se registran en más de 2-3 millones de personas cada año. La causa más importante de la aparición de esta enfermedad es el efecto de la radiación UV en las áreas dañadas de la piel, marcas de nacimiento o piel sensible (ligera, capaz de quemarse). La dermatoscopia es uno de los métodos más importantes para determinar la etapa de desarrollo del tumor, y el método de tratamiento más simple en las etapas iniciales es el uso de agentes inmunosupresores que reducen el trabajo del sistema inmunológico al prevenir la formación de anticuerpos. **Objetivo:** El objetivo del trabajo fue mostrar que el tratamiento del paciente (en el ejemplo de un hombre con sarcoma) con fármacos inmunosupresores apropiados tiene una dinámica positiva de recuperación y puede ser utilizado en el futuro para el tratamiento de cáncer de piel. Los inmunomoduladores pueden influir en las causas del melanoma al impedir que el sistema inmunitario responda al tumor y al hacer que la piel sea más sensible a la luz solar. Este trabajo epidemiológico investiga la conexión entre el uso de fármacos inmunomoduladores (incluidos los corticosteroides sistémicos y los inmunosupresores) prescritos para cualquier indicación. **Métodos:** Para este estudio se tomó un caso de sarcoma de Kaposi de un hombre de 82 años. El paciente tomó 122 dosis del fármaco inmunosupresor Nivolumab durante 2 semanas. **Resultados:** Después del final de la ingesta del fármaco, se examinaron las partes del tracto gastrointestinal y, como resultado, se encontró que el paciente se recuperó. Cuando se compara con personas que no toman medicamentos

inmunosupresores, existe un alto riesgo de desarrollar melanoma; además, el mayor riesgo se ha encontrado en los fármacos utilizados para prevenir el rechazo del órgano trasplantado. Los efectos negativos de los fármacos inmunosupresores como la inmunosupresión y la fotosensibilidad de la piel pueden explicar estos resultados. Estos hallazgos pueden ayudar a reducir el riesgo de enfermedades oncológicas de la piel a través de una mayor vigilancia y conciencia y una exposición solar más cuidadosa para los médicos y usuarios de estos medicamentos.

Palabras clave: Farmacocinética, sarcoma de Kaposi, corticoides, síndrome de células de lisina, dermatosis, adenocarcinoma.

INTRODUCTION

In recent years, advances in immunotherapy have revolutionized the field of oncology, offering innovative strategies to combat cancer by harnessing the body's own immune system. One area of exploration within this realm is the treatment of skin oncological diseases using immunosuppressive medications. In light of the evolving landscape of cancer treatments and the increasing use of immunosuppressive therapies, it becomes paramount to comprehend the implications of these medications on both the management of skin cancer and the likelihood of developing it.

The contemporary landscape of oncology is marked by the advent of checkpoint inhibitor therapies, a groundbreaking approach that utilizes immunomodulation to counter advanced cancers. As seen in recent research by Saller et al. (1) and Uldrick et al. (2), the intricate nature of complex cancers demands prompt diagnosis and proactive treatment strategies to mitigate both mortality and morbidity. In this context, understanding the dynamics of immunosuppressive medications and their potential role in shaping cancer outcomes becomes even more crucial.

The modern understanding of cancer underscores the critical role of the immune system in identifying and combating abnormal cells that arise due to tumor formation. While the immune system possesses the ability to recognize and target cancerous cells, the adaptability of cancer cells to mutate poses a significant challenge. This adaptive behavior necessitates

the activation of the immune system to effectively recognize and combat these evolving cancer cells. Immunotherapy emerges as a potent tool to enhance the body's immune response against atypical cells, holding promise as an effective strategy in the fight against oncological disorders.

However, the application of immunosuppressive medications in various medical contexts introduces complexities that warrant thorough investigation. This study recognizes the need to explore the potential interplay between immunosuppressive drugs and the risk of developing skin cancer, particularly focusing on the case of melanoma. The rarity of certain skin malignancies, like Kaposi's sarcoma caused by human herpes virus 8 (HHV-8) (3), further accentuates the importance of this research, as it provides insights into the impact of immunosuppression on the treatment outcomes and susceptibility to these rare cancer types.

The previous studies specifically focused on the relationship between the use of immunomodulatory drugs, such as systemic corticosteroids and immunosuppressants, and the risk of developing melanoma at a national level. The existing literature lacks comprehensive studies that directly investigate the interplay between immunosuppressive therapies and the risk of developing skin cancer, particularly melanoma, on a broader scale. This research aims to fill this gap by providing insights into how these medications might influence the susceptibility to melanoma and the subsequent treatment outcomes.

This study not only seeks to contribute to the growing body of knowledge surrounding the effects of immunosuppressive therapies on skin cancer risk and treatment but also aims to contextualize its findings within the broader landscape of immunotherapy's evolution. By developing the delicate balance between immune suppression and cancer management, this research ultimately strives to provide clinicians and researchers with valuable insights into optimizing treatment strategies and minimizing the risk of adverse outcomes in the dynamic field of oncology.

The novelty of this study lies in its exploration of the relationship between the use of immunomodulatory drugs, such as systemic

corticosteroids and immunosuppressants, and the risk of melanoma at a national level. The study examines the impact of immunosuppressive therapy on the treatment of skin cancer and the relationship between the use of immunosuppressive drugs and the risk of developing melanoma. Given that Kaposi's sarcoma is a rare type of cancer and the study looks at a specific case of a patient with this disease, the results are valuable for understanding the impact of immunosuppressive drugs on the treatment and risk of developing skin cancer.

MATERIALS AND METHODS

This study included 102 patients with non-Hodgkin's lymphoma (NHL) with high Tumor lysis syndrome (TLS), which amounted to 42 %, but only 6 % of TLS had clinical significance. The research methods employed in this study encompassed a series of diagnostic and therapeutic approaches to investigate the case of an 82-year-old patient presenting with an erythematous pruritic rash on the posterior femoral condyles that did not disappear within 4 weeks. Pathological diagnosis of puncture biopsy corresponded to Kaposi's sarcoma.

Diagnostic techniques used in the study included ELISA testing to assess human immunodeficiency virus (HIV) status, Computer Tomography (CT) Scan to visualize anatomical structures and identify lymphadenopathies, multiparametric MRI to evaluate the prostate gland, and Positron Emission Tomography and Computed Tomography (PET-CT) Scans imaging to detect potential metastases. These diagnostic tools were crucial for characterizing the patient's health condition, pinpointing abnormalities, and establishing the presence of various medical issues.

Histopathological analysis played a pivotal role in confirming suspected diagnoses. Puncture biopsies and endoscopic procedures were performed to obtain tissue samples for examination, aiding in the accurate identification of Kaposi's sarcoma and the presence of metastatic lesions in the stomach. The combination of these diagnostic procedures provided a comprehensive and detailed understanding of the patient's health

status and disease progression.

The study involved a multidisciplinary approach to treatment decision-making. The patient's preferences and medical condition were taken into consideration, leading to the proposal and discussion of alternative treatment options. These discussions encompassed potential interventions such as interferon therapy and immunotherapy. Ultimately, the patient chose to undergo immunotherapy using Nivolumab.

Nivolumab, a monoclonal antibody targeting cell death receptor-1 and hindering immune cell apoptosis, was administered to the patient at regular intervals. The efficacy of the treatment was monitored through subsequent assessments, including F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography and endoscopy. After a series of Nivolumab administrations, a complete response to the treatment was observed, with lesions being notably reduced. The patient's subsequent remission and sustained recovery over a 12-month follow-up period, achieved without resorting to standard chemotherapy due to his fragile health condition, marked a significant and successful outcome.

This case not only showed the potential effectiveness of immunotherapy in cases where traditional treatments are unsuitable but also highlighted the importance of tailoring medical interventions to individual patient's needs and health status. The combination of diverse diagnostic methods, thoughtful treatment discussions, and the strategic application of immunotherapy underscored the value of a comprehensive approach to patient care in complex medical scenarios.

This study aligned with the ethical principles of research, including anonymity, confidentiality, and beneficence. Ethical approval of the study was obtained from the Health Research Ethics Commission of the Riga Stradins University with No. LR-098.

RESULTS

The results of the study regarding the relationship between immunosuppressants and

the occurrence of melanoma show a preferential inhibition of the growth of melanoma cells, mainly through the proapoptotic mechanisms. Immunosuppressant drug therapy often consists of several drugs administered simultaneously as part of a program collective treatment regimen. The combination and amount of drug administration may change during the treatment. A positive result is achieved with high doses of immunosuppressants. Preventive strategies play an important role in patients with immunosuppression, considering the increased frequency and speed of development of precancerous and malignant skin lesions. Sun protection is a modified risk factor for skin cancer, and it should be discussed with all immunosuppressed patients. Patients should receive detailed consultations regarding sun avoidance, the use of sunscreen, and the use of sun-protective clothing.

Unfortunately, immunosuppressive regimens have a non-specific effect, causing a profound and non-specific impairment of humoral and cellular immunity. The following fact is the unintended consequence of immunosuppression: internal and cutaneous malignancies occur at markedly increased rates in transplant recipients. Modern methods of fighting malignant tumors have been able to prove that chemotherapy is not the sole effective method of treatment.

New research findings have shown that Nivolumab in combination with chemotherapy or without it may have better results than conventional chemotherapy regarding improving the well-being of patients (4). Lipson et al. (5) have stated that it is also possible to administer a new immune checkpoint inhibitor of Relatlimab to Nivolumab, which significantly prolongs the patients' lives with advanced melanoma, which was previously untreated. Unlike Nivolumab, Relatlimab has a different mechanism of action. It is not an immune checkpoint inhibitor that act on PD-L1. Relatlimab, in contrast, acts as an antibody that will affect the lymphocyte activation gene (LAG-3), which will suppress the immune response of T-cells to the body. Thus, studies confirm the positive effect of immunosuppressants on inhibiting melanoma cell growth, especially when using combination regimens, such as the addition of a new immune checkpoint inhibitor Relatlimab to Nivolumab.

The case study presented a unique patient scenario that prompted the consideration of various diagnostic and treatment strategies. HIV testing using the ELISA method returned negative results, eliminating it as a contributing factor. The CT scan revealed multiple lymphadenopathies in the right inguinal region, raising concern about potential malignancies. After radiotherapy, regular follow-ups tracked the patient's progress. A subsequent chest imaging due to back pain uncovered metastatic lesions in the T3 vertebral body, signaling disease progression. The accompanying increase in prostate-specific antigen led to a multiparametric MRI of the prostate, which confirmed prostate adenocarcinoma. Further investigations involved a prostate biopsy and a series of procedures like FGDS and PET-CT to identify lesions and exclude metastases. Notably, the patient's complex health status hindered the prescription of systemic chemotherapy, necessitating alternative treatment options.

Despite suggested interferon therapy, the patient declined and instead underwent a diagnostic endoscopy due to persistent anemia. The endoscopy revealed metastatic Kaposi's sarcoma in the stomach, while PET-CT highlighted parenchymal formations in the lungs. Given the patient's frail health, treatment decisions require careful consideration. Consultations introduced alternative interventions including interferon therapy and immunotherapy, with the patient opting for immunotherapy. Nivolumab, a monoclonal antibody that inhibits cell death receptor-1, was administered at a two-week interval. This choice was informed by its positive outcomes in metastatic lung cancer treatment. After 12 doses of Nivolumab, FDG-PET scans and endoscopy demonstrated a complete response, with no lesions present. Remarkably, the patient remained in remission for 12 months without further drug use. This outcome is noteworthy, particularly for patients unfit for standard treatments due to their health status.

Table 1
Different types of development of cancer

Form	Manifestation
Synchronous	The development of all cancers at the same time. A person may be diagnosed with multiple types of cancer simultaneously.
Sequential	The sequential development of different types of cancer. A person may be diagnosed with one type of cancer, and later develop another type of cancer.
Affecting each other	The interaction between tumors. A tumor in one part of the body may affect the development or progression of a tumor in another part of the body.

It is important to note that the dynamics of the disease in a patient with several types of malignant tumors can be different (Table 1). It depends on the type of cancer, stage, location, and interaction between them.

Symptoms will vary depending on the location and stage of each cancer and may include both general signs of weight loss, weakness, fatigue, and specific symptoms associated with each type of cancer. The details of the dynamics of manifestations depend on the specific clinical

case. It is also worth noting that HIV-infected patients may have not only complications such as AIDS but also a high risk of cancerous tumors such as Kaposi's sarcoma and others. The cancer-causing action of HIV has not yet been studied, but some studies show that HIV damages many tissues (intestine, lungs, and brain) due to the activation of mononuclear cells and infection (6).

HIV negatively affects cellular immunity, which may be the cause of carcinogenesis. In the absence of effective ART (antiretroviral

therapy), uncontrolled HIV infection leads to a significant decrease in HIV-infected CD4+ cells and uninfected CD4+ satellite cells in the blood and tissues. Under the same conditions, the CD8 count often increases, resulting in a change in the CD4/CD8 half ratio, an independent marker of immune dysfunction. In addition, HIV increases the expression of immune protein markers (PD-1), CD8-marker of T-cell depletion and dysfunction, which lead to dysregulation and systemic immune dysfunction. Undiagnosed HIV reduces the amount and range of T-cell immunity; HIV causes a decrease in undifferentiated T-cells, a regression in the diversity of the total number of T-cells in the blood, and a decrease in the number of T-cell receptors (TCR) due to CD4+ depletion and expansion of the CD8 oligoclonal population. Because of its high virulence, HIV is rapidly inhibited with modern ART. After the prescription of ART, CD4+ is restored, while CD8 on the contrary decreases.

The earlier the diagnosis is made and the younger the age for ART, the greater the likelihood of complete immune recovery, although the immune recovery is often incomplete. The worsening of the inflammatory state associated with curable and incurable HIV stages contributes to adverse long-term results. Given the above, HIV infection increases the risk of developing cancer, including Kaposi's sarcoma. Poor control of HIV infection and the impact of HIV on the immune system may contribute to carcinogenesis. Antiretroviral therapy can improve the immune system, but undiagnosed and uncontrolled HIV infection can lead to systemic immune dysfunction and adversely affect treatment outcomes (2).

Immunodeficiency is one of the risk factors for sarcoma; the unprogrammed cell division with cancer viruses and insufficient immune status are the main causes of immunodeficiency. Many carcinogenic viruses cause cancer in other immunodeficiency conditions such as congenital immunodeficiency and organ transplantation; CD4+ deficiency is strongly associated with malignancies independent of HIV infection (6).

The presence, number, and function of CD4+ T-cells are important in many stages of carcinogenic way, including the recognition of tumor antigens, the development of effective neutralizing antibodies, and cellular responses to

viral pathogens and precancerous lesions. The risk of developing cancer in humans depends on a decrease in CD4+ levels, which may indicate a synergistic relationship between chronic inflammation and a decrease in the immune status. A decrease in the number of CD4+ lymphocytes, ineffective CD8 response, and the associated immune dysfunction led to a decrease in the immune response, an important mechanism associated with HIV carcinogenesis (2).

This can be explained by the relationship between HIV, immune status, and cervical cancer: people with HIV are more likely to be infected with high-risk HPV, they are less likely to recover from HPV and more likely to develop high-grade malignancies. People living with HIV and low levels of CD4+ are also more likely to go from dysplasia to invasive cancer. During the clinical trial of the HPV vaccine (human papillomavirus) in HIV-infected adolescents, the induced antibody titers positively correlated with the CD4+ count, which is a key correlate of protection against the HPV vaccine, confirming the need for CD4+ T-cells in the synthesis of highly specific antibodies, which is the major inhibitory factor of HPV vaccines. HIV-specific CD4+ and CD8 T-cells are also localized in tissues, which can have a major impact on tumor regression. Immunosuppression and aging of T-cells are observed in chronic viral infections and malignant tumors (2).

In people living with HIV (PLHIV), poor function of T-cell is most associated with the development of lymphoma and Kaposi sarcoma (KS), associated with Epstein-Barr virus (EBV); in HIV-associated non-Hodgkin's B-cell lymphoma, T-cell multifunctionality and the reduced diversity of T-cell receptor are associated with a poor prognosis. These observations raised the interest in correcting immune dysfunction for the treatment of malignancies in HIV-infected people.

ART is one of the most effective immunotherapies. Improvements in ART in 1996 reduced the frequency and severity of KS and changed its natural course. The decrease in the risk of death from KS at the same levels of (HIV) RNA and CD4+ indicates that ART both improves the immune control in KS and reduces the immunomodulatory disorders. ART restores

immunity in approximately 80 % of PLHIV in the early stages of KS and regression of KS lesions. However, in advanced SC, ART alone is often insufficient (7). Several immunotherapies have shown their effectiveness in the treatment of SM and other HIV-associated cancers. Interferon- α (IFN- α) was the first true immunotherapy used to treat cancer.

During the latent phase, the sarcoma does not cause obvious pathological symptoms in the patient. After the penetration of the virus into the host's cell, a latent phase begins, during which some genes are expressed in very limited quantities. These are the proteins, corresponding to the genes: latent-associated nuclear antigen (LANA), regulatory factor of the viral interferon (vIRF3/LANA2), viral inhibitory protein FLICE (vFLIP), caposin, and viral microRNA. So, antiretroviral therapy is one of the most effective immunotherapy methods for the treatment of HIV infection and its complications. Improved outcomes in the treatment of HIV-associated diseases, including Kaposi's sarcoma, have been observed with ART, which reduces the frequency and severity of these diseases, restores immune control, and regresses lesions. However, in advanced Kaposi's sarcoma, ART alone may often be insufficient, and there are other immunotherapies, such as interferon- α (IFN- α), that are effective in treating various HIV-associated cancers.

Reactivation of the lytic cycle is an important factor in carcinogenesis; it is evidenced by the discovery that inhibition of the lytic cycle by ganciclovir reduces the risk of developing sarcoma by 74 %. It is believed that the lysogenic cycle provides a signal that stimulates the growth of latent cells and therefore tumors. This stage of viral infection involves the expression of viral proteins, genome replication, and the assembly of new virions by the host cell, which then come out of the cell using budding. The stimulus that initiates the lysogenic cycle is not well defined, but the process can be initiated by substances such as 12-O-tetradecanoyl-formaldehyde-13-phorbol-13-acetate (TPA), sodium butyrate, ionosine (calcium ionophore), epinephrine, and norepinephrine. At physiological concentrations, several cellular factors (X-box binding protein 1 (XBP-1), CREB binding protein (CBP), a complex of chromatin remodeling SWI/SNF,

TRAP/Mediator complex, RBPJ κ , human Notch intracellular domain and High Mobility Group Window 1 (HMGB1) influence on the nervous system, vegetative activity, hypoxia, and reactive oxygen species (ROS) in AIDS patients.

Recently, nitric oxide (NO) also plays an important role in the development of sarcoma tumors. According to Herrera-Ortiz et al. (3), NO inhibition resulted in a decrease in the infectious virus, lysogenic transcript, and protein. Proteins of the SARS-CoV-2 virus, namely the S and N proteins, cause tic reactivation and accelerate carcinogenesis. In addition, it has also been reported that some of the anti-COVID-19 drugs have been used in the study; ACE2 receptor expression is high in the AIDS- KS tissues, but there is no clear correlation between the femur and Kaposi's sarcoma and activation (as it is stated in the report). CD147, a multifunctional glycoprotein that is activated in the case of new infections of sarcoma and the Kaposi's sarcoma tissue, is also a co-receptor for the penetration of SARS-CoV-2 into the host's cells (8). Other viruses can also cause reactivation of the lysis cycle of Kaposi's sarcoma, such as HIV, herpes simplex virus type 1 (HSV-1), HSV-2, human cytomegalovirus (CMV), human herpesvirus 6 (HHV-6) and HHV-7. Since the cancer cells and spindle cells tend to isolate latent viral genomes, it is necessary to conduct the hemolytic reactivation of populations of small cells to maintain the presence and latency of the virus.

Thus, the reactivation of the lytic cycle in Kaposi's sarcoma plays an important role in carcinogenesis, and the use of ganciclovir to inhibit this cycle has shown a significant positive effect, reducing the risk of developing sarcoma by 74 %. The lysogenic cycle of viral infection, which includes gene activity and genome replication, also contributes to the stimulation of latent cell growth and tumor development. Various substances and factors, such as 12-O-tetradecanoyl-formaldehyde-13-phorbol-13-acetate (TPA), sodium butyrate, ionosine, epinephrine, norepinephrine, and others, can initiate the lysogenic cycle. In addition, nitric oxide (NO), as well as proteins of the SARS-CoV-2 virus, cause reactivation and promote carcinogenesis. Other viruses, such as HIV, HSV-1, HSV-2, CMV, HSV-6, and HSV-7, can also cause reactivation of the lysogenic cycle in

Table 2

Gene phases in the hemolytic cycle

Phase	Expression
Immediate early (IE)	Expressed early in the hemolytic cycle, and typically involved in the initiation of the cycle and the early stages of hemolysis.
Early (E)	Expressed slightly later in the hemolytic cycle than IE genes and involved in the amplification of the hemolytic response.
Late (L)	Expressed later in the hemolytic cycle than E genes, and involved in the terminal stages of hemolysis and the clearance of damaged cells

Kaposi's sarcoma. Hemolytic reactivation of cell populations is necessary to maintain viral presence and latency. Genes that are expressed during the hemolytic cycle can be divided into three groups (Table 2).

Therefore, skin cancer is an abnormal growth of skin cells. It often occurs under the influence of solar radiation. However, the common forms of cancer can also be caused by other factors. There are three forms of skin cancer – basalioma, squamous cell carcinoma, and melanoma. Kaposi's sarcoma is a less common form of skin cancer that affects the blood vessels in the skin and causes red or purple spots on the mucous membrane or skin.

The studied case underscores the significance of individualized treatment approaches and highlights the potential of immunotherapy, like Nivolumab, in situations where conventional options are unsuitable. It also emphasizes the importance of diagnostic precision in complex medical cases, showcasing how a multidisciplinary approach can yield positive outcomes. Furthermore, the findings align with emerging research, demonstrating the effectiveness of immunotherapy regimens in conjunction with standard therapy. Thus, the overall conclusion from the positive treatment outcomes is that immunotherapy, including the use of drugs that support the immune system and suppress tumor development, has significant potential in the fight against cancer. The introduction of new therapies, such as ART, has reduced the incidence and severity of certain cancers, improved immune control, and increased the chances of full immune recovery in patients. In addition, studies of immunotherapy in the context of other HIV-associated cancers,

such as Kaposi's sarcoma, have also shown positive results. Given this, further research and development of immunotherapeutic approaches may lead to further improvement in the treatment outcomes of cancer patients.

DISCUSSION

The results revealed immunosuppressants' potential as targeted melanoma treatment and the effectiveness of new immunotherapies like Nivolumab with Relatlimab in advanced melanoma. It is necessary to explore the broader implications of exploiting immunosuppression therapeutically and optimizing immunomodulatory approaches for cancer.

Volkow et al. (9) note the following in their article on the mortality in severe Kaposi's syndrome: In HIV-infected patients who receive ART, the HIV RNA in the blood plasma may not be detectable using the simple laboratory tests, but there is still a reservoir of potentially HIV-infected cells that can reappear after stopping ART. Maintenance of the HIV reservoir may depend on the duration of the existence of the CD4+ T-cell memory that is in the resting phase (G0). There is growing evidence that their stability does not change its values through the clonal extensions. In genomic studies, HIV penetration stimulates the transcriptional regions of active genes that promote HIV replication and delay, as well as stimulates the ways associated with carcinogenesis. The HIV reservoir is the hub of research on functional HIV therapy. The so-called "hit and kill" theory suggests HIV delaying during ART; the change in duration

(activation of HIV replication in the latently infected cells) increases the immunogenicity of HIV-infected cells and immunity to HIV, which leads to increased cell death (10, 11).

Various immunotherapeutic drugs used to inhibit cancer cells can destroy the HIV-respository by causing a change in delay or increased cell killing. Several drugs are under diagnostic testing for the HIV reservoir: CPI, an immune checkpoint inhibitor. These studies are given in the work of Dupin et al. (12) on the diagnosis of Kaposi's sarcoma. Some immunotherapeutic agents used in cancer treatment have a targeted effect aimed at changing the delay and/or persistence of HIV. Anti-PD-1 therapy is a therapy with anticancer agents that reduce CD4+ count and HIV RNA, which are aimed at the HIV reservoir. Expression of PD-1 and CTLA-4 may be increased due to chronic HIV infection, and HIV DNA and unconjugated RNA are diagnosed in tests of HIV patients who receive ART, and lymph nodes are infiltrated with PD-1+ cells.

Several cases and recent studies report an increase in transcriptions of tumor HIV CD4+ in patients with HIV-associated sarcomas who were prescribed the drugs against PD-(L)1. As a result of the administration of the corresponding drugs, many of these patients experienced HIV suppression after a certain period of time. General edema may be associated with a syndrome of inflammatory immune restructuring and change in the immune responses in people living with HIV. Reduction in the viral levels was observed in 2 patients out of 28 ones with indeterminate HIV RNA before CPI treatment, and viremia was identified in 5 patients out of 6 (13, 14). Colston et al. (15) studied the effects of Ipilimumab in 24 HIV patients without iridemia and cancer, and the research showed good results in suppressing this virus: two patients had a slight decrease in HIV RNA level and a slight increase after 14 years. Those who showed significant changes in CD4+ count or CD8 count T-cell, did not experience the abo-mentioned results. These observations support the effect of CPI in scaling down delay. Currently, additional studies are being carried out to evaluate the effect of CPI on the action of T-cells to eliminate HIV.

The effect of anti-CD30 monoclonal antibodies against latent HIV is being studied; the study

conducted by Biswas et al. (16) showed that CD30 cross-linking in the latently infected CD4+ T-cells induced HIV transcription. Recently, it has been shown that the use of Brentuximab Vedotin leads to the temporary disappearance of detected HIV RNA in CD4+ T-cells and a decrease in the HIV level in blood plasma. Thus, CD30 is a latent but transcriptionally active marker of HIV-infected cells and is proposed as an innovative therapeutic agent for the treatment of HIV (17,18).

Alemtuzumab is a monoclonal antibody aimed at CD52, which is expressed on T-cells as well as HIV-infected T-cells, regardless of CD4+ count in the blood plasma. Unnoticed CD4-infected T-cells were eliminated *in vitro* with the help of Alemtuzumab (19). According to Caby et al. (20), the effective treatment with Alemtuzumab *in vivo* in patients with HIV and Cesari syndrome reduced the ratio of CD4/CD8 and the risk of Kaposi's sarcoma or non-Hodgkin's lymphoma, but it did not eliminate the frequency of HIV-infected CD4+ T-cells. Alemtuzumab has also been used to treat patients with persistent HIV-negative disease after HSCT.

Severin et al. (21) have conducted a comparative study of the classic Kaposi's sarcoma and HIV viremia in AIDS, which has shown that a number of T-cell growth factors (studied as tumor markers) can influence the HIV pool. Interleukin-7 (IL-7) is a homeostatic cytokine that proliferates the diversity of T-cell lineage by enhancing the division of T-cell predecessors and it is used in various malignant neoplasms. It is also used IL-7, which is associated with a dose-dependent increase in T-cell division with CD4+ and CD8 markers, including CD8 T-cells (an HIV marker), in patients receiving ART. In patients with HIV suppression, the administration of IL-7 temporarily increased the HIV viral load, and there were no clinical consequences. CD8 activity against HIV was increased without clinical consequences. Another T-cell growth factor, IL-15, induced the proliferation of antigen-specific T-cells, mainly in the CD8 compartment; IL-15 is produced during acute HIV infection (22-24).

In vivo, stimulation of IL-15 NK cells from HIV-suppressed participants during ART resulted in a significant increase in infected CD4+ T-cells with cytotoxic CD8 T-cells (25). The cells were eliminated *in vivo* by cytotoxic CD8 T-cells – as

described in the articles by Cesmecci et al. (26) and Poizot-Martin et al. (27) regarding the cases of metastatic Kaposi's sarcoma that have been successfully treated with immunotherapy against PD-1. Preliminary studies of IL-7 and IL-15 in various cancers are ongoing (28-30).

In 2007, a man with HIV and leukemia underwent a hematopoietic stem cell transplantation (HSCT) using cells from a donor with CD4+ cells, homozygous for the CCR5-delta32 mutation, which makes the immune system not susceptible to CCR5-targeted HIV. Even though ART was discontinued after transplantation, HIV was not detected in either blood or biopsy. The second patient has been treated for Hodgkin's lymphoma using cells from a homozygous CCR5-delta32 donor; HIV is still negative in this patient 18 months after stopping ART (31). The allogeneic transplantation of stem cells significantly reduces the HIV reservoir: in European practice, 5 patients out of 6 (who received ART and underwent the hematopoietic stem cell transplantation from the donors of wild-type CCR5) received complete donor transplantation and continued to receive ART. The patients had CD4+ markers in the blood and tissues did not contain HIV DNA, and the tests of virus growth in mice did not show the signs of HIV (32).

However, ART should be stopped to demonstrate functional recovery, and in the case of allogeneic donor transplants with the CCR5 marker, it is impossible to achieve long-term viral suppression without ART in the transplantation of hematopoietic stem cells (33-36). In a study regarding the discontinuation of ART, two patients who received HSCT for treating haemoblastosis from wild-type CCR5 donors and had a null level of HIV RNA during ART for several years after transplantation, they both had a detectable viremia after the discontinuation of ART. In patients, it was detected on day 225 (26), and in some sick people - it was detected on day 24.

After the successful allogeneic transplantation from a homozygous CCR5-delta32 donor, a mutant CCR5 cell product was developed utilizing gene editing, which demonstrated its safety when administered to participants with chronic seropositive diseases (21,37-40). After the discontinuation of ART, the treated CD4+ cells are more resistant. Although these results

are more than positive, further research is needed to develop global approaches to combat HIV persistence during ART.

Since PLHIV live longer, cancer becomes the main cause of death, significantly outweighing the risks that threaten the population in general (41-43); the incidence of malignant neoplasms that have been provoked by AIDS is decreasing, but the mortality associated with NADM is increasing (44,45). The immune response does not produce the desired response, despite ART and its impact on the cancer risk; immunotherapy has the unique potential to improve the outcome of HIV-related cancer (46-48). To improve understanding, PLWH should be included in immuno-oncology research. Recent recommendations guide the appropriate inclusion of PLHIV and cancer patients in clinical trials (14,49,50). In addition, the study of cancer immunotherapy provides an opportunity to better understand the impact of HIV on the occurrence of sarcomas. Analysis of immunological and virological response to cancer immunotherapy in PLHIV will provide new insights into the eradication of HIV, and importantly, new insights regarding the development of new strategies for the treatment of HIV and cancer for people with HIV and cancer.

Therefore, by comparing the results of this study with other cases of using immunosuppressive drugs, it is possible to see a successful recovery of people with cancer. However, the correct combination of immunosuppressive drugs and immunomodulating agents is the main criterion for achieving treatment success, which in turn will stimulate an adequate response of the body to changes in the genetic apparatus of cells of the skin and mucous membranes.

CONCLUSIONS

Currently, there is significant progress in medicine in discovering the pathogenesis of the disease, but some research is still needed to understand the biochemical mechanisms necessary for the development of sarcoma. These are the places of damage with Kaposi's sarcoma: skin, mucous membranes, lymph nodes, and internal organs.

The study demonstrated the potential of immunotherapy, specifically Nivolumab, as an effective treatment approach for complex presentations of metastatic cancers when conventional options are unsuitable. Also, the results showed how detailed diagnostics and multidisciplinary care can inform individualized treatment decisions and lead to positive outcomes even in elderly, medically frail patients. The patient's complete response and extended remission highlighted the efficacy of adapted immunotherapy regimens, providing further evidence to support emerging research on immunomodulatory therapies. This research aligned with broader trends indicating the promise of harnessing the immune system in the fight against cancer. It underscored the need for continued development and optimization of immunotherapeutic strategies.

Further investigation is necessary to understand the intricate interplay between immunosuppression, immune response modulation, and susceptibility to cancers like melanoma. Elucidating these dynamics may reveal novel therapeutic avenues. This paper substantiates the merit of immunotherapy along side conventional modalities and personalized diagnostic approaches for managing complex presentations and improving cancer treatment outcomes. Thus, the potential of immunotherapy, the value of personalized care, the need for more research, and the role of immunomodulation in advancing cancer treatment can be emphasized.

REFERENCES

1. Saller J, Walko CM, Millis SZ, Henderson-Jackson E, Makanji R, Brohl SA. Response to checkpoint inhibitor therapy in advanced classic Kaposi sarcoma: A case report and immunogenomic study. *J Natl Compr Canc Netw*. 2018;16(7):797-800.
2. Uldrick TS, Goncalves PH, Abdul-Hay M, Claeys AJ, Emu B, Ernstoff MS, et al. Assessment of the Safety of Pembrolizumab in Patients with HIV and Advanced Cancer-A Phase 1 Study. *JAMA Oncol*. 2019;5(9):1332-1339.
3. Herrera-Ortiz A, Meng W, Gao S. Nitric oxide is induced and required for efficient Kaposi's sarcoma-associated herpesvirus lytic replication. *J Med Virol*. 2021;93(11):6323-6332.
4. Doki Y, Ajani JA, Kato K, Xu J, Wyrwicz L, Motoyama S, et al. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. *N Engl J Med*. 2022;386(5):449-462.
5. Lipson EJ, Velculescu VE, Pritchard TS, Sausen M, Pardoll DM, Topalian SL, et al. Circulating tumor DNA analysis as a real-time method for monitoring tumor burden in melanoma patients undergoing treatment with immune checkpoint blockade. *J Immunother Cancer*. 2014; 2:42.
6. Abbar B, Veyri M, Solas C, Poizot-Martin I, Spano J-P. HIV and cancer: Update 2020. *Bull Cancer*. 2020;107(1):21-29.
7. Barbari C, Fontaine T, Parajuli P, Lamichhane N, Jakubski S, Lamichhane P, et al. Immunotherapies and combination strategies for immuno-oncology. *Int J Mol Sci*. 2020;21(14):5009.
8. Wang K, Chen W, Zhang Z, Deng Y, Lian J-Q, Du P, et al. CD147-spike protein is a novel route for SARS-CoV-2 infection to host cells. *Signal Transduct Target Ther*. 2020;5(1):283.
9. Volkow P, Chávez-Galán L, Ramón-Luing L, Cruz-Velazquez J, Cornejo-Juárez P, Sada-Ovalle I, et al. Impact of valganciclovir therapy on severe IRIS-Kaposi Sarcoma mortality: An open-label, parallel, randomized controlled trial. *PLoS One*. 2023;18(5):e0280209.
10. Wightman F, Solomon A, Kumar SS, Urriola N, Gallagher K, Hiener B, et al. Effect of ipilimumab on the HIV reservoir in an HIV-infected individual with metastatic melanoma. *AIDS*. 2015;29:504-506.
11. Offersen R, Nissen SK, Rasmussen TA, Østergaard L, Denton PW, Søgaaard OS, et al. Pembrolizumab Induces HIV Latency Reversal in HIV+ Individuals on ART with Cancer. In: Conference on Retroviruses and Opportunistic Infections (CROI). Seattle, WA: 2019.
12. Dupin N, Jary A, Boussouar S, Syrykh C, Gandjbakhche A, Bergeret S, et al. Current and Future Tools for Diagnosis of Kaposi's Sarcoma. *Cancers*. 2021;13(23):5927.
13. Addula D, Das CJ, Kundra V. Imaging of Kaposi sarcoma. *Abdom Radiol*. 2021;46:5297-5306.
14. Vinhaes CL, Araujo-Pereira M, Tibúrcio R, Cubillos-Angulo JM, Demitto FO, Akrami KM, et al. Systemic Inflammation Associated with Immune Reconstitution Inflammatory Syndrome in Persons Living with HIV. *Life*. 2021;11(1):65.
15. Colston E, Grasela D, Gardiner D, Bucy RP, Vakkalagadda B, Korman AJ, et al. An open-label, multiple ascending dose study of the anti-CTLA-4 antibody ipilimumab in viremic HIV patients. *PLoS One*. 2018;13: e0198158.

16. Biswas P, Smith CA, Goletti D, Hardy EC, Jackson RW, Fauci AS. Cross-linking of CD30 induces HIV expression in chronically infected T cells. *Immunity*. 1995;2:587-596.
17. Wang CC, Thanh C, Gibson EA, Ball-Burack M, Hogan LE, Descours B, et al. Transient loss of detectable HIV-1 RNA following brentuximab vedotin anti-CD30 therapy for Hodgkin lymphoma. *Blood Adv*. 2018;2:3479-3482.
18. Hogan LE, Vasquez J, Hobbs KS, Hanhauser E, Aguilar-Rodriguez B, Hussien R, et al. Increased HIV-1 transcriptional activity and infectious burden in peripheral blood and gut-associated CD4+ T cells expressing CD30. *PLoS Pathog*. 2018;14:e1006856.
12. Ruxrungtham K, Sirivichayakul S, Buranapraditkun S, Krause W. Alemtuzumab-induced elimination of HIV-1-infected immune cells. *J Virus Erad*. 2016;2:12-18.
13. Caby F, Guiguet M, Weiss L, Winston A, Miro JM, Konopnicki D, et al. CD4/CD8 Ratio and the Risk of Kaposi Sarcoma or Non-Hodgkin Lymphoma in the Context of Efficiently Treated Human Immunodeficiency Virus (HIV) Infection: A Collaborative Analysis of 20 European Cohort Studies. *Clin Infect Dis*. 2021;73(1):50-59.
14. Séverin D, Bessaoud F, Meftah N, Du Thanh A, Tretarre B, Guillot B, et al. A comparative study of classic and HIV-viremic and aviremic AIDS Kaposi sarcoma. *AIDS*. 2021;35(3):399-405.
15. Chulembayeva L, Ilderbayev O, Taldykbayev Z, Ilderbayeva G, Argybekova A. Phytocorrection of immunological and biochemical changes in the combined impact of coal dust and high dose of radiation. *Georg Med News*. 2018;(Issue):141-150.
16. Dmitriev DV, Katilov OV, Kalinchuk OV. The role of early enteral nutrition in multimodal program fast track surgery in children. *Klinich Khirurg / Minister Okhor Zdorov Ukr, Nauk Tov Khirurg Ukr*. 2014;(9):36-38.
17. Tatenov AM, Tuleuhanov ST, Amanbayeva MB. Research of the mechanism of recognition of cancer cells by T-lymphocytes of immune system. *Physics and chemistry of this mechanism*. *Res J Med Sci*. 2015;9(4):237-239.
18. Rasmussen TA, McMahon J, Chang JJ, Symons J, Roche M, Dantanarayana A, et al. Impact of alemtuzumab on HIV persistence in an HIV-infected individual on antiretroviral therapy with Sezary syndrome. *AIDS*. 2017;31:1839-1845.
19. Cesmeçi E, Guven DC, Aktas BY, Aksoy S. Case of metastatic Kaposi sarcoma successfully treated with anti-PD-1 immunotherapy. *J Oncol Pharm Pract*. 2021;27(7):1766-1769.
20. Poizot-Martin I, Lions C, Allavena C, Huleux T, Bani-Sadr F, Cheret A, et al. Spectrum and Incidence Trends of AIDS- and Non-AIDS-Defining Cancers between 2010 and 2015 in the French Dat' AIDS Cohort. *Cancer Epidemiol Biomarkers Prev*. 2021;30(3):554-563.
21. Polatova DSh, Madaminov AY. Molecular and clinical aspects of oropharyngeal squamous cell carcinoma associated with Human Papillomavirus. *Opuhol Gol Sei*. 2021;11(2):31-40.
22. Tusupkaliev BT, Zhumalina AK, Zhekeyeva BA, Baizhanova RM. The state of proinflammatory and anti-inflammatory cytokines in blood serum of infants with low birth weight in the presence of intrauterine infection. *Int J Pharm Technol*. 2016;8(2):13676-13693.
23. Gambichler T, Susok L. PD-1 blockade for disseminated Kaposi sarcoma in a patient with atopic dermatitis and chronic CD8 lymphopenia. *Immunotherapy*. 2020;12(7):451-457.
24. Hütter G, Nowak D, Mossner M, Ganepola S, Müssig A, Allers K, et al. Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. *N Engl J Med*. 2009; 360:692-698.
25. Salgado M, Kwon M, Gálvez C, Badiola J, Nijhuis M, Bandera A, et al. Mechanisms that contribute to a profound reduction of the HIV-1 reservoir after allogeneic stem cell transplant. *Ann Intern Med*. 2018;169:674-683.
26. Bersimbaev R, Bulgakova O, Aripova A, Kussainova A, Ilderbayev O. Role of microRNAs in lung carcinogenesis induced by asbestos. *J Person Med*. 2021;11(2):1-23.
27. Zazorin BV, Ermukhanova LS. Influence of environmental factors on the body's immunological resistance. *Gig Sanit*. 2012;(3):8-9.
28. Kozłowski P, Parfieniuk-Kowerda A, Tarasik A, Januszkiewicz M, Czauz-Andrzejuk A, Łapiński TW, et al. Occurrence and clinical characteristics of hepatocellular carcinoma in the north-eastern Poland. *Przegl Epidemiol*. 2017;71(3):405-415.
29. Salimova AZ, Kutuev IA, Khusainova RI, Akhmetova VL, Svyatova GS, Berezina GM, et al. Analysis of ethnogeographic groups of Kazakhs based on nuclear genome DNA polymorphism. *Russ J Genet*. 2005;41(7):794-800.
30. Saduakassova KZ, Svyatova GS. Population features of alleles and genotypes frequency distribution of polymorphic genetic markers of antipsychotic medications pharmacokinetics in the Kazakh population. *Am J Med Genet, Part B*. 2022;189(3-4):100-107.
31. Nazarchuk O, Dmyrtriiev D, Babina Y, Faustova M, Burkot V. Research of the activity of local anesthetics and antiseptics regarding clinical isolates of *Acinetobacter baumannii* as pathogens of postoperative infectious complications. *Acta Biomed*. 2022;93(1):e2022003.

32. Hajiyeva NN. Value of immunological markers in the prognosis of development of atopic dermatitis in children. *Azerb Med J.* 2021;(4):19-25.
33. Hajiyeva N, Gafarov I, Hajiyeva A, Sultanova N, Panahova T. Forecasting of atopic dermatitis in newborns. *Indian J Dermatol.* 2022;67(3):311.
34. Bezshapochny SB, Zachepylo SV, Polyanskaya VP, Bobrova NA, Fedorchenko VI. Opportunistic mycoses of ENT organs. Part 1. *Vestn Otorinolaringol.* 2018;83(6):67-71.
35. Suleymanov TA, Balayeva EZ, Mammadov FI, Huseynova GH. Development and validation of a method for the determination of the amount of immunosuppressants in the blood by high-performance liquid chromatography. *Azerb Pharm Pharmacother J.* 2022;22(1):5-12.
36. Zazorin BV, Kurmangaliev OM, Ermukhanova LS. Features of the immune status in the population of urban areas with a high content of heavy metals. *Gig Sanit.* 2012;(3):17-19.
37. Polatova DSh, Madaminov AYu. Molecular and clinical aspects of oropharyngeal squamous cell carcinoma associated with human Papillomavirus. *Opuholi Golovy i Sei.* 2021;11(2):31-40.
38. Sulcymanov TA, Shukurov RT. Validation of the radiochemical purity determination method by high effective liquid chromatography for 18f-psma-1007 radiopharmaceutical medicine. *Azerb Pharm Pharmacother J.* 2021;21(1):5-11.
39. Bezshapochnyy SB, Zachepylo SV, Polianskaya VP, Bobrova NA, Fedorchenko VI. Opportunistic fungal infections of ENT organs. Part 2. *Vestn Otorinolaringol.* 2019;84(3):74-81.
40. Kashanskiĭ SV, Zhetpisbaev BA, Il'derbaev OZ, Ermenbaĭ OT. Mesothelioma in the Republic of Kazakhstan: A review. *Gig Sanit.* 2008;(5):13-17.
41. Lewandowska A, Lewandowski T, Rudzki G, Próchnicki M, Laskowska B, Pavlov S, et al. The Risk of Melanoma due to Exposure to Sun and Solarium Use in Poland: A Large-Scale, Hospital Based Case-Control Study. *Asian Pacific J Cancer Prevent.* 2023;24(7):2259-2269.
42. Grishin A, Spaska A, Kayumova L. Correction of overactive bladder with botulinum toxin type A (BTX-A). *Toxicon.* 2021;200:96-101.
43. Galanina N, Goodman AM, Cohen PR, Frampton GM, Kurzrock R. Successful treatment of HIV-associated Kaposi sarcoma with immune checkpoint blockade. *Cancer Immunol Res.* 2018;6(10):1129-1135.

Managing Challenges in a Symptomatic Patient with Moderate Pulmonary Stenosis: A Case Report

Manejo de los Desafíos en un Paciente Sintomático con Estenosis Pulmonar Moderada: Reporte de un Caso

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SUMMARY

Introduction: Pulmonary stenosis is a common form of obstruction in the right ventricular outflow tract, characterized by the narrowing of the pulmonary valve, which results in obstructed blood flow. **Case Presentation:** A 17-year-old female presented with recurring shortness of breath, chest pain, and palpitations, especially during physical activity. On examination, a grade III/VI continuous murmur was heard at the upper left sternal border. Echocardiography confirmed moderate pulmonary valve stenosis, a left-to-right patent ductus arteriosus (PDA), and mild to moderate pulmonary regurgitation. Treatment involved intravenous normal saline, ceftriaxone premedication at 2 grams/24 hours

intravenously, and oral propranolol at 10 mg every 8 hours. Subsequently, a successful balloon pulmonary valvuloplasty (BPV) was performed, and the patient's symptoms improved. **Conclusion:** Timely intervention with BPV is the primary therapeutic approach, emphasizing the importance of early treatment, irrespective of symptom onset.

Keywords: Balloon pulmonary valvuloplasty, congenital heart disease, case report, pulmonary stenosis, symptomatic moderate pulmonary stenosis.

RESUMEN

Introducción: La estenosis pulmonar es una forma común de obstrucción en la vía de salida del ventrículo derecho, caracterizada por el estrechamiento de la válvula pulmonar, lo que resulta en un flujo sanguíneo obstruido. **Presentación del caso:** Una joven de 17 años se presentó con episodios recurrentes de

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*falta de aire, dolor en el pecho y palpitaciones, especialmente durante la actividad física. En la exploración física, se escuchó un soplo continuo de grado III/VI en el borde esternal izquierdo superior. La ecocardiografía confirmó una estenosis moderada de la válvula pulmonar, un conducto arterioso permeable de izquierda a derecha (PDA) y una regurgitación pulmonar leve a moderada. El tratamiento incluyó suero fisiológico intravenoso, premedicación con ceftriaxona a 2 gramos/24 horas intravenosamente y propranolol oral a 10 mg cada 8 horas. Posteriormente, se realizó con éxito una valvuloplastia pulmonar con balón (BPV), y los síntomas de la paciente mejoraron. **Conclusión:** La intervención oportuna con BPV es el enfoque terapéutico primario, enfatizando la importancia del tratamiento temprano, independientemente del inicio de los síntomas.*

Palabras clave: Valvuloplastia pulmonar con balón, enfermedad cardíaca congénita, informe de caso, estenosis pulmonar, estenosis pulmonar moderada sintomática.

INTRODUCTION

Right ventricular outflow tract (RVOT) obstruction is an anatomic blockage in the right ventricular output and is typically caused by pulmonary valve stenosis, a condition characterized by the narrowing of the pulmonary valve, leading to restricted blood flow. This ailment is most frequently congenital, generally benign, and can affect both pediatric and adult patients (1,2).

While pulmonary stenosis may occur independently in 8 %-10 % of congenital heart diseases, it is frequently observed in conjunction with other congenital anomalies. Congenital pulmonary stenosis is commonly associated with genetic syndromes like Noonan syndrome, Alagille syndrome, Williams syndrome, and congenital rubella. Additionally, it can manifest as an acquired condition, resulting from factors such as rheumatic heart disease, carcinoid syndrome, infective endocarditis, or trauma. Pulmonary valve diseases often coincide with pulmonary regurgitation, attributed to valve irregularities or prior interventions (2).

Therapeutic strategies are determined based on the hemodynamic severity of the obstruction. In

cases of severe pulmonary stenosis, intervention is warranted. Furthermore, it is essential to consider intervention in instances of non-severe stenosis accompanied by symptoms such as congestive heart failure, right-to-left interatrial cyanosis, and exercise intolerance. Balloon pulmonary valvuloplasty (BPV) stands as the primary intervention for pulmonary stenosis and should be promptly administered upon diagnosis, regardless of the presence of symptoms (3-5). In this present case, we report our approach to managing symptomatic moderate pulmonary stenosis in a young female patient.

Case Illustration

A 17-year-old female patient has presented with a chief complaint of experiencing shortness of breath, especially during physical activities. Additionally, the patient reports a history of chest pain and palpitations over the past two years, with intermittent symptoms. The patient has a background of recurrent cough, fever, chest pain, and palpitations. Furthermore, the patient has been diagnosed with a congenital heart disease since the year 2020 and is currently undergoing propranolol treatment. There is no evidence of cyanosis, and there is no family history of congenital heart disease.

The patient is the oldest among four siblings, born after a full-term pregnancy, and cried immediately upon birth. She had a birth weight of over 2500 grams. During the pregnancy, the mother attended regular hospital check-ups, followed a vitamin regimen, and consistently took iron supplements.

Upon physical examination, the patient presents with a weight of 44 kg and a height of 163 cm. She is alert, and fully oriented, with vital signs within the normal range, including a blood pressure of 115/66 mmHg, a heart rate of 86 beats per minute, a respiratory rate of 24 breaths per minute, a temperature of 36.8°C, and oxygen saturation consistently ranging between 97 %-99 % in all extremities while breathing room air. There were no observable signs of jaundice or anemia during the head examination. The chest x-ray displayed normal findings (Figure 1).

Echocardiography findings indicated the presence of moderate valvular pulmonary

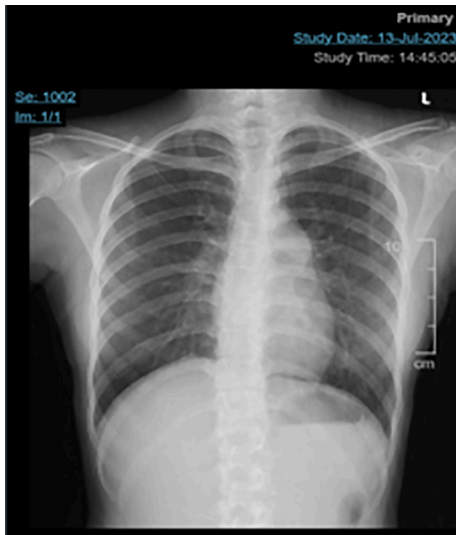


Figure 1. Chest X-ray examination of this patient.

stenosis (maximum pressure gradient (maxPG) of 46 mmHg, a left-to-right shunt through a patent ductus arteriosus (PDA) (sized 2.1 mm, with systolic PG of 12 mmHg and diastolic PG of 2 mmHg), and mild to moderate pulmonary regurgitation (PR PHT 151 ms, width >1/3 RVOT) (Figure 2).

During auscultation, vesicular breath sounds were observed, with no signs of rhonchi, wheezing, or retractions. Cardiac examination revealed a single S1 and a continuous murmur graded as III/VI at the upper left sternal border. Abdominal examination showed no dullness upon percussion and no organomegaly. Examination of the extremities did not reveal any peripheral edema, cyanosis, or clubbing of the fingers. Table 1 provides the laboratory findings of the patient conducted on July 13, 2023.

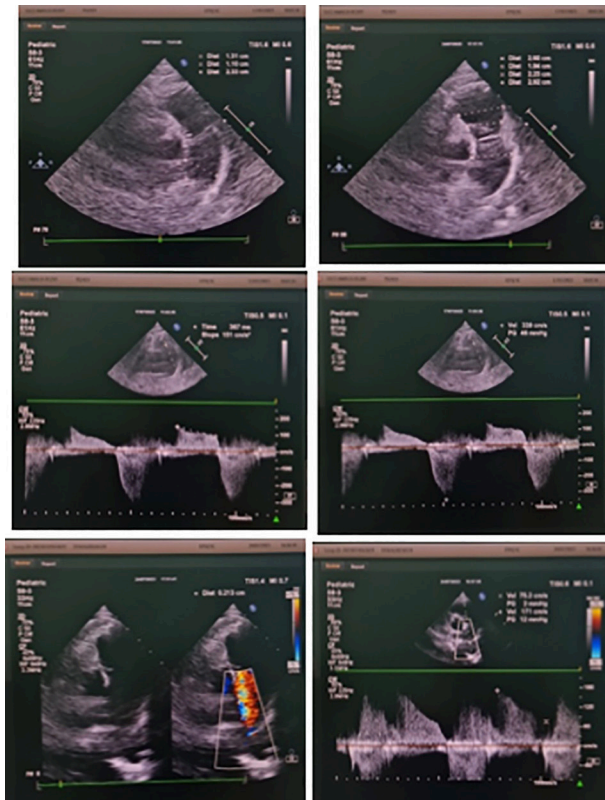


Figure 2. Echocardiography findings of the patient.

Table 1
Laboratory findings in this patient

Laboratory	Results	Normal range
Routine Haematology		
WBC	6.1	4.00 – 10.0
RBC	4.92	4.00 – 6.00
HGB	14.1	12.0 – 16.0
HCT	42	37.0 – 48.0
PLT	380	150 – 400
NEUT	49.6	52.0 – 75.0
LYMPH	41.4	20.0 – 40.0
Coagulation		
INR	1.05	-
PT	11.3	10-14
APTT	31.3	22.0 – 30.0
Blood Chemistry		
Urea	19	10 – 50
Creatinine	0.88	M(<1.3);F(<1.1)
ALT	22	< 38
AST	20	< 41
Electrolyte		
Sodium	140	136 – 145
Potassium	4.0	3.5 – 5.1
Chloride	107	97 – 111
Hepatitis Markers		
Hbs Ag (Elisa)	Non-Reactive	Non-Reactive
Anti-HCV (Elisa)	Non-Reactive	Non-Reactive

Previously, the patient underwent an RHC procedure on April 12, 2023. The RHC findings indicated the presence of moderate subvalvar pulmonary stenosis and a left-to-right shunt through the PDA characterized by low flow and low resistance. A BPV procedure with an estimated balloon size of 25 to 28 mm was scheduled. During hospitalization, the patient received intravenous administration of normal saline (NaCl 0.9 %) at a rate of 500 cc over 24 hours, intravenous ceftriaxone at a dosage of 2 grams every 24 hours as premedication, and oral propranolol at a dosage of 10 mg every 8 hours. The patient then underwent the BPV procedure on July 26, 2023. Following the RHC, which revealed the presence of pulmonary stenosis (pulmonary artery annulus 20.75 mm) and a small PDA, the BPV procedure was successfully performed using a nucleus balloon sized 25 x 40 mm. Oxygen saturation improved from 76 % to 91 % at the pulmonary artery (Figure 3).

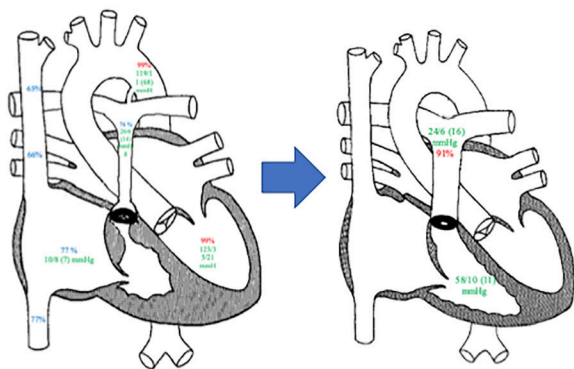


Figure 3. Comparison of oxygen saturation at pulmonary artery before and after BPV.

Following the percutaneous BPV (Figure 4), the patient has reported a significant improvement in her symptoms, and the shortness of breath has disappeared. A physical examination conducted before discharge showed normal vital signs, with oxygen saturation consistently ranging from 98 % to 99 % while breathing room air.

DISCUSSION

Pulmonary stenosis represents a relatively prevalent congenital heart disease, occurring in approximately 8 % to 10 % of the population and frequently co-occurring with other congenital anomalies. In the current case, the patient's primary complaints include dyspnea on exertion, chest discomfort, and intermittent palpitations. These symptoms are consistent with the documented clinical presentations associated with pulmonary stenosis. These manifestations typically tend to emerge and, in many cases, progress over time in patients with moderate to severe stenosis. In conditions marked by severe stenosis, the incapacity of the right ventricle to enhance cardiac output can lead to chest pain during physical activity, instances of fainting, and, although uncommon, sudden cardiac death (2).

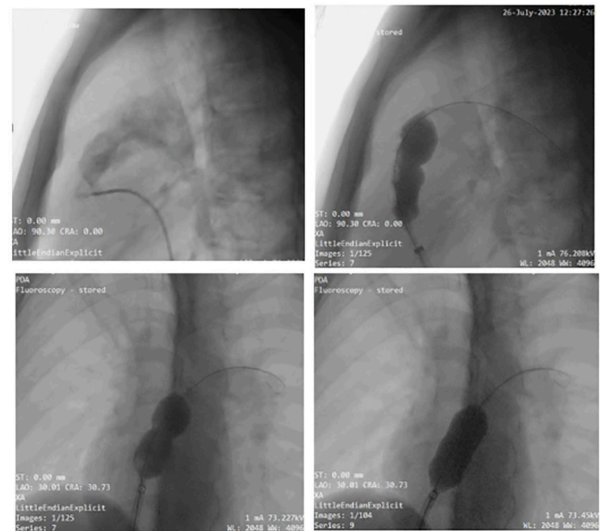


Figure 4. Percutaneous balloon pulmonary valvuloplasty was performed in patients with symptomatic moderate PS.

During the physical examination, the patient showed a singular S1 heart sound, a regular cardiac rhythm, and a continuous grade III/VI murmur at the upper left sternal border. As indicated in the existing medical literature, pulmonary stenosis

commonly presents with a systolic ejection murmur, primarily audible at the left cardiac base, with accentuation during inspiration. With increasing severity of pulmonary stenosis, the ejection click progressively approaches S1, eventually becoming inaudible in instances of severe pulmonary stenosis. In cases of pronounced pulmonary stenosis, jugular venous pressure (JVP) demonstrates conspicuous waves, and manual palpation may uncover an enlarged right ventricle; however, this was not observed in our present case (6).

Echocardiography serves as the primary diagnostic method for evaluating pulmonary stenosis (7). In this examination, the patient was diagnosed with patent ductus arteriosus featuring a left-to-right shunt, moderate valvular pulmonary stenosis, and mild to moderate pulmonary regurgitation. Consequently, the patient is scheduled for a balloon pulmonary valvuloplasty procedure. In cases of moderate pulmonary stenosis, it is advisable to undergo regular follow-up assessments, ideally on an annual basis. If there is evidence of right ventricular (RV) enlargement or the emergence of symptoms indicative of RV dysfunction, intervention becomes necessary (5). In the present case, the patient displays symptoms associated with pulmonary stenosis and an RV pressure exceeding 50 mmHg, necessitating intervention (8).

According to the American Cardiology College/ American Heart Association (ACC/ AHA) guidelines, our patient meets the criteria for undergoing balloon pulmonary valvuloplasty. This procedure is recommended for patients who show symptoms and have been diagnosed with either moderate or severe pulmonary stenosis, as well as those with valvar pulmonary stenosis. In our patient, who has been diagnosed with symptomatic moderate valvar pulmonary stenosis, the indication for balloon pulmonary valvuloplasty is fulfilled.

CONCLUSIONS

Balloon pulmonary valvuloplasty is the first-line treatment for pulmonary stenosis and should be performed promptly upon diagnosis.

Intervention is not only considered in patients with severe pulmonary stenosis but also in non-severe cases with symptoms.

DECLARATIONS

Ethics approval and consent to participate.

Not applicable

Consent for publication

The authors certify that the patient and family have obtained all appropriate patient consent forms. The patient's parents understand that names and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Availability of data and material

Not applicable

Competing interests

The authors declare no competing interests.

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Authors' contributions

AAU, YP, and AMD made the initial conception and idea. AAU and AMD prepared the initial manuscript. AQ revised and prepared the submitted manuscript. YP, AAU, IM, and MZ reviewed and advised for critical revisions. All contributing authors approved the final draft.

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REFERENCES

1. Heaton J, Kyriakopoulos C. Pulmonic stenosis. StatPearls. 2023. Available from URL: <https://www.ncbi.nlm.nih.gov/books/NBK560750/>

2. Ruckdeschel E, Kim YY. Pulmonary valve stenosis in the adult patient: Pathophysiology, diagnosis and management. *Heart*. 2019;105(5):414-422.
3. Marchini F, Meossi S, Passarini G, Campo G, Pavasini R. Pulmonary valve stenosis: From diagnosis to current management techniques and future prospects. *Vasc Health Risk Manag*. 2023;19: 379-390.
4. Muneuchi J, Watanabe M, Sugitani Y, Kawaguchi N, Matsuoka R, Ando Y, et al. Early palliative balloon pulmonary valvuloplasty in neonates and young infants with tetralogy of fallot. *Heart Vessels*. 2020;35(2):252-258.
5. Mitchell B, Mhlongo M. The diagnosis and management of congenital pulmonary valve stenosis. *SA Heart*. 2018;15(1):36-45.
6. Mann DL, Zipes DP, Libby P, Bonow RO, Braunwald E. Braunwald's heart disease. A textbook of cardiovascular medicine, 10th edition. Philadelphia: Elsevier Inc; 2015.
7. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2019;32(1):1-64.
8. Cuypers JA, Witsenburg M, van der Linde D, Roos-Hesselink JW. Pulmonary stenosis: Update on diagnosis and therapeutic Options. *Heart*. 2013;99(5):339-347.

Case of Myocardial Infarction with Nonobstructive Coronary Arteries Caused by Thebesian Veins Thrombosis

Caso de Infarto de Miocardio con Arterias Coronarias No Obstructivas por Trombosis de las Venas de Tebesio

Oleksandr Savchenko¹, Yuliia Tyravska^{2*}, Yuliia Moshkovska³, Tetiana Motsak⁴, Liudmyla Kuzmenko⁵

SUMMARY

Introduction: The causes of myocardial infarction with nonobstructive coronary arteries are heterogeneous and include different reasons. Clinical cases of myocardial infarction without obstruction represent a difficult diagnostic task where cardiac magnetic resonance is increasingly used. **Objective:** This research aimed to demonstrate the evaluation protocol of myocardial infarction with nonobstructive arteries. **Method:** The object of this study was a 49-year-old male patient who presented at the emergency department with atypical chest pain, notably elevated troponin levels. To establish the diagnosis were performed electrocardiogram, echocardiography, stress-echocardiography, coronary angiography, and cardiac magnetic resonance. **Results:** Echocardiography

didn't demonstrate significant abnormalities of the heart's wall movement but due to elevated troponin level and were performed coronary angiography and the myocardial infarction with nonobstructive coronary arteries were established. Further cardiac magnetic resonance confirmed the diagnosis and established that the cause of myocardial infarction was Thebesian vein thrombosis. A cardiac magnetic resonance imaging (MRI) was performed, which showed myocardial edema in the inferior wall on T2-weighted visualization. Late gadolinium enhancement showed focal areas of subendocardial infarction. The patient received appropriate medical treatment and experienced good clinical outcomes. This case study demonstrates how the role of cardiac MRI in the diagnosis and management of myocardial infarction with nonobstructive coronary arteries (MINOCA) patients has become increasingly crucial, as the understanding of troponin elevation and its various mechanisms continues to evolve.

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RESUMEN

Introducción: *Las causas del infarto de miocardio con arterias coronarias no obstructivas son heterogéneas e incluyen diferentes motivos. Los casos clínicos de infarto de miocardio sin obstrucción representan una tarea diagnóstica difícil donde se utiliza cada vez más la resonancia magnética cardíaca. Objetivo:* Esta investigación tuvo como objetivo demostrar el protocolo de evaluación del infarto de miocardio con arterias no obstructivas. **Método:** *El objeto de este estudio fue un paciente varón de 49 años que acudió al servicio de urgencias por dolor torácico atípico, destacando niveles elevados de troponina. Para establecer el diagnóstico se realizaron electrocardiograma, ecocardiografía, ecocardiografía de estrés, angiografía coronaria y resonancia magnética cardíaca. Resultados:* La ecocardiografía no demostró anomalías significativas del movimiento de la pared del corazón, pero debido al nivel elevado de troponina se realizó una angiografía coronaria y se estableció el infarto de miocardio con arterias coronarias no obstructivas. Una resonancia magnética cardíaca adicional confirmó el diagnóstico y estableció que la causa del infarto de miocardio fue la trombosis de la vena de Tebas. Se realizó una resonancia magnética (MRI) cardíaca, que mostró edema miocárdico en la pared inferior en la visualización potenciada en T2. El realce tardío con gadolinio mostró áreas focales de infarto subendocárdico. El paciente recibió tratamiento médico adecuado y experimentó buenos resultados clínicos. Este estudio de caso demuestra cómo el papel de la resonancia magnética cardíaca en el diagnóstico y tratamiento de pacientes con infarto de miocardio con arterias coronarias no obstructivas (MINOCA) se ha vuelto cada vez más crucial, a medida que la comprensión de la elevación de troponina y sus diversos mecanismos continúa evolucionando.

Palabras clave: *Resonancia magnética cardiovascular, angiografía coronaria, MINOCA, ecocardiografía de estrés.*

INTRODUCTION

The traditional approach to acute chest pain is considered to be closely related to myocardial ischemic conditions, which in most cases are expected to be the result of coronary atherosclerosis. This conception conditioned diagnostic, therapeutic management, and prognostic evaluation of myocardial ischemic conditions. Guidelines of 4th Universal

Definitions of Myocardial Infarction, which were published by (1), presented new conceptions in understanding myocardial infarction. Since then, there have been clear demarcations between myocardial infarction and myocardial injury. Today myocardial injury means non-obstructive coronary artery myocardial infarction (MINOCA) and Takotsubo syndrome. The consequences of this new conception consider large changes in future protocols of evaluation and management of patients with acute ischemic myocardial pain (2). Currently, in most clinical cases of patients with typical symptoms of myocardial infarction but no atherosclerotic obstruction, cardiologists often face skepticism, and the diagnosis is frequently denied (3). Despite the numerous reviews from Ukrainian and European societies, that specialize in the evaluation and management of patients with acute coronary syndromes, a lot of clinicians still deny the possibility of myocardial infarction in cases with non-obstructive coronary arteries.

The first stage when cardiologists are faced with a case of non-obstructive myocardial infarction is to determine which instrumental diagnostic methods can confirm this diagnosis. After changes in terminology, it was established that cardiac magnetic resonance (CMR) plays a crucial role in the differential diagnosis of non-ischemic causes of myocardial infarction. Lintingre et al. (4) and Pathik et al. (5) consider that the efficacy of CMR diagnostic of conditions with suspected MINOCA is between 60 % and 87 %. The issues regarding patient selection criteria for CMR diagnosis, the timing of CMR diagnosis (early or late), and the choice of CMR protocol for visualization still need to be addressed. After establishing a diagnosis, cardiologists are faced with the challenge of determining the treatment protocol. MINOCA encompasses various underlying causes, including coronary artery spasms, microvascular dysfunction, myocarditis, etc. Each etiology demands a distinct therapeutic approach, making it challenging to adopt a uniform treatment protocol. Besides, unlike the well-established guidelines for myocardial infarction with obstructive coronary arteries, there is a lack of standardized protocols for managing MINOCA. The absence of clear guidelines can lead to uncertainty among cardiologists regarding the most appropriate course of action. It remains unclear if the treatment protocols for patients

with acute myocardial infarction with obstructed coronary arteries are suitable for MINOCA cases.

Matta et al. (6) divided all pathological mechanisms of MINOCA into two groups: ischemic reasons and non-ischemic reasons. Ischemic reasons include spontaneous coronary artery dissection (SCAD), disruption of plaques, coronary spasm, dysfunction of the microvascular net, embolism or thrombus in coronary arteries, and mismatch in supply-demand mechanisms. The non-ischemic reasons include myocarditis, cardiomyopathy of Takotsubo, hypertensive disease of the heart, tachyarrhythmias, chemotherapeutic agents, cardiomyopathies, and intoxications with cardiotoxins. Fedorov et al. (7) analyzed the current position regarding MINOCA and consider that management of MINOCA remains challenging. Pharmacological treatment, indeed, remains relevant but uncertain due to the unclear etiology. Khanyukov et al. (8) consider that results from randomized trials in multicenter studies are eagerly awaited to find new pathobiological treatments.

This research aims to represent the typical case of MINOCA and describe the standard protocol of evaluation and treatment based on etiology.

Literature Review

Physicians can often misdiagnose acute myocardial infarction in cases of absence obstruction process in coronary arteries. As a result, the patients without correct diagnosis do not receive appropriate medical therapy and are wrongly reassured and discharged. Previous studies by Tamis-Holland et al. (9) and Talebi et al. (10) have examined the etiologies, diagnosis, and treatment of MINOCA. Specifically, Tamis-Holland et al. summarized the different possible causes of MINOCA and outlined appropriate diagnostic and therapeutic approaches in their conclusions. Meanwhile, Talebi et al.'s review highlighted the value of using diverse imaging modalities to determine the underlying etiology in all MINOCA cases. These two studies underscore the need for a thorough diagnostic workup using multiple imaging techniques to identify the specific causes of MINOCA and guide appropriate management.

Reynolds et al. (11) highlighted the use of intracoronary imaging and advanced methods of imaging modalities to determine the etiology of MINOCA. His study showed that nearly 40 % of patients with MINOCA cases have had signs of plaque disruptions in the past. These plaque disruptions include ruptured plaque, erosion of vessels, and calcified areas of the vessels. The performing of intracoronary imaging approved these signs. MINOCA cases with plaque disruption, approved by intracoronary imaging, on CMR imaging showed large areas of edema, which testified about the temporary ischemic condition in large vessels. Sometimes, a necrotic area was observed within the edema area (12). The only way to distinguish what reasons could lead to such appearances is the intracoronary provocative test or CMR imaging in a smaller, well-defined area of gadolinium enhancement in the late period (LGE) which can indicate that the most likely reason for myocardial necrosis was atherothrombotic debris embolization from the area of disruption (13). The CMR imaging is preferable to the intracoronary provocative test.

Collet et al. (2) in current guidelines for the management of MINOCA cases with ruptured plaque recommended medical treatment similar to plaque rupture in cases of obstructive coronary artery disease. Patients diagnosed with both plaque disruption and MINOCA are recommended to undergo dual antiplatelet therapy for one year, followed by single antiplatelet therapy for the remainder of their life. Patients with non-obstructive coronary artery disease, even if the atherosclerosis is at an early stage, are prescribed statin therapy as a treatment option. Lee et al. (14) described the case of MINOCA in a patient with sickle cell disease. In this research, a 49-year-old man with sickle cell disease in the past medical history with complaints of chest pain was hospitalized. Diagnosis of MINOCA used as secondary to microvascular obstruction. The patient received antiplatelet therapy and was discharged.

Despite the growing recognition of MINOCA as a distinct entity within the spectrum of acute myocardial conditions, several research gaps remain that merit further exploration. The absence of universally accepted treatment guidelines for MINOCA patients poses a

significant challenge. While guidelines for myocardial infarction with obstructive coronary arteries are well-established, MINOCA patients present a diverse array of underlying causes. The development of standardized protocols according to different etiologies is essential for optimizing patient outcomes. The optimal choice and timing of imaging modalities for diagnosing MINOCA remain uncertain. Comparative studies assessing the effectiveness of different modalities, such as CMR, echocardiography (ECG), and intracoronary imaging, could guide clinical decision-making. The mechanisms underlying subendocardial ischemia, as observed in some MINOCA cases, warrant further investigation. Advancing an understanding of potential biomarkers or imaging features that can predict treatment outcomes would facilitate more precise targeting of therapeutic strategies. Addressing these knowledge gaps through further investigation is key to unraveling the intricacies of MINOCA, optimizing diagnostic and management protocols, and ultimately improving prognosis and quality of life for patients affected by this complex syndrome.

MATERIALS AND METHODS

The object of this research is the clinical case of a 49-year-old male patient, who has visited the cardiologists with complaints of mild pain, “pressure” and “heaviness” behind the sternum

radiating to his left arm. After significant physical exertion, shortness of breath and diaphoresis were observed. A case of this patient included previous cardiac ischemia. During a previous visit to the cardiologist, echocardiography was performed and mitral regurgitation of the I stage was established. Blood chemistry established hyperlipidemia, but the patient did not take prescribed statin therapy for the last 2 years. Holter monitoring registered supraventricular tachycardia. At the time of hospitalization, his blood pressure was 114/56 mm Hg. The heart rate was 57 bpm. The temperature was 36.4°C (97.6°F). The respiratory rate was 21 per minute. Blood saturation in room air was 98 %. The 12-lead ECG didn't show specific changes in the ST segment (Figure 1), but troponin increased to 11.5 ng/mL. ECG also did not show the disturbed function of the left ventricle. Coronary angiography didn't reveal any coronary segments with more than 50 % obstruction. A CMR was performed, which showed myocardial edema in the inferior wall on T2-weighted visualization. Late gadolinium enhancement showed focal areas of subendocardial infarction.

Table 1 shows laboratory results, which were sampled at the moment of hospitalization.

A transthoracic echocardiogram (TTE) was performed according to the guidelines of the British Society of Echocardiography (15). TTE showed no significant wall motion disorders. The ejection fraction was 59 %, and the heart volumes and wall thickness were normal.



Figure 1. ECG of the patient

CASE OF MYOCARDIAL INFARCTION WITH NONOBSTRUCTIVE CORONARY ARTERIES

Table 1

Shows laboratory results, which were sampled at the moment of hospitalization

Table 1. Laboratory tests

Parameter	Result	Reference range
Complete blood count		
Leukocytes, x10 ⁹ /L	16.4	3.5-10.6
Erythrocytes, x10 ¹² /L	4.63	4.0-5.2
Haemoglobin, g/L	129	110-160
Haematocrit, %	24	35-47
Mean corpuscular volume, fl	95.7	75-98
Mean corpuscular haemoglobin, pg	31.7	27-34
Mean corpuscular haemoglobin concentration, g/dL	34.4	31.5-36
Platelets, x10 ⁹ /L	469	150-390
Erythrocytes distribution width (RDW-SD)	47.1	37-54
Erythrocytes distribution width (RDW-CV)	14.2	11-16
Platelets distribution width, fl	15.3	10-18
Mean platelets volume, fl	9.2	6.5-11
Erythrocyte sedimentation rate, mm/h	24	<15
Blood differential test		
Neutrophils, x10 ⁹ /L	4.57	1.7-7
Lymphocytes, x10 ⁹ /L	2.87	1-4.8
Monocytes, x10 ⁹ /L	0.38	0-0.8
Eosinophils, x10 ⁹ /L	0.08	0-0.45
Basophils, x10 ⁹ /L	0.01	0-0.02
Coagulogram		
Prothrombin time, s	10.2	9.8-12.5
Prothrombin index, %	96.3	70-130
International normalization ratio	1	
Activated partially thromboplastin time, s	30.5	22-32
D-fibrinogen, g/L	3.15	2-4
Thrombin time, s	18.4	14-21
Lipidogram		
Cholesterol, mmol/L	6.2*	<5.2
Triglycerides, mmol/L	2.12	<2.26
High-density lipoproteins, mmol/L	1.51*	>1.68 – no risk
Low-density lipoproteins, mmol/L	3.8*	<2.59 – the optimal level
Biochemistry		
Serum glucose, mmol/L	4.92	4.11-5.89
Creatine phosphokinase, U/L	1234	39-308
C-reactive protein, mg/dL	1.34	5

Evidence of pericardial effusion was absent. Aortic dimensions were within the normal range. In the apical projection, increased trabeculation of the apex of the left ventricle was noticed. Pulmonary regurgitation of the I stage and mitral regurgitation of the I stage was noted. Complaints of discomfort behind the sternum and shortness of breath after physical exertion, dyslipidemia, and the age of the patient become the prescription

to undergo stress echocardiography (stress EchoCG). Stress EchoCG was carried out on a horizontal bicycle ergometer Shiller erg 911L on a Toshiba Aplio 50 scanner and a Mortara scribe electrocardiograph and performed according to the ABCDE Stress-Echo protocol (16). The results showed that the patient was indicated to pass over coronary angiography.

This study aligned with the ethical principles of research, including anonymity, confidentiality, and beneficence. Ethical approval of the study was obtained from the Health Research Ethics Commission of the Bogomolets National Medical University with No. MO-178.

RESULTS

After the diagnosis of MINOCA was established, the goal of the treatment strategy was to identify the underlying etiology and prescribe appropriate pathoetiological medical treatment. To achieve this, a follow-up TTE was ordered after the coronary angiography. Protocol of TTE on MINOCA cases was performed on expert class devices. In this case, TTE was performed on the GE Vivid E9 scanner. All measurement calculations were performed during three cardiac cycles, except continuous wave (CW) Doppler and pulse wave (PW) Doppler. The ejection fraction was recalculated to Simpson's rule and became 58 %. Classification of regional movements of cardiac walls made by visual interpretation of the wall's width. Segments, which become thicker more than 30 %, are regarded as normokinetic. Less than 10 % are regarded as akinetic. Segments can be regarded as dyskinetic if there is systolic thinning or eccentric excursion. In this patient, pathological dismovement was not observed.

2D loops from the projection of three apical cameras were analyzed with the use of the Q-analysis module in longitudinal 2D strain in EchoPAC BT11.2. When the area of interest is marked with the borders, this module generates strain curves and peak systolic strains in semi-automatic mode. The software utilized in this study automatically generated strain curves and peak systolic strains by marking the myocardial borders as the region of interest (ROI). Additionally, it calculated the post-systolic index, which measures the proportion of shortening after aortic valve closure and was found to be less than 0.2. Temporal derivation of strain rate was also performed. Both Global longitudinal strain (GLS) and segmental values for all variables are recorded. The Tissue Doppler Imaging (TDI) Q-analysis module utilized in this study analyzed loops from color-coded tissue Doppler obtained

from the same views in apical projection. The software module placed ROIs in the two basal segments in each imaging view to evaluate the maximal systolic and diastolic velocities in the early stages, the timing of the cardiac cycle events, and the myocardial performance index for both ventricles. The analysis revealed a myocardial performance index of 0.3.

Mitral inflow velocities, which include E-speed (850 mm/s) and A-speed (550 mm/s) were calculated. E/E' was 6, and pulmonary venous flow was 450 mm/s. In this investigation, a custom interface designed in LabVIEW was utilized to examine the E waves during free breathing and after the Valsalva maneuver. To study the E waves, the equation for a simple harmonic oscillator was applied, and the constants k , c , and x were calculated by fitting the curve to the maximum velocity envelope of each E wave. The values of these constants represent chamber stiffness, viscoelastic energy loss, and load, respectively. Moreover, the time constant of isovolumic chamber relaxation (IVRT) was assessed and was found to be 84 ms in the patient under observation. The stiffness and relaxation components of the deceleration time (DT) of the E wave were measured to be approximately 180 ms. These outcomes facilitated the computation of a load-independent index of diastolic filling and stiffness.

Considering complaints of discomfort behind the sternum and shortness of breath during physical exertion, dyslipidemia (increased levels of total cholesterol and low-density lipoproteins, decreased level of high-density lipoproteins), as well as age, the patient was indicated to undergo stress echocardiography (stress EchoCG) (Table 2).

On the initial ECG, a sinus regular rhythm and a slightly negative T wave in lead III were recorded. On the initial echogram, there was a zone of hypo-/akinesis in the region of the apical lateral segment in the 4-chamber view and the local effect of spontaneous contrasting of the rounded shape with a diameter of about 1.2 cm, which was suspicious of a hypoechoic intracardiac thrombus located in the region of the trabeculae of the apex-lateral walls of the left ventricle. At a load of 50 W, in the apex-lateral segment of the left ventricle, normokinesis

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Table 2
Stress-Echo protocol

Stage	Workload, W	Time, min	Heart Rate, bpm	BP, mmHg	ECG	EchoCG	Complaints
Initial (0)	0	3:00	67	120/75	“-” T wave in lead III	Hypo-/akinesis of the apical lateral segment in the 4-chamber view, the local effect of spontaneous contrasting in the region of the apex-lateral wall of LV	none
1	50	3:00	111	130/80	-/-	normokinesis	none
2	100	1:03	130	130/80	Horizontal depression 1.2 mm in V5-6, deepening of “-” T in lead III.	Normo-/hypokinesis of the apical lateral segment in the 4-chamber view, a small rupture of the lateral wall of the LV, the release of the part of the thrombus beyond the pericardium of LV lateral wall	cyanosis dyspnoea
Restitution	0	3:00	105	125/75	“-” T in lead III	normokinesis	none
Rest	0	5:00	67	120/70	As initial	Hypo-/akinesis of the apical lateral segment of LV	none

Note: LV – left ventricle.

is registered in contrast to hypo-/akinesis as previously at the initial stage. It was decided to continue the study, as there were no complaints or negative ECG trends. At a workload of 100 W after 1 min. 3 s., the appearance of shortness of breath, and mild cyanosis of the lips were noticed, as well as horizontal depression of the ST segment with a maximum amplitude of 1.2 mm in leads V5-6, deepening of the negative T wave in lead III were registered on ECG. On the echogram, attention is drawn to a small rupture of the lateral wall, the lumen of which was filled with a thrombus with the release of a part of the thrombus beyond the pericardium of the lateral wall. At the same time, the size of the cardiac thrombus within the left ventricle was decreased. In addition, there was mild hypokinesis in the apical segment of the intraventricular septum in the 4-chamber view (Figure 2).

The restitution period was normal. At 5 minutes of rest, the condition of the patient, ECG, and contractility of the left ventricle on EchoCG returned to baseline. Given the fact that the

patient was suspected of myocardial infarction, coronary angiography was performed. Based on the findings from the coronary angiography, it was concluded that the patient did not have any significant obstructive lesions in the left coronary artery. Nevertheless, a distinct contrast blush was observed at the endocardial surface, generating a ventriculogram through the extensive presence of multiple micro fistulae originating from the diagonal branch of the left anterior descending artery and emptying into the left ventricular cavity (Figure 3).

A peculiar contrast blush was observed in both the left (A and B) and right (C and D) coronary arteries. This unusual flow drained into the left ventricular chamber, and it was traced to the Thebesian venous network by following the arrows. Interestingly, the visualization of the endocardial border was facilitated by this contrast blush, which was particularly evident in images B and D (Figure 3). The intermittent visualization of these fistulae may indicate thrombosis in the Thebesian veins, which could

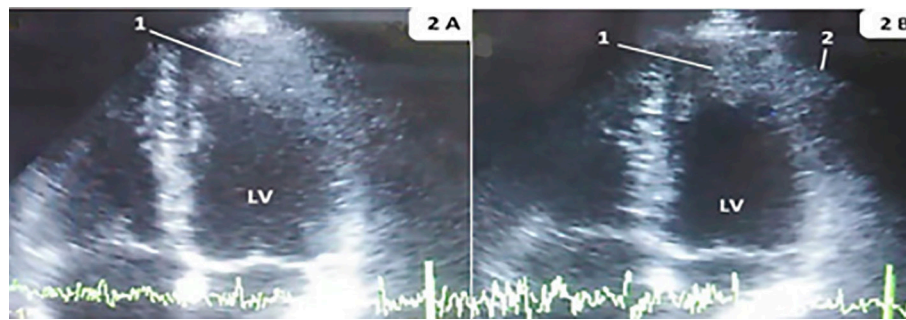


Figure 2. Apical 4-chamber view during stress-EchoCG test: 2A – before the test; 2B – after stage 2 (1 – the local effect of spontaneous contrasting; 2 – the part of the thrombus beyond the pericardium).

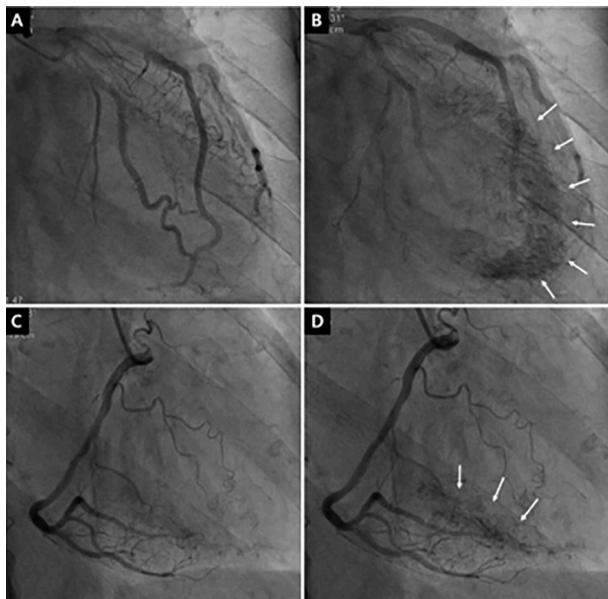


Figure 3. Coronary angiography showing the absence of significant stenosis.

be the underlying cause of the symptoms. Based on a retrospective analysis of this clinical case, it was determined that the most effective laboratory investigations should encompass routine clinical chemistry. In addition, it is recommended to perform a comprehensive array of tests to evaluate different domains, such as haematology, cystatin C, glucose, hsTroponinT, lipids, NT-proBNP, thyroid function, D-dimer, electrolytes, metoxycatecholamines, and the

albumin to creatinine ratio in the urine. In every case, an oral glucose tolerance test (OGTT) must be performed along with measurements of HbA1C and cortisol levels in saliva (morning and evening). Additionally, all patients, which are suspected of MINOCA should undergo haematological testing after 6 months to rule out the risk of thromboembolism and systemic lupus erythematosus.

Moreover, during the right coronary angiography, a comparable capillary blush was noticed, which drained into the left ventricular cavity. This capillary blush was identified as originating from the branch of the posterolateral artery and posterior descending artery. The observed results suggested the existence of an arterioluminal form of the Thebesian venous network that collects blood from the coronary arteries and empties it directly into the ventricle. Further testing with CMR revealed a definite subendocardial perfusion defect at the level of the base to the middle part of the left ventricle during the rest perfusion sequence. The discovery implies that noticeable Thebesian veins may instigate subendocardial ischemia, even when at rest, and present as an acute coronary syndrome. Late enhancement of gadolinium, signifying myocardial infarction in the subendocardial layer, was confirmed at a later stage. To treat the patient's condition, bisoprolol, valsartan, and a small dose of anticoagulants to decrease cardiac afterload were administered alongside antiplatelet therapy. The patient's symptoms ameliorated, and he was subsequently released from medical care. Follow-up at the outpatient

clinic revealed that the patient remained stable for three months.

It is crucial to conduct an outcomes-based clinical trial to assess the efficacy of MINOCA patient management treatment guided by CMR. A thorough CMR evaluation including functional imaging and advanced tissue characterization techniques like mapping and late gadolinium enhancement can help diagnose and predict outcomes in MINOCA patients, enabling personalized treatment. It should be included as a primary diagnostic test in clinical guidelines. This protocol should be performed within one week of acute presentation with complete coverage of the left ventricle to provide a thorough evaluation. In cases where patients exhibit a clear non-ischemic cause, the typical protocol for acute coronary syndrome may not be beneficial and could even be harmful. Additional research is needed to determine whether the standard heart failure treatments, including beta-blockers and ACE inhibitors, can reduce the risk of progressing dilated cardiomyopathy and severe arrhythmias for patients with acute myocarditis, especially those who have impaired left ventricular ejection fraction, regional wall motion abnormalities, or extensive late gadolinium enhancement imaging. The benefits of utilizing CMR to guide treatment strategy in MINOCA patients extend beyond a precise diagnosis of myocardial infarction and distinguishing it from non-ischemic causes. It also provides valuable information about the extent and functional impact of acute myocardial injury, allowing for a more individualized treatment approach for each patient. This can include identifying the presence of myocardial inflammation, fibrosis, or scarring, which may require specific therapies or interventions. Additionally, CMR can help monitor the response to treatment over time, allowing for adjustments as necessary to optimize patient outcomes.

An optimal approach for managing MINOCA patients would involve a thorough and non-invasive assessment of both the upstream coronary arteries and downstream myocardium, which would enable the development of a personalized treatment plan. The use of a comprehensive evaluation, such as multiparametric CMR imaging, would be highly beneficial for diagnosing and predicting outcomes in MINOCA patients and should be considered a primary

diagnostic tool in clinical guidelines. It is promising that CMR has demonstrated additional clinical benefits in diagnosing and forecasting outcomes in patients with MINOCA, and it should be included in clinical guidelines as one of the primary diagnostic tests to allow for further classification of these patients. This integration will provide a more comprehensive understanding of the extent and functional consequences of acute myocardial injury, as well as inform personalized treatment plans.

DISCUSSION

The results of this study provide valuable insights into the diagnostic and treatment challenges associated with MINOCA, particularly when caused by intracardiac thrombosis involving Thebesian veins. The case demonstrates that MINOCA can present with mild or atypical symptoms, minimal changes on ECG, and even absent pain syndrome, highlighting the importance of considering alternative diagnostic methods beyond traditional markers of acute coronary syndromes. The utility of cardiac magnetic resonance (CMR) as a comprehensive diagnostic tool is underscored, as it enables the identification of subtle myocardial abnormalities and the differentiation between ischemic and non-ischemic causes.

Thygesen et al. (1) defined 5 types of myocardial infarction. It was highlighted that myocardial injury taxonomy needs improvement, as it is still rather challenging to differentiate its subtypes and choose appropriate therapeutic approaches depending on the cause.

MINOCA is not associated with stenosing atherothrombosis of the coronary arteries and occurs in patients with intact coronary arteries or initial coronary atherosclerosis when atherosclerotic plaque is less than 50%. At the same time, atherosclerotic lesion of the coronary arteries with the presence of “young” plaques with a thin fibrous cap and a large lipid core, which can be damaged under various conditions and lead to partial or complete thrombosis followed by spontaneous thrombolysis, is considered as one of the causes of MINOCA. As a result, Sucato et al. (17) defined that interrupted myocardial

infarction can occur when the area of necrosis is noticeably smaller or even in very rare cases is not registered. This clinical case represents a similar situation when the area of necrosis was so small, that even ECG didn't show significant abnormalities. In such situations, Kovacs noticed the phenomenon of spontaneous thrombolysis with reflow. In addition, Meah and Williams (18) noted that an atherosclerotic plaque can be completely or partially located eccentrically (so-called "positive" remodeling) when there is no narrowing of the coronary arteries lumen, but the risk of injury and myocardial infarction still exists. The experience of this study confirms that MINOCA cases require investigation of every abnormality that was noted.

The heart veins in their number and size significantly exceed the arteries. The coronary venous system is divided into two groups of veins. While coronary sinus and tributary veins, as well as veins draining the right ventricle and the atria, belong to the greater cardiac venous system, the lesser cardiac venous system is represented by Thebesian veins, particularly small vascular channels, and venous sinusoids. Thebesian veins with a diameter of 50 to 200 microns are localized within the myocardium. Sirjuddin et al. (19) studied that in the atrium, their structure is similar to veins, and in the ventricles, Thebesian veins look like sinusoids – narrow vascular fissures with the endothelium in the myocardium. In this research, knowledge of variant coronary venous anatomy in CMR played a role in the diagnosis of Thebesian vein thrombosis. Four types of Thebesian veins are described. The first one has a short tree-like trunk, which is the basis of a network of vessels extending into the deep layers of the thickest sections of the myocardium. The second type of vessels occur in areas of the myocardium of small thickness, practically do not have a trunk, and immediately diverge in a star-like manner in the form of thin branches anastomosing with each other. The third type of vessel – long channels, almost without branches and passing through the myocardium. Finally, the fourth type of vessel is small veins with a small number of branches passing through the deep layers of the heart muscle.

Heart veins are mentioned mostly regarding resynchronization therapy, left ventricle pacing and arrhythmia ablation, drug-targeted therapy,

and delivery of stem cells to the infarcted myocardium. In this case, the patient's medical history is not burdened by anything like this and it remains unclear what led to thrombosis of the Thebesian veins. Ansari (20) considered the significance of Thebesian veins and defined that they supply blood to the myocardium in coronary arterial occlusion, acting as a natural nutrient channel. Consequently, Thebesian veins are of great compensatory importance in conditions of insufficient coronary blood supply. Moreover, Boonysirinant et al. (21) established that they can regress and even disappear after myocardial infarction. It is logical to assume the theory that in this case, Thebesian veins could have appeared as a compensatory mechanism for previously occurred myocardial ischemia and will regress over time, but it is not possible to verify this theory. The connection of sinusoids with the branches of the coronary system of the heart is noted. Cernica et al. (22) assumed that it may be a compensatory mechanism of myocardial blood supply, especially in ischemic patients. In the current patient, thrombosis of Thebesian veins opening on the endocardium of the left ventricle was noted in the region of myocardial infarction.

Padfield (23) described similar to this research clinical case where Thebesian veins were localized in the region of the trabeculation of the left ventricle and were sclerosed during coronary atherosclerosis. In addition, turbulent blood flows develop in the area of trabeculae and chords, which eventually damage the endothelium of these vessels (24). It is in these places that a venular intraventricular thrombus can form. It is formed, as a rule, due to increased blood turbulence and, possibly, due to aseptic inflammation and sclerosis of Thebesian veins (25, 26). In this case, a thrombus can cause microembolization and thrombosis of the microvasculature of the myocardium, followed by focal necrosis and gradual thinning of the myocardium which, perhaps, leads to myocardial microrupture in the left ventricle of the current patient.

At the same time, these processes can occur gradually and strictly locally, which significantly changes the clinical manifestations of MINOCA. The pain syndrome can be mild or atypical or absent with insufficient or even no changes on ECG, as it happened in the current patient (27). Regarding EchoCG, in the area of myocardial

damage in the apical lateral segment of the left ventricle, hypo-/akinesis developed as a protective reaction to injury (stunning of the myocardium) (28-30). At stage, I, the area of the viable myocardium had to be differentiated from the hibernating myocardium. Consequently, it was decided to increase the load. At stage II, normo-/hyperkinesis was registered, which made it possible to exclude the hibernating myocardium due to severe coronary atherosclerosis. However, it was under this load that a micro-rupture of the lateral wall of the left ventricle was registered, which was the main cause of myocardial stunning.

As for the tactics of the management of this patient regarding a cardiac thrombus, most likely it is necessary to highlight two tactical points. First, if a fresh intracardiac thrombus was located in the area of trabeculae without lateral wall hypokinesis, it is possible, after examining the patient for thrombophilia, to start using antiplatelet agents with small doses of new oral anticoagulants (31, 32). In the presence of hypokinesis of the left ventricle lateral wall, it is necessary to remember the possible damage not only to the fibrous capsule of the CA atherosclerotic plaque but also to the endomyocardium. Transesophageal echocardiography may be useful in these patients to evaluate endocardial damage. In such patients, anticoagulants should be used with caution, as the presence of an intracardiac clot may be beneficial for the patient's survival (33, 34). In this present case, the clot was located inside the heart and may have covered the microruptures in the left ventricle.

While this study provides important insights, some limitations should be noted when interpreting the findings. The research presented results from a single patient case, which may not fully represent the broader MINOCA population. The individual patient characteristics and clinical presentations could limit the applicability of the obtained results to other cases. The small sample size of one patient limits the statistical power and generalizability of the findings. A larger patient number is needed to validate the trends observed in this study. The short follow-up period post-treatment does not allow us to assess the long-term effectiveness and durability of the treatment strategy employed. Longer follow-up periods are necessary to evaluate the sustained benefits.

CONCLUSIONS

The results of this research showed that clarifying MINOCA diagnosis requires significant diagnostic capabilities. In this case, EchoCG, stress-EchoCG, coronary angiography, and CMR were required to discover the reason for MINOCA. As previously discussed, MINOCA should be established after coronary angiography. In this case, during stress-EchoCG, was observed the phenomenon of a partial release of the thrombus through small ruptures in the lateral wall of the left ventricle into the pericardial cavity. Although this event may not be the cause of the symptoms, it could be a step toward explaining their etiology. Coronary angiography showed a vast capillary blush of Thebesian veins, draining into the cavity of the left ventricle. Despite the low distinctiveness of such a small branch, obstruction is observed in some of them. Further, CMR with late gadolinium enhancement showed subendocardial myocardial infarction at the delayed phase. In this way, "suspicious" results of coronary angiography and diagnosed myocardial infarction on CMR make it possible to establish the etiology of this MINOCA case – thrombosis of Thebesian veins. The patient was prescribed bisoprolol, valsartan, and antiplatelet therapy with small doses of anticoagulants. The benefit of using CMR in the case of MINOCA is obtaining the accurate reason for myocardial infarction to differentiate it from non-ischemic reasons. This can help to make the treatment of each patient more effective and individualized. Based on the research findings, the following recommendations for future clinical practice can be made. The promotion of multi-center research involving a large number of patients who potentially have a diagnosis of MINOCA can improve the guidance of therapy and enhance the prognosis of such patients. These studies can refine diagnostic criteria, treatment approaches, and risk factor assessment. Long-term outcome assessments will shed light on the effectiveness of interventions guided by CMR findings. It is necessary to develop standardized protocols for CMR and stress-EchoCG, ensuring consistent diagnostic procedures across diverse clinical settings. This will facilitate meaningful comparisons of results and outcomes. Specialized training for healthcare

professionals, along with patient education initiatives, can elevate the accurate diagnosis and management of MINOCA cases and is crucial to enhancing awareness and education. Eventually, a collaborative, multidisciplinary approach involving cardiologists, radiologists, and other specialists is crucial to refining MINOCA diagnosis and management.

REFERENCES

1. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow, et al. Fourth universal definition of myocardial infarction. *Eur Heart J*. 2018;40(3):237-269.
2. Collet JP, Thiele H, Barbato E, Barthelémy O, Bauersachs J, Bhatt DL, et al. GCM. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2021;42(14):1289-1367.
3. Skybchyk VA, Skybchyk YV. Myocardial infarction with non-obstructive coronary artery disease (MINOCA): Approaches to diagnosis and treatment. *Medicines of Ukraine*. 2020;9(10):27-33.
4. Lintingre PF, Nivet H, Clement-Guinaudeau S, Camaioni C, Sridi S, Corneloup O, et al. High-resolution late gadolinium enhancement magnetic resonance for the diagnosis of myocardial infarction with nonobstructed coronary arteries. *JACC: Cardiovascular Imaging*. 2020;13(5):1135-1148.
5. Pathik B, Raman B, Amin NHM, Mahadavan D, Rajendran S, McGavigan AD, et al. Troponin-positive chest pain with unobstructed coronary arteries: Incremental diagnostic value of cardiovascular magnetic resonance imaging. *Eur Heart J Cardiovasc Imag*. 2016;17(10):1146-1152.
6. Matta AG, Nader V, Roncalli J. Management of myocardial infarction with nonobstructive coronary arteries (MINOCA): A subset of acute coronary syndrome patients. *Review Cardiovascular Medicine*. 2021;22(3):625-634.
7. Fedorov S, Kozlova S, Szhytska S, Kulpok-Baginski T, Nadolny K. Myocardial infarction with non-obstructive coronary arteries: Novelty and perspectives. *Pharma Innovation*. 2017;6(9):527-529.
8. Khanyukov OO, Sapozhnychenko LV, Samilyk MV, Perepelytsya KD. Management of patients with myocardial infarction without coronary artery obstruction (MINOCA): Literature review and own data. *Ukrainian Therapeutic J*. 2021;4.
9. Tamis-Holland JE, Jneid H, Reynolds HR, Agewall S, Brilakis ES, Brown TM, et al. Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary artery disease: A scientific statement from the American Heart Association. *Circulation*. 2019;139(18):e891-e908.
10. Talebi S, Moreno P, Dominguez AC, Tamis-Holland JE. The imaging toolbox to assess patients with suspected myocardial infarction in the absence of obstructive coronary artery disease (MINOCA). *Current Cardiology Reports*. 2020;22(11):134.
11. Reynolds HR, Maehara A, Kwong RY, Sedlak T, Saw J, Smilowitz NR, et al. Coronary optical coherence tomography and cardiac magnetic resonance imaging to determine underlying causes of myocardial infarction with nonobstructive coronary arteries in women. *Circulation*. 2021;143(7):624-640.
12. Ouldzein H, Elbaz M, Roncalli J, Cagnac R, Carrie D, Puel J, et al. Plaque rupture and morphological characteristics of the culprit lesion in acute coronary syndromes without significant angiographic lesion: Analysis by intravascular ultrasound. *Annals of Cardiology and Angiology*. 2012; 61(1):20-26.
13. Reynolds HR, Srichai MB, Iqbal SN, Slater JN, Mancini GB, Feit F, et al. Mechanisms of myocardial infarction in women without angiographically obstructive coronary artery disease. *Circulation*. 2011;124(13):1414-1425.
14. Lee S, Kaplin S, Tamis-Holland J, Talebi S. MINOCA in a patient with sickle cell disease. *Am J Med*. 2020;133(8):E425-E426.
15. Robinson S, Rana B, Oxborough D, Steeds R, Monaghan M, Stout M, et al. A practical guideline for performing a comprehensive transthoracic echocardiogram in adults: The British Society of Echocardiography minimum dataset. *Echo Research & Practice*. 2020;7(4):G59-G93.
16. Picano E, Ciampi Q, Cortigiani L, Arruda-Olson AM, Borguezan-Daros C, Pretto JLCES, et al. Stress Echo 2030: The novel ABCDE-(FGLPR) protocol to define the future of imaging. *J Clin Med*. 2021;10(16):3641.
17. Sucato V, Testa G, Puglisi S, Evola S, Galassi AR, Novo G. Myocardial infarction with non-obstructive coronary arteries (MINOCA): Intracoronary imaging-based diagnosis and management. *J Cardiology*. 2021;77(5):444-451.
18. Meah MN, Williams MC. Clinical relevance of coronary computed tomography angiography beyond coronary artery stenosis. *RoFo*. 2020;193(10):1162-1170.
19. Sirajuddin A, Chen MY, White CS, Arai AE. Coronary venous anatomy and anomalies. *J Cardiovasc Computer Tomogr*. 2020;14(1):80-86.
20. Ansari A. Anatomy and clinical significance of ventricular Thebesian veins. *Clin Anatomy*. 2001;14(2):102-110.

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21. Boonyasirinant T, Halliburton SS, Schoenhagen P, Lieber ML, Flamm SD. Absence of coronary sinus tributaries in ischemic cardiomyopathy: An insight from multidetector computed tomography cardiac venographic study. *J Cardiovasc Computer Tomogr* 2016;10(2):156-161.
22. Cernica D, Bordi L, Beganu E, Rodean I, Benedek I. Multiple coronary chamber micro fistulas or persistent Thebesian vessels? *J Interdiscip Med*. 2017;2(3):262-265.
23. Padfield GJ. A case of coronary cameral fistula. *Europe J Echocardiography*. 2009;10(5):718-720.
24. Razumnikova OM, Shandaulov AK, Mazhbich BI. The hemodynamics of the lesser circulation and blood indices in rats under long-term high-altitude hypoxia. *Byull Eksperiment Biol Med*. 1989;107(5):526-528.
25. Tatenov AM, Tuleuhanov ST, Amanbayeva MB. Research of the mechanism of recognition of cancer cells by T-lymphocytes of immune system. *Physics and chemistry of this mechanism*. *Res J Med Sci*. 2015;9(4):237-239.
26. Navruzov SN, Polatova DS, Geldieva MS, Nurieva EI. Possibilities of study of the main cytokines of the immune system in patients with osteogenic sarcoma. *Vopr Onkol*. 2013;59(5):599-602.
27. Dixit P, Shah R, Agrawal Y, Shah R, Rao A. Prominent Thebesian veins in association with Takotsubo cardiomyopathy. *Cureus*. 2021;13(7):e16204.
28. Atamanyuk IP, Kondratenko YP. Calculation method for a computer's diagnostics of cardiovascular diseases based on canonical decompositions of random sequences. *CEUR Workshop Proceed*. 2015;1356:108-120.
29. Pekur DV, Khmil DN, Bacherikov Y Yu, Mammadli AH, Naghiyev JA, Suleymanova NY, et al. Investigation of gamma-ray sensitivity of YAG: Ce-based scintillation structures. *Semicond Phys Quantum Electron Optoelectron*. 2023;26(1):89-96.
30. Tursynova A, Omarov B, Sakhipov A, Tukenova N. Brain Stroke Lesion Segmentation Using Computed Tomography Images based on Modified U-Net Model with ResNet Blocks. *Int J Online Biomed Engin*. 2022;18(13):97-112.
31. Dobrovanov O, Dmytriiev D, Prochotsky A, Vidiscak M, Furkova K. Pain in COVID-19: Quis est culpa? *Electron J Gen Med*. 2023;20(1):em435.
32. Dmytriiev D, Dobrovanov O. Post-COVID pain syndrome. *Anaesth Pain Intensive Care*. 2021;25(4):505-512.
33. Afandiyev RV. Development of regulatory acts of rules on conducting inspections of medicinal products manufacturers according to the good manufacturing practice requirements. *Azerb Pharm Pharmacother J*. 2021;21(2):25-33.
34. Pestun IV. Research of self-medication among population in Ukraine. *Azerb Pharm Pharmacother J*. 2021;21(2):34-41.

Uso de la Plataforma de Acceso Transanal *Gelpoint*[®] *Path* para la Resección Local de Neoplasias del Recto

Use of the *Gelpoint*[®] *Path* Transanal Access Platform for Local Rectal Neoplasms Resection

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RESUMEN

Objetivo: Presentar un caso de adenoma tubulovelloso con adenocarcinoma moderadamente diferenciado infiltrante, extirpado mediante el GelPOINT[®] Path como instrumental laparoscópico estándar. **Caso Clínico:** Paciente sin comorbilidades, llega a consulta externa por sensación de pujo después de cada comida, examen físico sin anomalías, en rectoscopia se detecta masa en el recto; se extirpada mediante el uso del GelPOINT[®] Path, 36 horas postquirúrgico es dado de alta. **Conclusión:** El uso de GelPOINT[®] Path fue la alternativa más adecuada, debido a que no se podía resecar endoscópicamente debido a la posición, el tamaño y riesgo quirúrgico y anatomopatológico.

Palabras clave: Cirugía mínimamente invasiva transanal, Neoplasias del Recto, Resección.

SUMMARY

Objective: To present a case of tubulovillous adenoma with infiltrating moderately differentiated adenocarcinoma, removed by GelPOINT[®] Path as standard laparoscopic instruments. **Clinical Case:** A patient without comorbidities, arrives at the outpatient clinic due to a pushing sensation after each meal, physical examination without abnormalities, rectoscopy detects a rectal mass; it is removed using GelPOINT[®] Path, 36 hours postoperative is discharged. **Conclusion:** The use of GelPOINT[®] Path was the most appropriate alternative because it could not be resected endoscopically due to the position, size, and surgical and pathological risk.

Keywords: Transanal minimally invasive surgery, rectal neoplasms, resection.

INTRODUCCIÓN

El cáncer de recto es uno de los tumores gastrointestinales más frecuentes, estando su relevancia e incidencia aumentando progresivamente. De acuerdo con la Organización Mundial de la Salud (OMS) el cáncer de colon y recto representa el 19,3 % de todas las neoplasias malignas a nivel mundial, con un 47 % de mortalidad anual (1). El riesgo

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de padecer cáncer rectal es de 1 en 26 para mujeres y de 1 en 23 para hombres; entre los tumores del recto encontramos en su gran mayoría adenocarcinomas (2).

Los adenomas son lesiones no cancerosas que se desarrollan a nivel de colon y recto, compuestos por epitelio displásico de la mucosa. Estas lesiones se clasifican histológicamente en adenomas tubulares, adenomas tubulovelloso (pólipos velloglandulares) o adenomas vellosos; la mayoría asintomáticos y descubiertos incidentalmente (2). El riesgo de malignización de los adenomas con displasia de alto y bajo riesgo es de 27 % y 5 %, respectivamente a los 15 años y pólipos < 1 cm se espera que se conviertan en adenocarcinoma invasivo, a los 10 años (2).

La cirugía es la piedra angular del tratamiento, pero este es un campo en constante cambio. La cirugía rectal es difícil de realizar, sobre todo para los pacientes con alto riesgo quirúrgico (sexo masculino, índice de masa corporal elevado, tumor rectal bajo, pelvis estrecha, mesorrecto graso, próstata voluminosa). La resección quirúrgica del cáncer de recto suele requerir en algunas ocasiones una proctectomía con la respectiva linfadenectomía (3,4). La proctectomía transanal se desarrolló inicialmente para evitar las conversiones en los pacientes en quienes es necesaria una anastomosis coloanal o una resección abdominoperineal (APR), dependiendo de la ubicación del cáncer en el recto. La técnica se ha ampliado en la actualidad a las proctectomías con anastomosis colorrectal. Suele denominarse escisión mesorrectal total transanal (*transanal total mesorectal excision*). Todos los autores coinciden en insistir en sus dificultades quirúrgicas específicas: la elección de un plano de disección inadecuado, con el riesgo uretral anterior en el tercio inferior y el riesgo lateral neurovascular en el tercio medio.

Estos procedimientos se han realizado tradicionalmente por vía transabdominal a través de una incisión abierta. Existen tres modalidades de la resección quirúrgica del cáncer de recto que complementan la operación abierta tradicional: cirugía laparoscópica, cirugía robótica y cirugía transanal (3,4).

En el 2009 surgió la Cirugía Mínimamente Invasiva Transanal (*Transanal minimally invasive surgery*, TAMIS) que es un híbrido entre la microcirugía transanal endoscópica o *transanal endoscopic microsurgery* (TEM), usada para reseccionar lesiones benignas y malignas en el recto distal a proximal, utilizando la plataforma de acceso transanal *GelPOINT® Path* (Applied Medical, Rancho Santa Margarita, CA, Estados Unidos) con instrumental laparoscópico estándar, diseñado específicamente para TAMIS. Estos dispositivos permiten utilizar cámaras, insufladores e instrumental laparoscópico convencional (3,4). *GelPOINT® Path* utiliza tres puertos para instrumental de 5 o 12 mm, que se insertan a través de una interfaz gelatinosa.

Se presenta un caso de adenoma tubulovelloso con adenocarcinoma moderadamente diferenciado infiltrante, extirpado mediante el *GelPOINT® Path* como instrumental laparoscópico estándar.

Caso Clínico

Se presenta el caso de un paciente de sexo masculino de 78 años de edad, sin antecedentes de relevancia, quien acude a médico tratante debido a que durante seis meses ha presentado dolor abdominal tipo cólico, de leve de intensidad EVA 4/10 acompañado de sensación de pujo después de cada comida. Se realiza el examen físico y exámenes complementarios, no se encuentra ninguna alteración. Debido a que el dolor aumenta se decide realizar rectoscopia donde se observa una masa de color pardo gris, una superficie aterciopelada y una consistencia elástica (Figura 1).

Debido a los antecedentes del paciente y a la evidencia en la literatura, se propuso como alternativa de tratamiento la TAMIS utilizando el *GelPOINT® Path* como instrumental laparoscópico estándar.

Se realizó la escisión de la masa rectal utilizando la plataforma para TAMIS mediante *GelPOINT® Path* puerto 5,5 cm fijado en el borde anal con seda 0 con aguja pequeña (SH) no absorbible. Se colocaron tres trocantes

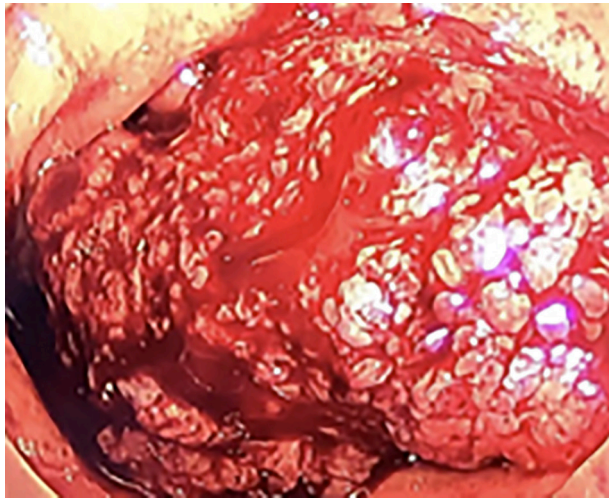


Figura 1. Colonoscopia del recto.

desechables de 5 mm de diámetro en forma de triángulo (Figura 2), el primero como cámara laparoscópica e iluminador, el segundo como pinza para agarrar el intestino, portaagujas y electrocauterio, finalmente el tercero como tijeras o dispositivo de sutura; llevando a cabo una disección transversal y en profundidad del tumor (Figura 3). Se realiza el cierre de la incisión con vycril 2/0, posteriormente se efectuó lavado transanal con 3000 mL de solución salina al 0,9 %, se retira el *GelPOINT® Path* y se traslada el paciente a hospitalización. La masa rectal es enviada a anatomía patológica.

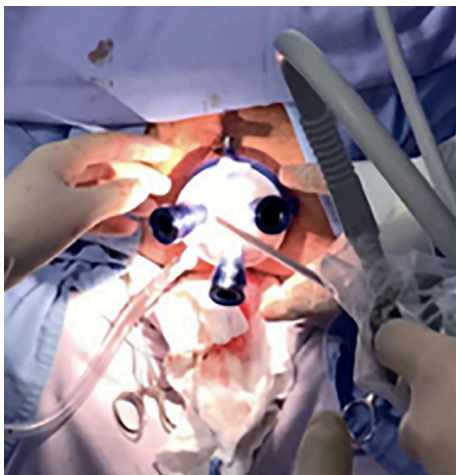


Figura 2. Dispositivo *GelPOINT® Path*.

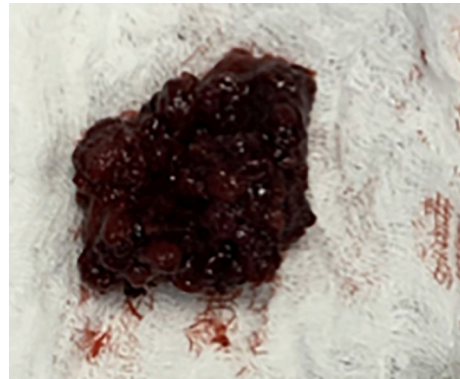


Figura 3. Tumor rectal diseccionado.

El paciente permanece 36 horas en hospitalización expresando dolor anal leve, soportable, que no requiere la administración de ningún medicamento, no presenta salida de líquido, ni sangrado a nivel anal, considerando el caso se otorga el alta al paciente.

El informe histopatológico revela un Adenoma túbulo vellosa con estructuras tubulares y vellosidades revestidas por células cilíndricas basófilas con displasia epitelial de alto grado que presenta en algunas zonas transformación de Adenoma carcinoma moderadamente diferenciado que infiltra la submucosa formando pequeños nidos celulares en medio de una respuesta linfoide poco significativa. Relacionando la clínica del individuo con el estudio anatomopatológico se diagnostica al paciente con tumor rectal: Adenoma tubulovelloso con adenocarcinoma moderadamente diferenciado infiltrante. El procedimiento quirúrgico resulto ser curativo.

DISCUSIÓN

El tratamiento del cáncer del recto localizado se ha transformado en un procedimiento muy complicado; para tumores localizados en el tercio medio y superior del recto normalmente se practica la técnica quirúrgica conocida como resección anterior baja, para tumores del tercio inferior del recto se aplica la resección abdomino-perineal o resección

abdomino-perineal ultra baja con anastomosis colo-anal (3,4). Actualmente como opción terapéutica de escisión local de neoplasias del recto proximal a distal se ha empleado la técnica de Cirugía Mínimamente Invasiva Transanal (*Transanal minimally invasive surgery*, TAMIS). Para que este método puede ser aplicado se necesita cumplir con los siguientes criterios de inclusión: tumores que midan menos de 4 cm de diámetro, que ocupen menos del 40 % de la luz del recto, sean móviles al examen del recto y tengan un grado de estadificación T1 (2).

Devane y col., indican que TAMIS es un procedimiento oncológicamente más seguro y rentable que la escisión transanal convencional (TAE) y microcirugía endoscópica transanal (TEM) debido a que utiliza instrumentos laparoscópicos y cámaras con un solo puerto de incisión, en lugar de un rectoscopio rígido fijo como TEM (4), además, TAMIS obtiene un ángulo de visión de 360° y la posición de la luz rectal permite operar en múltiples cuadrantes de proximal a distal usando la misma configuración, mientras que TEM requiere reposicionamiento del paciente o de la plataforma consiguiendo como máximo una visión binocular estable, por su lado TAE aunque se tenga una visión directa, la exposición es limitada para la porción media y proximal del recto menos para el tramo distal (5). Kim y Lee manifiestan que TAMIS proporciona ventajas como, el uso de la posición de litotomía independientemente de la localización de la masa, reduciendo el tiempo de ajuste del equipo en el quirófano, además, permite un mejor control de las vías respiratorias y disminuye el riesgo de complicaciones perioperatorios (6). Del mismo modo, esta técnica posibilita researse en el plano submucoso con márgenes de resección negativo de al menos 5 mm y en caso de lesiones malignas de 1 cm (6). En 1 241 procedimientos TAMIS realizados se ha demostrado que es un procedimiento seguro para resultados oncológicos y posoperatorios, lo que incluye la estancia hospitalaria, los márgenes de resección positivos, la baja fragmentación del espécimen, la alta tasa de concordancia entre el diagnóstico preoperatorio y posoperatorio y la baja recurrencia (6). Al comparar el TEM, la operación endoscópica

transanal (TEO) y TAMIS se demostró que TAMIS presenta ventajas en cuanto a menor pérdida de sangre, menor duración de la estancia hospitalaria y mayor tasa de cierre de defectos. La tasa de complicaciones es del 18,4 %, incluyendo hemorragia urinaria posoperatoria, fiebre y penetración de la cavidad peritoneal; la mayoría se resuelve con tratamientos conservadores como antibióticos y transfusiones sanguíneas (6). Con respecto a la calidad de vida, la TAMIS logra buenos resultados a largo plazo en la evaluación de la función intestinal mediante la puntuación del síndrome de resección anterior baja (LARS) (3-6). TAMIS disminuye las lesiones del esfínter en comparación con la TEM debido al menor diámetro de la plataforma y el material flexible del puerto. Ding y col., en China, indican con respecto a TAMIS, que el tiempo promedio de cirugía desde armar el dispositivo hasta retirarlo es de 46,13 a 111,94 minutos, el promedio de volumen de sangre perdida durante el procedimiento es de 19,19 a 22,64 mL y la estancia hospitalaria postoperatoria media fue de 4,56 a 1,76 días, sin muerte quirúrgica ni complicaciones graves (7).

CONCLUSIÓN

La elección de la técnica quirúrgica en el tratamiento del cáncer de recto se basa en diversos factores. La localización del tumor, su estadio, las características anatómicas del paciente y su calidad de vida poscirugía son aspectos fundamentales a tener en cuenta, con el objetivo de obtener los mejores resultados oncológicos posibles y la menor morbilidad para el paciente.

La evidencia indica que TAMIS con el *GelPOINT® Path*, fue la alternativa más adecuada para la resección realizada al paciente, lo que permitió su favorable recuperación. Este procedimiento fue realizado al encontrar una masa de características tumorales, que no se podía resear endoscópicamente por la posición, el tamaño y riesgo quirúrgico y anatomopatológico, siendo necesario optar por resolución quirúrgica. Antiguamente se realizaba a través de valvas anales con mucha dificultad y una visualización pobre,

sin embargo, actualmente se dispone de esta plataforma que permitió una mejor visualización, una resección con límites perilesionales en longitud y profundidad (1 cm) y ejecutándose en *full thickness* (grosor completo), precautelando así, una resección adecuada en caso de encontrarse lesión maligna T1 o ubicada en la mucosa. Posteriormente con histopatología de la lesión resecada, se corroboró que se trataba de un adenocarcinoma confinado a la mucosa, es decir, que la resección realizada fue curativa.

Conflictos de intereses

Los autores no reportan conflicto de interés.

Consentimiento para publicar

Los autores certifican que el documento anterior no ha sido previamente publicado; una vez aceptado para la publicación, los derechos de difusión serán transferidos a la Gaceta Médica de Caracas.

Aprobación ética y consentimiento de participación

Se solicita las autorizaciones pertinentes a las autoridades de la Clínica Latinoamericana para el desarrollo del presente artículo respetando la confidencialidad de la información de los pacientes. Le entidad de los individuos participantes del presente artículo fue protegida durante el desarrollo del mismo. Los autores cuentan con el consentimiento informado por parte del paciente para la publicación del caso clínico.

REFERENCIAS

1. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Cancer today. Int Agency for Research on Ca. 2020;36:14-17.
2. He F, He X, Cui M, Wang Y. Mixed small cell neuroendocrine carcinoma and squamous cell carcinoma covered by tubulovillous adenoma in the rectum: A case report and detailed molecular analyses. World J Surg Oncol. 2023;21:65.
3. Steele S, Church J, Delaney C, Hull T, Kalady M. Cleveland Clinic Illustrated Tips and Tricks in Colon and Rectal Surgery. Surrey, Reino Unido: Wolters Kluwer; 2021;1. Disponible: <https://axon.es/ficha/libros/9781975108250/cleveland-clinic-illustrated-tips-and-tricks-in-colon-and-rectal-surg>
4. The American Cancer Society medical and editorial content team (<https://www.cancer.org/cancer/acs-medical-content-and-news-staff.html>). Tratamiento contra el cáncer colorectal. cancer.org. 1.800.227.2345.
5. Devane L, Burke J, Kelly J, Albert M. Transanal minimally invasive surgery for rectal cancer. Ann Gast Surg. 2021;5:39-45.
6. Kim M, Lee T. Trans anal minimally invasive surgery using laparoscopic instruments of the rectum: A review. World J Gastrointest Surg. 2021;13:1149-1165.
7. Ding L, Ji G, Xu X, Xie Y, Hu D, Zhang H. Evaluation of transanal minimally invasive surgery for rectal benign lesions. J Laparoendosc Adv Surg Tech A. 2020;30:1160-1164.

Aspectos Bioéticos en la Enseñanza de la Anatomía Humana

Bioethical Aspects in the Teaching of Human Anatomy

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RESUMEN

La Anatomía Humana es una disciplina fundamental para los estudiantes de ciencias de la salud, generalmente, presente en los primeros semestres de la malla curricular. A lo largo de su historia, su aprendizaje se ha basado en la disección y proyección de cadáveres humanos o sus partes, por lo que amerita orientar su enseñanza desde un enfoque bioético; donde aspectos como la dignidad póstuma, procura y donación de cuerpos, gestión del cadáver, adaptación cultural apropiada, consideración de avances tecnológicos sin deshumanización o la prevención de prácticas ilícitas, deben ser considerados por los docentes. Es por ello que, se propuso realizar una revisión narrativa, con el objetivo de analizar el marco biojurídico y las consideraciones e implicaciones bioéticas en la enseñanza de la Anatomía Humana en países sudamericanos como Brasil, Chile, Colombia y Venezuela.

Palabras clave: Anatomía Humana; Bioética; Enseñanza.

SUMMARY

Human Anatomy is a fundamental discipline for health sciences students, generally present in the first semesters of the curriculum. Throughout its history, its learning has been based on the dissection and projection of human corpses or their parts, therefore, it deserves to guide its teaching from a bioethical approach; where aspects such as posthumous dignity, procurement and donation of bodies, management of the corpse, appropriate cultural adaptation, consideration of technological advances without dehumanization or the prevention of illicit practices, must be considered by teachers. For this reason, a narrative review was proposed to analyze the biolegal framework and the bioethical considerations and implications in the teaching of Human Anatomy in South American countries such as Brazil, Chile, Colombia, and Venezuela.

Keywords: Human anatomy, bioethics, teaching.

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INTRODUCCIÓN

La enseñanza de la anatomía humana es un pilar fundamental en la formación médica y científica, proporcionando a los estudiantes una comprensión profunda de la estructura y función del cuerpo humano (1). A pesar de todos los avances tecnológicos, la enseñanza de la anatomía durante este siglo es similar a la del siglo XIX, es decir, las prácticas y demostraciones docentes se realizan sobre un cadáver humano, en una sala de disección, no ocurriendo mayores cambios en las estrategias didácticas para la enseñanza anatómica desde el siglo XVII (2).

El proceso de enseñanza-aprendizaje de la anatomía, es un binomio entre profesores y alumnos, que buscan ampliar sus conocimientos basados en la disección cadavérica; por lo que este proceso debería enfocarse en el estudio de la anatomía sobre el estudio descriptivo de un cadáver y en su defecto partes de cadáveres, individuos vivos o incluso materiales obtenidos de los mismos, así como los medios didácticos virtuales deben ser una alternativa complementaria (1). Las diferentes modalidades de enseñanza de la anatomía (disección, maquetas o tecnología virtual) y las mejoras en los dominios cognitivos se ven subordinadas a cuestiones ético-legales y disponibilidad de material cadavérico, con incidencia en el proceso de enseñanza-aprendizaje y las respuestas subjetivas de los educandos (3).

En este sentido, la disección del cadáver ha sido la metodología preferida y utilizada clásicamente para el aprendizaje de la anatomía, inclusive los estudiantes nativos digitales siguen considerando tanto a la disección de cadáveres como el estudio de proyecciones, como las más adecuadas para la obtención de conocimientos básicos de anatomía descriptiva y funcional y de competencias en anatomía clínica (4). La formación académica en el estudio de las ciencias médicas está representada por un devenir de experiencias angustiantes o estresantes, sobre todo en el estudio de la anatomía humana, donde para su estudio se deben abordar cadáveres o material cadavérico humano, donde pueden converger una serie de cuestionamientos de tipo filosóficos, éticos y emocionales que están asociadas de una manera o de forma permanente

con la muerte (5); por tanto, aunque el uso del cadáver humano pasó a ser central instrumento de saber en la escuela médica clásica, se ha venido cuestionando la real utilidad de su utilización en el proceso global de enseñanza-aprendizaje y las repercusiones éticas que su uso acarrea (6).

Dado a esta circunstancia, en los últimos tiempos, se ha visto cómo la enseñanza tradicional de la anatomía se ha volcado hacia un enfoque más clínico, generando el reemplazo de los cadáveres y uso de especímenes anatómicos reales por modelos de plástico, por la anatomía radiológica, la anatomía viviente, el aprendizaje basado en problemas, en lecturas, uso de computadoras y sobre todo por herramientas tecnológicas (7). Sin embargo, se debe tener en cuenta que aunque estas nuevas tecnologías educativas contribuyen a la enseñanza de la anatomía, la manipulación de un cuerpo humano, no tiene sustitución posible, dado a que involucra otros sentidos fundamentales para la formación médica, como ver el grosor y forma real de estructuras con sus posibles y frecuentes variaciones, o el reconocimiento a través del tacto sobre elasticidad o consistencia, tamaño, bordes, relaciones; así como tampoco el proceso reflexivo que puede darse en el estudiante durante la disección, sobre la vida y la muerte, la salud y la enfermedad, sobre la persona o el cadáver en que está trabajando, son preguntas que no se pueden formular con el uso de estos programas de imágenes multiplanares o tridimensionales (8).

Aunque esta disciplina, hoy día, se encuentra consolidada, históricamente ha atravesado períodos de gran turbulencia, al punto de ser considerada un delito por autoridades políticas y religiosas; motivados, básicamente, porque se realizaron estudios e investigaciones en cadáveres humanos, lo cual era contrario a las ideas de sacralidad del cuerpo, defendidas por los clérigos, que lideraron la sociedad en el oscurantismo. De esta forma, el material de estudio de los anatomistas se tornó polémico, estableciendo una paradoja entre la necesidad y la curiosidad por estudiar el cuerpo humano y la inviolabilidad y santidad del cadáver, junto al cuestionamiento de su dignidad (9).

Lamentablemente, es necesario recalcar que algunos episodios de la historia de la anatomía han desprestigiado en determinados momentos su reputación, debido a las actitudes poco éticas

e irreverentes de algunas personas; tal como la práctica de la disección como entretenimiento y mercadería a través de manifestaciones públicas en grandes anfiteatros, con venta de entradas exorbitantes, es decir, sin ningún fin académico o científico (9). De igual manera, durante la Segunda Guerra Mundial, los anatomistas alemanes utilizaron los cuerpos de las víctimas del Holocausto en estudios anatómicos, como también se observó la aparición de algunas ilustraciones de la esvástica nazi en las páginas de algunos libros de esta disciplina en ese período (10).

Un registro del Hospital Colonia de Barbacena de Brasil, una institución para pacientes psiquiátricos en la que fueron asesinados por inanición, 60 000 brasileños mayoritariamente afrodescendientes, detalló que se vendieron 1 853 cadáveres a escuelas de medicina para ser usados en las clases de anatomía (11). Por su parte, en Colombia en 1992 se descubrió el caso de la Universidad Libre de Barranquilla, donde se evidenciaron prácticas tendientes a la disposición de cadáveres sin los procedimientos establecidos en las normas de carácter sanitario, tras la denuncia de asesinatos de habitantes de calle cuyos cadáveres fueron descubiertos en su morgue (12).

Asimismo, se manifiestan múltiples situaciones de ética cuestionable en cuanto a la manipulación de cadáveres en salas de anatomía, morgues y centros clínicos, las cuales se tratan de inadecuaciones técnicas y éticas que, en algunos casos, se han repetido sistemáticamente durante tanto tiempo, que casi nadie las cuestiona, pasándolas por habituales e inclusive por legítimas; tal como sería el caso de los estudiantes que registran y publican fotografías con cadáveres en plena sala de disección o cuando se realizan exposiciones anatómicas con fines banales y controvertidos que manifiestan un irrespeto al cadáver humano en cuerpo y memoria (6).

Hoy día, aunque la tendencia hacia el uso de simuladores y modelos anatómicos en la enseñanza anatómica está en aumento, la mayoría de los cadáveres utilizados en las aulas son de personas no identificadas, lo cual conlleva a dilemas éticos, dado a que estos individuos suelen ser marginados sociales, carecen de apoyo y a menudo son víctimas de violencia, a quienes no se

les reconocieron derechos fundamentales durante su vida y que tras su fallecimiento, mediante consentimiento presunto, sus cuerpos se utilizan en la disección anatómica, convirtiéndolos en recursos de enseñanza y activos de los anfiteatros anatómicos, a los que no se les reconoce dignidad, valor intrínseco como personas, pero sí un precio de intercambio a sus unidades corporales (13).

Como puede verse, la enseñanza de la anatomía humana, componente esencial en la malla curricular de las profesiones de las ciencias de la salud, debe abordarse con una conciencia constante de los aspectos bioéticos involucrados; puesto que su proceso educativo no está exento de desafíos éticos y morales. Este ensayo explora estos aspectos fundamentales, las principales leyes y normativas vigentes en países sudamericanos como Brasil, Chile, Colombia y Venezuela; así como su relevancia en la formación de profesionales de la salud.

Marco Biojurídico

La enseñanza de la anatomía humana está regida por principios éticos y legales destinados a garantizar el respeto a la dignidad y los derechos humanos, así como a promover una educación médica y científica responsable y ética; es esencial que tanto los educadores como estudiantes de las ciencias de la salud se mantengan informados sobre estos marcos biojurídicos y los tengan en consideración de manera rigurosa en su práctica educativa.

A nivel mundial existen diversas leyes y códigos que regulan la investigación y la enseñanza de las ciencias, donde la anatomía está incluida, puesto que tienen directrices y códigos de ética que influyen en la enseñanza de la anatomía humana y la utilización de cadáveres y tejidos. Dichas normas jurídicas desde siglos pasados han venido regularizando y cambiando el manejo de los cadáveres en las salas de disección. En Inglaterra por ejemplo, la Ley de Anatomía de 1832, prohibió el uso de los cuerpos de los criminales condenados y permitió la donación voluntaria del cuerpo; marcando el inicio de un cambio de paradigma en la adquisición de cadáveres para disección anatómica, de acuerdo con los derechos humanos y la dignidad (14).

En este sentido, la Declaración Universal sobre Bioética y Derechos Humanos (15), adoptada por la UNESCO, subraya la importancia de respetar la dignidad humana, los derechos humanos y las libertades fundamentales en la investigación científica, la cual debe realizarse en el marco de los principios éticos enunciados en esta Declaración. Por su parte, la Declaración de Helsinki, adoptada en la capital finlandesa por la Asamblea General de 1964 de la Asociación Médica Mundial (16), es el documento internacional más importante de regulación de la investigación en seres humanos desde el código de Nürenberg de 1947. Esta dispone los principios éticos para la investigación médica en humanos, incluida la importancia del consentimiento informado y la protección de los derechos de los donantes.

Vale resaltar que las leyes y regulaciones específicas que normatizan la utilización de cadáveres para la ciencia y/o la docencia médica pueden variar según el país y la jurisdicción; por ejemplo en Estados Unidos de Norteamérica, aunque estas regulaciones pueden variar de un estado a otro, a nivel federal, la Ley de Donantes de Cuerpos y Tejidos Humanos (“Uniform Anatomical Gift Act”) establece los principios generales para la donación de cuerpos y tejidos humanos con fines de investigación y educación (17).

En Brasil, de acuerdo con la Ley Federal No. 8501/92, promulgada el 30 de noviembre de 1992 por el Congreso Nacional, los cadáveres que no hayan sido reclamados dentro de un plazo de treinta días después del fallecimiento podrán ser enviados a las facultades de medicina; asimismo, tanto los cadáveres no identificados como los identificados, pero sin constancia del domicilio de la familia ni de los tutores legales, también pueden ser utilizados con fines científicos y académicos, con la salvedad de que solo los cadáveres de personas fallecidas por causas naturales pueden ser utilizados para la investigación, por lo que cuando existan indicios de que la muerte fue producto de un hecho delictivo, el cadáver no podrá ser utilizado para estos fines (18).

Además, los derechos de la persona también están regulados por el Código Civil brasileño, el cual en su artículo 11 garantiza que los derechos de la persona son intransferibles, inalienables e irrevocables, por lo tanto, para el

ordenamiento jurídico del país, el cadáver tiene huellas de personalidad y por lo tanto no puede ser considerado un ser inanimado; mientras que el artículo 1.857 (párrafo 2) contempla la intención de donar el propio cuerpo con fines científicos después de la muerte, teniendo validez como disposición testamentaria de carácter no patrimonial, cuya vigencia persiste aunque el testador se haya limitado a ellas (19). Sin embargo, la Ley 9.434/1997 (20) requiere el consentimiento de la familia del fallecido. Más recientemente, la Resolución 196/1996 del Consejo Nacional de Salud (21), expone, con relación al uso de cadáveres con fines de investigación, establece los requisitos para la donación de cuerpos, los cuales incluyen la declaración de intención del donante o la autorización para donar el cuerpo por parte de miembros de la familia y/o representantes legales; además de contemplar, el respeto total a la dignidad del ser humano sin mutilación ni violación del cuerpo.

En Chile, la Ley N° 20.584 sobre Derechos y Deberes de los Pacientes (22) establece los derechos y deberes de los pacientes, incluyendo el consentimiento informado para cualquier intervención médica; si bien no se centra específicamente en la enseñanza de la anatomía, el principio del consentimiento informado es fundamental en la utilización de cuerpos y tejidos humanos con fines educativos. Por su parte, el libro IX del Código Sanitario chileno (23), regula el aprovechamiento de tejidos o partes del cuerpo de un donante vivo y de la utilización de cadáveres o parte de ellos con fines científicos o terapéuticos, siempre y cuando el donante haya otorgado en vida su consentimiento informado (Artículo 146); asimismo en su artículo 147 regula el aprovechamiento para la investigación científica de los cadáveres fallecidos en instituciones sanitarias cuyos cuerpos no fuesen reclamados en el tiempo previsto.

A su vez, en el Decreto 240 promulgado en junio de 1983 y modificado en diciembre de 1997, se establece el reglamento del libro noveno del código sanitario (24), en el cual se disponen los requisitos para la obtención, almacenamiento, manejo y disposición de cadáveres y tejidos humanos utilizados en la investigación científica y docencia universitaria (artículos 5-7); así como la obligación de las instituciones sanitarias de promocionar e informar sobre la donación de

órganos o tejidos, el tiempo de procura para cuerpos no reclamados (artículo 10), restos humanos exhumados no reclamados (artículo 16) o productos de la concepción que no lleguen a nacer vivos (artículo 17).

En Colombia, la Dirección General del Instituto Nacional de Medicina Legal y Ciencias Forenses publica la resolución 382 de 2015 (25), por la cual se reglamenta la inscripción de entidades para la obtención de cadáveres, componentes anatómicos y tejidos con fines de trasplante, docencia e investigación y se dictan otras disposiciones. Asimismo, el Decreto 786 (26) reglamenta la práctica de autopsias medicolegales y viscerotomías, las cuales se han clasificado en sanitarias, docentes e investigativas y deben ser realizadas sólo por personal avalado por el Instituto de Medicina Legal o en servicio social obligatorio.

Por último, en Venezuela, no se establecen aspectos relacionados con la investigación, la enseñanza y la utilización de cadáveres y tejidos humanos con fines educativos y científicos, ni en la Ley Orgánica de Salud (27) ni en la Ley del Ejercicio de la Medicina (28); sin embargo, ciertos principios y disposiciones de estas leyes pueden ser relevantes para esta área. A su vez, la Reforma de la Ley sobre Trasplante de Órganos y materiales anatómicos en seres humanos (29) dispone que cada ciudadano, después de su fallecimiento, es un potencial donante de órganos para trasplante, a menos que exista una negativa explícita en este sentido; asimismo, establece los conceptos de cadáver e investigación y docencia (artículo 3), respeto de la dignidad de la persona fallecida (artículos 13 y 31), pero no hace ninguna consideración sobre la donación cadavérica para estudio anatómico.

El Código de Deontología Médica venezolano (30), en su artículo 72 (numeral 10) establece el derecho del enfermo a disponer de su cuerpo luego de su muerte, en los artículos 145 a 150, normatiza la práctica forense y la práctica de necropsias; mientras que en su título quinto, capítulo primero (artículos 161 -168) si bien regula tanto la docencia médica, la cual debe satisfacer los requerimientos de orden ético, como el trasplante de órganos (capítulo quinto, artículos 207-215), no considera específicamente la enseñanza con cadáveres ni la disposición de

cuerpos humanos para la ciencia. Por su parte, en sus artículos 20, 69 y 132 regula el derecho a la intimidad del paciente, la exhibición al público profano de actos médicos y la obligación de mantener el secreto médico aún después de la muerte; los cuales son aspectos que considerar en cuanto a garantizarles a las personas sus derechos a la privacidad e intimidad aún posterior al término de la vida humana.

En el caso venezolano, en el entorno legal no se ha legislado sobre la disposición del cadáver, o de partes de él, con el objeto de que sea utilizado en fines de investigación científica, para la docencia universitaria. No existe por lo tanto normativa alguna que exponga que aquellos cadáveres de personas fallecidas en establecimientos hospitalarios públicos o privados, o que se encuentren en los establecimientos del Servicio Nacional de Medicina y Ciencias Forenses, es decir en las morgues que no fueren reclamados dentro del plazo que señale el reglamento, podrán ser destinados a la docencia universitaria en las salas de disección de las Escuelas de Medicina del país (5).

Como puede inferirse de los párrafos anteriores, cada país tiene sus propias leyes y regulaciones que rigen la utilización de cadáveres y tejidos humanos con fines educativos; dichas leyes varían en cuanto a los requisitos de consentimiento, la disposición de los cuerpos y la supervisión de la enseñanza anatómica. A su vez, las instituciones educativas que ofrecen programas de ciencias de la salud deben cumplir con las regulaciones establecidas por las respectivas autoridades educativas y sanitarias para la utilización de cuerpos y tejidos humanos en la enseñanza de la anatomía, además de poder promulgar reglamentos internos dirigidos a normatizar el uso de las salas de disección y a hacer cumplir todo el marco biojurídico y bioético descrito.

Consideraciones bioéticas

Los aspectos bioéticos en la enseñanza de la anatomía humana abarcan desde el consentimiento informado hasta la utilización responsable de cadáveres y la adaptación culturalmente apropiada de la educación anatómica. A continuación, se analizan las

principales consideraciones bioéticas implicadas en la enseñanza de la Anatomía Humana:

a) Dignidad Póstuma

Uno de los principios fundamentales en la enseñanza de la anatomía humana es el respeto a la dignidad de los individuos cuyos cuerpos son utilizados con fines educativos. Sin embargo, según diversas teorías ontológicas sobre la dignidad, como las propuestas por Kant, John Rawls o Martha Nussbaum, basadas en la racionalidad, sintiencia o florecimiento de actividades vitales, respectivamente. Desde estas perspectivas, pareciera que el principio de dignidad no es atribuible al cadáver y a sus componentes macro y microscópicos (13). En este mismo orden de ideas, autores como Neto y col. (31), plantean que la ausencia de una biografía en el caso de los cadáveres no reclamados pudiese significar el fin de los derechos de la personalidad de un cuerpo, dado que no tiene intereses como persona, no tiene valor en sí mismo, no ha expresado una última voluntad y no tiene familiares que puedan proteger su historia.

No obstante, el cadáver y sus componentes deben ser objeto de la misma consideración moral que se debe a los seres humanos vivos, si bien sujeta a las particularidades del cuerpo muerto, pues son merecedores de dignidad póstuma. La dignidad póstuma se erige entonces como el valor reconocido al cuerpo sin vida de la persona, el cual constituye su memoria y la de su red de relaciones significativas, de lo cual se deriva una actitud de respeto a sus valores, creencias, preferencias religiosas, ideológicas y éticas, así como de su integridad, tanto física como ideológica; así pues, el tratamiento dado al cadáver y sus componentes refleja la consideración y el respeto que en vida se tiene por las personas y las comunidades (13).

Uno de los cimientos de la bioética en la enseñanza de la Anatomía Humana debe ser el respeto a la dignidad y privacidad de los individuos cuyos cuerpos son utilizados con fines educativos. Comentarios perniciosos de índole satírico, discriminatorio o sexual ejercidos sobre el cadáver, así como actos y situaciones vejatorias, ya sea en sala de disección, el museo o en el ámbito hospitalario, al ser actos realizados en la intimidad, por tal inmensurable, generalmente terminan como anecdóticos e impunes; nada

es más insensato e injusto que violentar lo que ontológicamente está imposibilitado de defenderse (6). Los profesionales involucrados en el proceso de enseñanza de la Anatomía Humana deben, como lección fundamental para todos sus estudiantes, compartir enseñanzas sobre actitudes éticas relacionadas con el respeto a los cadáveres y a la dignidad humana, de modo de sensibilizar a los estudiantes sobre la moralidad de sus acciones, para que entiendan que no siempre su autonomía y voluntad deben predominar en sus actitudes; por tanto, la preparación del estudiante, en cuanto a los conocimientos que implican los principios éticos y el estudio de anatomía humana con el uso de cadáveres es un proceso aún en construcción que necesita de la atención de los profesores involucrados (32).

b) Principio de Autonomía

Es imperativo obtener el consentimiento informado de los donantes de cadáveres o tejidos humanos para garantizar que sus deseos y valores sean respetados incluso después de su fallecimiento; este principio asegura que la enseñanza anatómica se realice de manera ética y con un sentido de responsabilidad hacia los donantes y sus familias. Aun posterior a la muerte se puede producir daño a los intereses y deseos expresados por la persona, cuando ésta en vida se negó a donar su cuerpo con fines de docencia o investigación o, cuando deseándolo, terceros lo impiden; en este contexto cobran relevancia las disposiciones que se hacen a través de voluntades anticipadas, dado a que, estos intereses persisten más allá de la persona que los porta, no sólo representan intereses individuales, sino también disposiciones compartidas con otros miembros de la comunidad y son una prolongación de la autodeterminación (33).

Esta reticencia cultural a la donación del cadáver, que puede venir tanto de su titular en vida o por su representante una vez fallecido, es lo que determina que generalmente se empleen con fines de docencia o investigación cuerpos de personas de las que se desconoce su identidad, lo que implica desafíos éticos y jurídicos ya mencionados; por lo que se deberá consultar la regulación existente en el país (13). La disponibilidad de cuerpos para docencia e investigación en Anatomía alcanza niveles críticos en muchas universidades latinoamericanas, las cuales mayoritariamente recibían cadáveres no

reclamados, provenientes de hospitales para internación de pacientes crónicos con los cuales tenían convenios o por normas loco-regionales que lo avalaban; sin embargo, los cambios legislativos, las nuevas formas de tratar a los enfermos crónicos y la imposición de la filosofía de la donación sobre aquella de la apropiación, que resulta acorde a los criterios éticos actuales, han modificado notoriamente la disponibilidad de cuerpos para su estudio (34).

No obstante, con base en el principio bioético de beneficencia y no maleficencia, la utilización de estos cadáveres no reclamados para la enseñanza de la Anatomía Humana puede ser beneficiosa al mejorar la formación de futuros profesionales de la salud y, en última instancia, contribuir a la atención médica de alta calidad; sin embargo, también es necesario garantizar que sean tratados con el máximo respeto y dignidad, al mismo tiempo que se busquen alternativas éticas como la donación voluntaria de cuerpos para la enseñanza e investigación biomédica. La dignidad póstuma es una condición *sine qua non* que debe garantizarse, aún se traten de cuerpos no reclamados o no identificados, en quienes sus actos morales se tornaron desconocidos, pues estos no se modifican, aunque hubieses cometido actos altamente reprochables desde lo jurídico o lo moral.

c) Respeto a la privacidad e intimidad

El secreto profesional debe prevalecer aún después de la muerte, salvo las excepciones previstas por la ley, por lo que se debe entonces garantizar la confidencialidad e impedir el acceso de terceros no autorizados a los espacios donde reposan cadáveres que han sido resguardados con fines de docencia o investigación, así como evitar la difusión de imágenes o videos en los que se pueda determinar la identidad del cadáver, tales obligaciones morales incluyen al recurso humano en formación (13). En muchos casos, el secreto profesional, que debe guardarse por respeto tanto al difunto como sus familiares, quedan al libre albedrío de quienes practiquen la disección cadavérica en los laboratorios universitarios, y sólo son inculcados por parte del profesor si éste decide hacerlo (35).

En este contexto, es prioritario que las instituciones educativas establezcan reglamentos de comportamiento en las salas de disección

y anfiteatros anatómicos, los cuales sean sociabilizados con sus estudiantes y se exija el cumplimiento de los mismos; las nuevas generaciones de estudiantes, nativos tecnológicos, asiduos consumidores de redes sociales, pueden verse tentados a subir en las mismas imágenes donde se puedan exponer el cadáver o sus partes, conllevando a la pérdida de la privacidad. El cumplimiento del secreto médico incluye tanto al equipo de salud como al recurso humano en formación, por lo que tanto profesores como estudiantes deben evitar la difusión de imágenes o videos de los cuerpos estudiados, y más aún si en ellas se pueda determinar la identidad del cadáver (13).

En este sentido, en los últimos tiempos, la tendencia a compartir digitalmente cada detalle de nuestras vidas ha perpetrado las más impensadas esferas de la intimidad propia y ajena, conllevando a un descontrolado registro foto-videográfico y exposición de procedimientos biomédicos; de interés en este segmento son los innúmeros casos de registro y exposición innecesaria de cadáveres (total o parte) por parte de estudiantes y profesores de ciencias médicas en el ámbito educativo. Al respecto, el registro y exposición innecesaria de cadáveres o sus partes por parte de estudiantes y profesores de ciencias médicas se considera inapropiado; este puede ser de tipo situacional o registro francamente pernicioso, ambos son prescindibles, sin embargo, la ofensa moral del segundo es mayor pues preconcebidamente se actúa de mala fe. No obstante, el carácter moral de estas acciones estará siempre supeditado a la intencionalidad, la real necesidad, la utilidad y/o un legítimo consentimiento (6).

Esta situación, se ha venido tornando cada vez más problemática en diversas partes del mundo, así en marzo del año 2009, se conoció la denuncia contra estudiantes de enfermería de la Universidade Federal de Juiz de Fora (UFJF) en Brasil, quienes fueron denunciados por compartir en redes sociales, fotos dentro del laboratorio de Anatomía con partes de cadáveres donde se mostraban estudiantes jugando con huesos humanos; lo cual no sólo representaba una conducta antiética sino que también puede ser considerado un crimen según las leyes brasileñas, conllevando a pena de uno a tres años de privación de la libertad (36). Asimismo, previamente estudiantes de enfermería de la

ciudad de Bahía, habían publicado en Internet imágenes de cadáveres tomadas en el laboratorio de Anatomía de la Universidade Estadual de Feira de Santana (UEFS), lo cual va contra los principios éticos y representa una falla de las universidades, quienes deben garantizar y velar sigilosamente los datos e imágenes tanto de los pacientes como de los cadáveres (37).

Por su parte, considerando al Código de Deontología Médica venezolano (30), en su artículo 69 establece que el enfermo tiene derecho a que se le respete su intimidad, en tanto que en el artículo 132 obliga a mantener el secreto médico aún después de la muerte y en el artículo 20 considera contrario a la moral médica permitir la exhibición al público profano de actos médicos, quirúrgicos u obstétricos que hayan sido fotografiados o filmados; sólo en caso de que fuesen con fines educativos podría hacerse siempre y cuando que se tenga la aprobación del Colegio de Médico respectivo. Por tanto, si se considera que los derechos de las personas continúan aún posterior a la muerte, los docentes de anatomía humana deben garantizar el resguardo de la privacidad e impedir que sus estudiantes fotografíen y exhiban intencionalmente o no, el cadáver o sus partes en redes sociales.

d) Utilización Ética de Cadáveres y Tejidos Humanos

El uso de cadáveres y tejidos humanos en la enseñanza anatómica plantea cuestiones éticas relacionadas con la adquisición, manipulación y disposición de estos materiales. Los protocolos éticos adecuados son esenciales para garantizar un tratamiento respetuoso y responsable de los donantes; además, es crucial prevenir el comercio ilegal de cuerpos y tejidos humanos, protegiendo así la integridad de los procesos educativos y evitando la explotación de individuos vulnerables. Por tanto, si bien la docencia y la investigación son fines lícitos, se debe prestar especial cuidado al proceso de obtención, distribución, almacenamiento, manipulación, uso y destino final de los cadáveres y sus componentes anatómicos de personas que no han sido reclamados por sus familias (38).

Desde el descubrimiento del formaldehído en el siglo XIX, el estudio de la anatomía pudo prolongarse durante el tiempo que el espécimen soportara la disección y la putrefacción de ser

un problema; desde entonces, se dio inicio a una carrera en busca de nuevas y mejores técnicas de preservación en pro de la enseñanza, el estudio de la anatomía y la libertad para ejercerla, dejando de lado muchas veces las consideraciones éticas que la utilización de dichas técnicas podría acarrear; como en el caso de la plastinación (35).

Aunque en las sala de disección el cuerpo humano pueda materializarse y convertirse en un espécimen, lo que está en cuestión es el tipo de cuerpo en anatomización que surge como experiencia y materialidad para el estudiante se hace de un cuerpo cuyas estructuras anatómicas son frágiles y que está abierto a la variación, adquiriendo las habilidades para explorar y no memorizar un cuerpo normal y desarrollando la habilidad para aprender a tocar consistencias con cierta firmeza, lo cual al inculcarle, incluso, a ser cuidadoso con esa materialidad, les enseña ética en la práctica (39).

Sobre manipulación inadecuada del cadáver sin duda el caso más penosamente emblemático y de registro reciente sucedió en el laboratorio de morfología de la reconocida Universidad Complutense de Madrid, donde una investigación judicial demostró el manejo inadecuado de un total de 534 cadáveres que en distintos estados de descomposición yacían agolpados y hacinados en el anfiteatro; la mayoría de éstos eran de personas que habían donado su cuerpo a la ciencia, específicamente, para su uso en didáctica médica. Este escenario se repite en innumerables facultades de medicina del mundo, en donde los cuerpos son reducidos a instrumentos materiales, operados sin el cuidado ni decoro debido y, por veces, con grosera manipulación técnica; la corporalidad del cadáver es el sustrato tangible de su dignidad especial que, así como su *memoria defuncti* deben ser respetadas, más aún en didáctica médica en donde el cuerpo del fallecido debe recibir un trato notable en retribución al enorme servicio prestado (6).

La gratuidad es un principio relativo a la donación de componentes anatómicos con fines de docencia, investigación o trasplante; el cadáver, sus órganos, tejidos y líquidos no pueden ser objeto de lucro, comercio o enriquecimiento de terceros (13). La captación ilícita de cadáveres para estudio e investigación en ciencias médicas es más que conocida y practicada, entre otros, por estudiantes, ya sea en calidad de ejecutores

o adquirentes, bien sea por profanación de sepulcros, compras ilegales o intercambio o compra-venta de huesos; prácticas que confieren una extrema instrumentalización de las piezas cadavéricas, las cuales quedan como simples utensilios, deshumanizados y ajenos a de todo tipo de consideración que no sea en principio la didáctica o la comercial (6).

e) Principio de Justicia

Todo cadáver utilizado en didáctica médica tiene un ciclo de vida útil que cuando cumplido se le debe procurar un depósito final acorde. La privación de los restos cadavéricos de un depósito final digno menosprecia al cadáver y, en consecuencia, a la persona que proporcionó su cuerpo a la enseñanza médica; mantener las piezas cadavéricas sin un papel cierto les delega un estatus mobiliario y tal materialización es contraria a la dignidad y tamaña privación es un acto de injusticia. Se debe establecer un proceso de gestión cadavérica, ya sea por ley o por decreto reglamentario, que permita un seguimiento de los restos humanos, desde su adquisición hasta su sepultura o cremación (40).

f) Educación Sensible y Culturalmente Apropiable

De acuerdo con Grilli (41), cuando el recurso didáctico es el organismo propiamente dicho, es importante evitar mensajes contradictorios entre el discurso teórico explícito y las acciones pedagógicas que en los hechos se dan, aunque en el discurso teórico se promueve el respeto a la vida en sus diferentes manifestaciones, en su enseñanza se muestran muchas veces al alumno prácticas de laboratorio contradictorias con el discurso; por tanto, el trabajo práctico con material natural debe permitirle al alumno desarrollar tanto habilidades manipulativas como cognitivas de observación e interpretación de datos. Tanto profesores como alumnos que se inclinan sobre estos cuerpos inertes para estudiarlos exhaustivamente no pueden permanecer indiferentes ante su material de estudio. A pesar de ser un símbolo de la muerte, el cadáver también lleva todo el simbolismo de la vida de alguien, el cuerpo preservado muestra las marcas y cicatrices de su viaje, aunque no haya familiares y amigos que salvaguarden su memoria; aunque está desprovisto de alma o espíritu, su rostro aún revela expresión facial, rasgos de un ser humano único y la biografía de

un sujeto de derecho que debe tener su dignidad preservada, aunque solo quede su vulnerabilidad y debilidad (9).

Así pues, es de fundamental importancia en la enseñanza de las ciencias de salud, que tanto los profesores como el resto del personal involucrados en el proceso de enseñanza-aprendizaje, figuren como los principales responsables de la humanización de la enseñanza morfológica, posibilitando en los alumnos un nuevo horizonte de comprensión sobre la muerte y que los cadáveres sean visto como la expresión de la vida que partió; como el vehículo didáctico dirigido a los alumnos en la enseñanza de ética y dignidad humana, ya que, futuramente, estarán delante de sus pacientes, inclusive en una posible situación de muerte (42).

Al respecto, una experiencia en una universidad costarricense demostró que al incluir una clase de ética al inicio del curso, que abarque temas como el respeto por el donante, conductas dentro de las salas de disección y que enfatizen al donante como primer paciente, lograron cambios significativos en la conducta de los estudiantes hacia los cuerpos utilizados en los laboratorios, desarrollando en ellos conductas más humanistas (43). Por tanto, debe enfatizarse la necesidad de un proceso educativo en la disciplina de la anatomía, que resalte la importancia de las cuestiones éticas en el trato con cadáveres; por lo que los estudiantes necesitan conocer un poco de la historia de esta materia esencial y ser guiados por sus profesores antes de ingresar al laboratorio de anatomía, ya que traen consigo miedos y dudas que van más allá del universo biológico y, en muchos casos, necesitan superarse barreras culturales y religiosas en el trato y manejo del cadáver (9).

Por otra parte, la diversidad cultural y religiosa presenta desafíos adicionales en la enseñanza de la anatomía humana, por lo que adaptar los enfoques educativos para respetar las creencias y valores de diversas comunidades es un aspecto clave de la bioética; sobre todo la utilización de cadáveres humanos en la enseñanza anatómica que demanda una sensibilidad cultural y religiosa, dado el significado que puede tener el cadáver humano dependiendo de estos aspectos. Ajustar los enfoques educativos para respetar las creencias y valores de diversas comunidades es crucial para promover la inclusión y el entendimiento; por tanto, la educación anatómica debe ser

culturalmente apropiada y sensible, evitando la insensibilidad o la falta de respeto hacia las creencias de los estudiantes y la sociedad en general; con lo cual no solo se fomenta la inclusión, sino que también se promueve una comprensión más profunda y respetuosa del cuerpo humano.

En la actualidad, muchas universidades enfrentan la problemática de la escasez de cuerpos humanos para la enseñanza anatómica; por lo que la creación de un programa de donación de cuerpos podría servir como medio para viabilizar la donación voluntaria y propiciaría mejoras significativas en la calidad de la enseñanza de los estudiantes y una mejor formación del profesional médico (44). A su vez, la disponibilidad en la sociedad de información objetiva y clara sobre el proceso de donación posibilitaría el aumento de la tasa de adhesión de los potenciales donantes, para lo cual son fundamentales estrategias de comunicación más efectiva como la difusión a través de programas de radio y televisión, internet, centros académicos, carteles colocados en los tableros de anuncios de las escuelas, juntas de vecinos y centros comunitarios (45).

g) Avances Tecnológicos y Ética en la Enseñanza

De acuerdo con Zambrano (2), el profesor de anatomía más que un instructor de un conocimiento especializado, debe ser un educador, que no sólo cubra aspectos inherentes a la materia en sí misma, sino que a través de ella procure la consecución de objetivos colaterales trascendentales, tales como: el respeto al cuerpo como parte consustancial del ser humano, facilitar una aproximación temprana a la formación ética del profesional, estimular el respeto a la vida, para protegerla y tratar de prolongarla combatiendo las enfermedades, y enseñar a interpretar el significado de la muerte como resultado inevitable del devenir humano y el sentido de responsabilidad ante las acciones ejecutadas.

La tecnología ha revolucionado la enseñanza de la anatomía humana, permitiendo la creación de modelos anatómicos virtuales y la simulación de procedimientos médicos. Aunque estos avances ofrecen oportunidades educativas innovadoras, también plantean interrogantes éticos; la simulación virtual y la impresión en 3D, si bien pueden ser herramientas valiosas, no

deben desvincular por completo a los estudiantes de la realidad ética de tratar con cuerpos humanos reales; es esencial equilibrar la tecnología con la formación ética integral.

Al respecto, detractores de la realidad virtual en la enseñanza de la anatomía humana, considera que ésta es una simulación, por lo que al sustituir al ser humano vivo o al cadáver y sus estructuras por elementos virtuales, se estaría distorsionando la realidad y condicionando al alumno a un estudio indirecto del cuerpo humano, con lo cual se estaría contribuyendo consciente o inconscientemente a la deshumanización de la medicina. El médico se debe entrenar con seres humanos para trabajar con seres humanos y no sólo con máquinas, lo cual debe ser un complemento para el estudiante, un medio y no un fin; por lo que la realidad virtual podría traer consecuencias negativas como: la ausencia de trabajo en equipo; su artificialidad distorsionaría la relación médico-paciente; convertirse en factor coadyuvante a la deshumanización de la medicina; y la exclusión del derecho del mundo virtual, donde las acciones realizadas no generan consecuencias que impliquen asumir responsabilidades, enseñándole al estudiante que no importa cometer errores, al no haber responsabilidad ante terceros (2).

Por otra parte, según Cordeiro y Menezes (40), debido tanto a la escasez y dificultades para la obtención de cuerpos para la investigación y docencia universitaria como a su alta demanda, países como Brasil, Argentina, Turquía, Arabia Saudita o Egipto, han tenido que recurrir a adquirirlos legalmente en un mercado a encomienda de cadáveres o sus partes, exportados desde países como Estados Unidos de Norteamérica o China. Cuando las universidades o instituciones que ofrezcan capacitaciones en cadáveres hayan tenido que importar restos humanos para la docencia e investigación, se debería establecer un proceso de gestión cadavérica, ya sea por ley o por decreto reglamentario, que permita rastrear los restos humanos, desde el despacho de aduana hasta su sepultura o cremación.

Es importante que los académicos tengan un mayor conocimiento sobre la preservación, manejo e importancia del cadáver para la formación técnica y humanizada de sus alumnos; por lo tanto, es necesario que estén claros todos

los procesos legales involucrados, así como la forma en que los cuerpos serán preparados, conservados y utilizados en todas las áreas del conocimiento (45).

CONCLUSIONES Y RECOMENDACIONES

En el estudio de la Anatomía Humana, a lo largo de su historia, la disección del cuerpo humano o la proyección de sus partes, han sido las principales estrategias utilizadas para su aprendizaje; durante siglos los cadáveres humanos han sido utilizados como principal herramienta instruccional para la enseñanza de la Anatomía a los estudiantes de las ciencias de salud. Por tanto, el proceso de enseñanza – aprendizaje de esta disciplina, además de considerar los aspectos técnicos y académicos, debe estar centrado en valores; de modo, que los educandos desde las etapas iniciales de su formación, cuando generalmente cursan esta asignatura, vayan adquiriendo competencias y actitudes que fomente el respeto por la vida y la dignidad humana, aún después del cese de las funciones vitales.

Al ser el cadáver o sus partes los principales medios para el aprendizaje de esta disciplina, debe tenerse en consideración que enfrentar la muerte humana conlleva una serie de implicancias que van desde la cosmovisión de las diferentes culturas sobre el cese de la vida hasta las creencias religiosas de las personas; por otro lado, no debe obviarse que aún, a pesar de la muerte, los derechos de la persona se mantienen vigentes, por lo que el manejo y disposición del cuerpo humano debe ser tratado adecuadamente y respetando siempre su dignidad póstuma. Así pues, aunque la enseñanza de la anatomía humana es esencial para la formación de profesionales de la salud, también plantea importantes consideraciones éticas, tales como el respeto por la dignidad de los cadáveres, la transparencia en el consentimiento y la promoción de alternativas éticas como la donación voluntaria en vida del cuerpo para la docencia e investigación biomédica; el equilibrio entre la necesidad de educación médica y el respeto por la autonomía y la dignidad póstuma es esencial para abordar adecuadamente los dilemas y cuestionamientos bioéticos que puedan

acompañar a la enseñanza anatómica, como sería la utilización de cadáveres no reclamados.

Aunque en muchos países sudamericanos, el marco legal ha venido ajustándose y regulando el uso de cadáveres para la ciencia e investigación; aun en algunos países, como es el caso de Venezuela, no existen disposiciones legales que rijan sobre la materia en cuestión; sin embargo, esta situación no exime de la responsabilidad para gestionar y materializar valores en deberes que respeten los derechos y dignidad de las personas que, después de la vida, continúan aportando valor al proceso de enseñanza de la anatomía humana. Por tanto, es prioritario que las autoridades, las universidades y asociaciones gremiales de Médicos y demás profesionales sanitarios, promuevan iniciativas y proyectos de ley que legislen sobre voluntades anticipadas para la donación al final de la vida y sobre la disposición de los cadáveres no reconocidos o solicitados para fines académicos.

Asimismo, las Facultades de Medicina deben cumplir con su deber, gestionando y conservar de manera óptima los cadáveres con los que se impartirá la docencia, velando por que se respete el derecho a la privacidad evitando la difusión de imágenes fútiles de los cuerpos, así como también deliberar acerca del tema en los programas de la asignatura que dictan. Al integrar los aspectos bioéticos en la enseñanza de la anatomía humana, se está asegurando que los futuros profesionales de la salud sean no solo expertos en su campo, sino también individuos conscientes de sus responsabilidades éticas hacia los donantes, las comunidades y la sociedad en general; futuros profesionales humanizados, respetuosos con el sufrimiento de sus pacientes y conscientes de sus obligaciones éticas en su búsqueda del conocimiento y de la excelencia médica.

REFERENCIAS

1. Araujo JC. Aspectos históricos de la enseñanza de la anatomía humana desde la época primitiva hasta el siglo XXI en el desarrollo de las ciencias morfológicas. *Rev Arg Anat Online*. 2018;9(3):87-97.
2. Zambrano A. Ética y realidad virtual en la enseñanza de la Anatomía Humana. Universidad del los Andes: Mérida, Venezuela. 2011. Disponible

- en: <http://bdigital2.ula.ve:8080/xmlui/bitstream/handle/654321/6856/Etica%20y%20realidad%20virtual.pdf?sequence=1&isAllowed=y> Fecha de consulta: 21 de agosto de 2023.
3. Mazzoglio MJ, Algieri RD, Tornese EB, Ferrante S, Broffman C, Algieri A. Ludoaprendizaje en Anatomía: Impacto en las Concepciones Culturales y el Afrontamiento Cadavérico desde la Neurociencia Cognitiva. *Int J Morphol.* 2020;38(4):1065-1073.
 4. Mompeó B. Metodologías y materiales para el aprendizaje de la anatomía humana: percepciones de los estudiantes de medicina 'nativos digitales'. *FEM.* 2014;17(2):99-104.
 5. Araujo JC. Reacciones de los estudiantes del primer año de medicina en el estudio práctico de la anatomía con el cadáver ante la sala de disección y su influencia en el proceso de aprendizaje. *Avan Biomed.* 2018;7(2):90-105.
 6. Guzmán JA. Aspectos bioéticos y jurídicos del manejo del cadáver. Un análisis del estatus mortem y su consonancia ética en la praxis. *Vida y Ética.* 2018;19(2):77-141.
 7. Bravo AC. La anatomía ha evolucionado: enseñar y aprender anatomía en el siglo XXI; ¿Qué ha cambiado?. *Morfología.* 2019;11(1).
 8. Araujo JC. Del cadáver a la realidad virtual en el aprendizaje de la anatomía humana en la Escuela de Medicina de la Universidad del Zulia. *Rev Arg Anat Online.* 2017;8(3):98-101.
 9. Gonçalves SB, Binda da Silva de Jesus AR, Duarte LA. A dignidade do cadáver desconhecido enquanto material de estudo da Anatomia Humana. *UNESC.* 2022;5(2):51-66.
 10. Aumüller G, Grundmann K. Anatomy during the Third Reich. *Ann Anat (Germany).* 2002;184(3):295-303.
 11. Greco D, Welsh J. Derechos humanos, ética y práctica médica. *Rev Bioét.* 2016;24(3):443-519.
 12. Redacción El Tiempo. Cierran Morgue de la Universidad Libre. Disponible en <https://www.eltiempo.com/archivo/documento/MAM-53904>
 13. Pinto BJ, Gómez AI, Marulanda J, León AH. Necroética: el cuerpo muerto y su dignidad póstuma. *Repert Med Cir.* 2018;27(1):55-64.
 14. Bezerra PM, Borba M, Guerriero ICZ, Dallari SG. Análisis ético y legal de la investigación científica con cadáveres en Brasil. *Rev Bioética.* 2020;28(3):554-564.
 15. Organización de las Naciones Unidas para la Educación, la Ciencia y la Cultura. División de la Ética de las Ciencias y de las Tecnologías Sector de Ciencias Humanas y Sociales. Declaración Universal sobre Bioética y Derechos Humanos. París: UNESCO. 2006. Disponible en: https://unesdoc.unesco.org/ark:/48223/pf0000146180_spa
 16. Asociación Médica Mundial. Declaración de Helsinki de la Asociación Médica Mundial - Principios éticos para las investigaciones médicas en seres humanos. Disponible en: <https://www.wma.net/es/politicas-post-declaracion-de-helsinki-de-la-amm-principios-eticos-para-las-investigaciones-medicas-en-seres-humanos/>
 17. National Conference of Commissioners on Uniform State Laws. Uniform Anatomical Gift Act. 1987. Disponible en: http://www.uniformlaws.org/shared/docs/anatomical_gift/uaga87.pdf
 18. Lei Nº 8.501, de 30 de novembro de 1992. Diário Oficial da União - Seção 1. p. 16519. (1-12-1992). Disponible: <https://www2.camara.leg.br/legin/fed/lei/1992/lei-8501-30-novembro-1992-363726-publicacaooriginal-1-pl.html>
 19. Novo Código Civil Brasileiro. Curitiba/PR, Câmara Municipal de Curitiba, Diretoria de Informática, (10-01-2002). Disponible en: <http://www.cmc.pr.gov.br/download/ccivil.pdf>.
 20. Lei Nº 9.434, de 4 de febrero de 1997. Dispõe sobre a remoção de órgãos, tecidos e partes do corpo humano para fins de transplante e tratamento e dá outras providências. Diário Oficial da União. (05-02-1997). Disponible en: http://www.planalto.gov.br/ccivil_03/LEIS/L9434.htm
 21. Conselho Nacional de Saúde. Resolução CNS Nº 466, de 12 de diciembre de 2012. Aprovadiretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos. Diário Oficial da União. (13-06-2013). Disponible en: https://bvsms.saude.gov.br/bvs/saudelegis/cns/2013/res0466_12_12_2012.html
 22. Ley Núm. 20584. Regula los derechos y deberes que tienen las personas en relación con acciones vinculadas a su atención en salud. Diario Oficial de Chile. (24-04-2012). Disponible en: <https://www.bcn.cl/leychile/navegar?idNorma=1039348>
 23. Decreto Núm. 725. Código Sanitario. 11ª edición. Santiago de Chile: Jurídica de Chile. 2004. Disponible en: <https://www.bcn.cl/leychile/navegar?idNorma=5595>
 24. Decreto Núm. 240. Reglamento del Libro Noveno del Código Sanitario. Diario Oficial de Chile. (3-12-1983). Disponible en: <https://www.bcn.cl/leychile/navegar?idNorma=5595>
 25. Resolución 382 de 2015. Diario Oficial de de la República de Colombia. No. 49.517. (20-05-2015). Disponible en: https://jurinfo.jep.gov.co/normograma/compilacion/docs/resolucion_medicallegal_0382_2015.htm
 26. Decreto 786 de 1990. Por el cual se reglamenta parcialmente el título IX de la Ley 09 de 1979, en cuanto a la práctica de autopsias clínicas y médico - legales, así como viscerotomías y se dictan otras disposiciones. Diario Oficial de la República de Colombia. No 39.300. (17-04-1990). Disponible

- en: https://www.icbf.gov.co/cargues/avance/docs/decreto_0786_1990.htm
27. Ley Orgánica de Salud. Gaceta Oficial de la República de Venezuela. N.º 36.579. (11-11-1998). Disponible en: <https://www.asambleanacional.gob.ve/storage/documentos/leyes/ley-organi-20220316141637.pdf>
 28. Ley del Ejercicio de la Medicina. Gaceta Oficial de la República Bolivariana de Venezuela N.º 39.823. (19-12-2011). Disponible en: <https://alc.com.ve/wp-content/uploads/2013/10/Ley-del-Ejercicio-de-la-Medicina.pdf>
 29. Ley de Reforma de la Ley sobre Trasplante de Órganos y materiales anatómicos en seres humanos. Gaceta Oficial de la República Bolivariana de Venezuela. N.º 39.808. (25-11-2011). Disponible en: <https://www.asambleanacional.gob.ve/storage/documentos/leyes/ley-sobre--20220110153629.pdf>
 30. Código de Deontología Médica. LXXVI Reunión Extraordinaria de la Asamblea de la Federación Médica Venezolana. (20-03-1985). Disponible en: <https://docs.venezuela.justia.com/federales/codigos/codigo-de-deontologia-medica.pdf>
 31. Neto JB, Feijó A, Loch J, Bilhalva G, Baú M. O valor social do cadáver humano: personalidade, pesquisa científica, doação de órgãos e corpos. *Direito & Justiça*. 2008;34(1):60-73.
 32. Borba K. O estudo de Anatomia no ensino de enfermagem: reflexões sobre princípios éticos. *Cienc Cuid Saude* 2017;16(1).
 33. Perosino MC. Un cadáver humano. *Cuadernos de ética*. 2014;29(42):1-22.
 34. Biasutto SN, Cárdenas J, Prat GD, Romero R, Medina BA, Tamayo S, et al. Situación de las universidades argentinas y latinoamericanas en relación al material cadavérico para la enseñanza de la anatomía. *Rev Arg Anat Clin*. 10(2):52-76.
 35. Rueda RJ, Hernández JD. Anatomía Humana: Ciencia, Ética, Desarrollo y Educación. *Rev Fac Med*. 2012;20(2):6-8.
 36. Harnik S. Federal de Juiz de Fora investiga fotos de brincadeira com cadáver em aula de anatomia. UOL Educao. Disponible en: <https://educacao.uol.com.br/ultnot/2009/03/13/ult105u7719.jhtm>
 37. Aragaki B. Estudante de enfermagem vaza fotos de cadáveres na Web. UOL Educao. Disponible en: <https://educacao.uol.com.br/ultnot/2008/06/05/ult105u6573.jhtm>
 38. Araujo JC. Naturaleza jurídica del cadáver o componentes anatómicos utilizado con fines docentes: Perspectiva bioética y biojurídica. *Rev Bioet Latinoam*. 2019;23:73-97.
 39. Martínez S. Hacer arteria carótida en el Laboratorio de Anatomía. Práctica y materialidad en una asignatura de Medicina. *Rev Colomb Soc*. 2016;39(2):31-47.
 40. Cordeiro RG, Menezes RF. Lack of Corpses for Teaching and Research. *Rev Bras Educ Med*. 2019;43(1):579-587.
 41. Grilli J. El material natural en la Biología escolar. Consideraciones éticas y didáctica sobre las actividades prácticas de laboratorio. *Rev Eureka sobre Enseñanza y Divulgación de las Ciencias*. 2018;15(1):1-19.
 42. Castilho MAS, Oda JY, Sant'Ana DMG. Fear and Deshumanization: A Critical View on the Daily Routine of the Human Anatomy Laboratory. *Int J Morphol*. 2009;27(3):909-912.
 43. González J, Salazar L. La importancia del Programa de Donación de Cuerpos en la formación médica antes y después de la pandemia: experiencia de la Escuela de Medicina de la Universidad de Costa Rica. *Universidades*. 2022;(92):19-31.
 44. Prohmann LAV, Figueiredo RR, Mendes VS, Carvalho MBB de, Almeida FS de, Gama Filho OP. Perspectivas de uma comunidade universitária acerca da doação de corpos para estudo em anatomia humana. *Rev Bras Educ Med*. 2023;7(1): e038.
 45. Marani RB, Hermes-Uliana C, Silva AP da, Silva Edos A, Martins HA. Knowledge between academics about body donation for the teaching of Human Anatomy. *RSD*. 2021;10(2): e55110212881.

Perla de Observación Clínica

El Síndrome de la Nariz Sin Límites.

Una Amenaza Otorrinolaringológica Encubierta de
Iatrogenesis y Malapaxis

Pearl of Clinical Observation.

The Nose No Bounds Syndrome.

A Hidden Otorhinolaryngological Threat of Iatrogenesis and Malpractice

Aderito De Sousa Fontes¹, María José Zamora Santil²

RESUMEN

Una amplia diversidad de alteraciones de la nariz y senos paranasales (SPN) pueden ser susceptibles de tratamiento quirúrgico, cuando falla la terapia médica máxima o cuando el objetivo es generar un cambio estético o cosmético en un paciente. Los riesgos de resultados adversos de una cirugía electiva de este tipo pueden ser notables y altamente probables, más aún cuando la decisión de operar no ha sido valorada previamente de manera rigurosa. Este escenario se

vuelve aún más preocupante, con el ofrecimiento publicitario desenfrenado y sin escrúpulos, de tratamientos falsos y poco claros, que son una amenaza encubierta de iatrogenesis y malapaxis otorrinolaringológica y que están asociados a una variedad de manifestaciones clínicas intolerables y a menudo irreversibles para la salud física y mental del paciente, que terminan desencadenando un nuevo trastorno en los tiempos actuales, que hemos querido denominar como el “Síndrome de la nariz sin límites”.

SUMMARY

A wide diversity of nose and sinus disturbances may be susceptible to surgical treatment when maximal medical therapy fails or when the goal is to generate

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an aesthetic or cosmetic change in a patient. The risks of adverse outcomes after elective nose and paranasal sinuses surgery can be notable and highly probable, even more so when the decision to operate has not been previously rigorously assessed. This scenario becomes even more worrying, with the unbridled and unscrupulous advertising offering of false and unclear treatments, which are a hidden threat of iatrogenesis and otorhinolaryngological malpractice that are associated with a variety of intolerable and often irreversible clinical manifestation for the physical and mental health of the patients, that end up triggering in a new disorder in current times, which we wanted to call as the “Nose no bounds syndrome”.

INTRODUCCIÓN

Generalmente, las cirugías en la nariz y SPN más frecuentes se indican en un importante volumen de pacientes en todos los grupos etarios, son de corta duración, en una elevadísima proporción se realizan de forma ambulatoria, ocasionalmente se asocian con comorbilidades importantes y el tipo y tiempo de anestesia varían de acuerdo a la complejidad de la intervención primaria realizada y a otros procedimientos simultáneamente realizados en la nariz de manera combinada, especialmente con fines cosméticos. Los resultados indeseables y a menudo perjudiciales ocasionados por la indicación de intervenciones quirúrgicas imprudentes y atrevidas en esta región anatómica, generalmente no son reportados por quienes los ejecutan y sus consecuencias habitualmente son atendidas por otros especialistas (1).

A pesar del progreso en la comprensión de la fisiopatología de las enfermedades de nasosinusales, los avances tecnológicos en el diagnóstico y los tratamientos de sus diferentes trastornos, los fracasos y resultados desfavorables derivados por una cirugía fallida, representan un problema importante con considerables consecuencias para la salud física, emocional y la economía de estos pacientes. Los aspectos técnicos y la capacitación adecuada del otorrinolaringólogo juegan un papel importante en minimizar las probabilidades de fracaso de una cirugía, especialmente cuando el objetivo principal del cirujano ha sido la indicación apresurada del acto operatorio sugerido, pasando por alto los protocolos previos de detección y

control de comorbilidades locales o sistémicas asociadas; la realización de procedimientos agresivos inoportunos y anticuados o la mala selección de pacientes a los que se le plantean además realizar otras cirugías combinadas que pueden ser desaconsejables en una gran cantidad de casos (ej. cirugías estéticas o de otro tipo) (2).

En muchos casos, en los que la cirugía primaria ha fracasado, los criterios de selección y planificación para una reintervención deben ajustarse aún más, ya que las perspectivas de éxito pueden depender de los daños ocasionados en la cirugía previa, más aún cuando han sido mutiladas o seriamente afectadas estructuras anatómicas importantes cruciales en el funcionalismo nasosinusal.

La anatomía de la nariz y SPN esta conformada por diferentes estructuras y cavidades aéreas ubicadas dentro de los huesos del cráneo y de la cara, intercomunicadas por diminutos drenajes y es probablemente una de las estructuras del cuerpo humano que posee más variaciones anatómicas. Aunado a esto, se agrega un complejo funcionalismo en el que su revestimiento epitelial juega un importante papel como barrera física, acondicionamiento del aire inhalado (calentamiento, humidificación y filtrado), sensorial (olfatoria) y defensa local innata y adaptativa en el inicio y configuración de respuestas inmunes (3).

La intrincada complejidad anatomo funcional de la nariz y los SPN y las diferentes estructuras anatómicas críticas y vulnerables que la rodean (cerebro, órbitas, importantes vasos y nervios), configuran además un escenario desafiante desde los puntos de vista clínico, diagnóstico y quirúrgico (4).

Cuando una cirugía de rutina y electiva sale mal

Los riesgos de resultados adversos después de una cirugía electiva nasosinusal pueden ser notablemente probables, a pesar del conocimiento fisiopatológico registrado hasta ahora, unido al perfeccionamiento de los estudios imagenológicos y las modernas técnicas quirúrgicas endoscópicas. Todos estos aspectos han contribuido en consecuencia a mejorar los niveles de precisión diagnóstica y los abordajes operatorios más convenientes.

Existen elementos que son claves en la decisión de una cirugía electiva. La palabra “electiva” puede hacernos pensar que se trata de algo opcional, pero esto no siempre es así. Una cirugía electiva es aquella que, a diferencia de una operación de emergencia, se programa con tiempo evaluando cuidadosamente los riesgos y beneficios de la intervención planteada, indicando las medidas previas para que la cirugía se efectúe en condiciones clínicas óptimas y planificando la estrategia operatoria más conveniente (5).

Conectado a lo antes mencionado, la selección de los pacientes programados para una cirugía electiva y la evaluación continua de las indicaciones formales de los diferentes procedimientos quirúrgicos nasosinuales y sus resultados, basados en el análisis de la evidencia publicada en la literatura, por encima de las opiniones anecdóticas de las experiencias particulares de algunos cirujanos, son aspectos fundamentales para llegar satisfactoriamente a los objetivos propuestos en un paciente con indicación quirúrgica electiva o por el contrario, fracasar en el intento de lograr un buen resultado (6).

Una buena parte de los casos con resultados quirúrgicos desfavorables y negativos se relacionan cuando se desestiman de los criterios establecidos de selección de pacientes cuando se realizan procedimientos quirúrgicos funcionales y/o estéticos de la nariz inadecuados y el paciente se despreocupa en buscar información que responda a preguntas como: ¿Por qué, para que y que tipo de cirugía nasal me han propuesto realizar?, ¿Quién me la va a realizar? y ¿Cómo y dónde se llevara a cabo? (7).

El síndrome de la nariz sin límites

La indicación de una cirugía nasal electiva debe ajustarse dentro de ciertos límites relacionados con la selección del paciente (edad, patología existente, comorbilidades) y la valoración de los criterios de la cirugía que se plantea realizar (beneficios, alteraciones fisiológicas posoperatorias, riesgos y pronósticos). La selección de pacientes y cirugías puede llegar a ser más desafiante cuando el propósito de la cirugía nasal se asocia a generar un cambio funcional y físico (cosmético o estético), bien sea por solicitud propia del paciente o por la recomendación

circunstancial de su cirujano tratante. En estos últimos casos, las motivaciones y expectativas de los pacientes son aún más complejas, por lo que además es necesario evaluar la esfera psicológica y sus expectativas y ponderar los potenciales daños físicos, emocionales y económicos que pueden presentarse en un paciente insatisfecho (7).

Precipitar los criterios de selección e indicación simultánea de intervenciones funcionales y estéticas desestimando todas estas consideraciones, sin lugar a duda puede potencialmente conducir a resultados intolerables y perjudiciales sin límites en un paciente (8,9).

Un importante fenómeno que hay que considerar en los actuales momentos, ha sido el impacto de los medios de comunicación modernos (radio, TV, internet, redes sociales) en la oferta sin límites, de tratamientos médicos o quirúrgicos de todo tipo. La carencia de barreras y regulaciones en la difusión de servicios de salud, han abierto un espectro de gran alcance para la creatividad del “negocio obscuro” en las que se promocionan procedimientos médicos y quirúrgicos dudosos, realizadas por individuos no calificados (charlatanes, intrusos y médicos sin escrúpulos). La injerencia mediática de estos actores genera un impacto de rechazo y desmoralización considerable, en los profesionales formalmente reconocidos y son un mal ejemplo para los profesionales de las nuevas generaciones médicas que formalmente cumplen con los requisitos necesarios para su preparación académica, por lo que deben considerarse enemigos internos desenfrenados del ejercicio correcto y honorable de la medicina. En el campo de la rinología la oferta de operaciones dudosas y desaconsejables ha comenzado a dar consecuencias perjudiciales en la salud y economía en varios pacientes (10).

La nomenclatura del “síndrome de la nariz sin límites” está inspirada en un capítulo de la serie American Greed (Codicia americana) de NBC - USA, titulada “Dr. Mark Weinberger - Nose no Bounds”, 2011; Temporada 5 - Episodio 50 (Figura 1) y se atribuye a los daños físicos, funcionales y psicológicos que algunos médicos especialistas, personal de salud no calificado que ejercen el intrusismo (médicos sin adiestramiento exhaustivo, esteticistas, odontólogos maxilo-faciales, enfermeras, fisioterapeutas, estudiantes de medicina o técnicos) y charlatanes (individuos

SÍNDROME DE LA NARIZ SIN LÍMITES

sin preparación), cuya actuación se manifiesta en una triada caracterizada por:

- Aplicar tratamientos médicos y/o quirúrgicos no consensuados científicamente que pueden ser engañosos, obsoletos y riesgosos.
- Poseer una capacitación y entrenamiento profesional deficiente o insuficiente.
- El objetivo principal es el lucro.

La práctica impropia, abusiva e inapropiada de los procedimientos quirúrgicos aplicados en la nariz (funcionales y/o estéticos), han derivado en serias perturbaciones (a menudo irreversibles) a la salud orgánica y mental de los pacientes que se han sometido a estos tratamientos. La larga lista de repercusiones indeseables ha sido descrita de manera independiente y entre ellas se han reportado: obstrucción y sequedad nasal persistentes, sangrados nasales regulares, asimetría externa de la nariz, perforación del tabique nasal, acumulación de costras nasales, mal olor nasal con halitosis, cefaleas, alteraciones olfatorias (anosmia) y el gusto (ageusia), trastornos respiratorios habituales durante el sueño, repercusiones en interacción social, irritabilidad emocional, hiperventilación, pérdida de autoestima, trastornos de atención y concentración (aproxia), ansiedad, depresión, suicidio y gastos asistenciales reiterados (2,4,5,7-9).

Antecedentes históricos

La denominación sugerida para este síndrome se inspiró en un sonado caso ocurrido en

Norteamérica protagonizado por el Dr. Mark Weinberger, quien impresionaba ser un médico de primer nivel en su práctica profesional en Weinberger Sinus Clinic (Merrillville, Indiana-USA), una población con altos niveles de contaminación.

Las investigaciones desarrolladas señalaron que la mayoría de los pacientes que consultaron a este médico por padecimientos otorrinolaringológicos (más del 95 %), tuvieron contrariamente a la práctica médica habitual una sobre-indicación de cirugías rinosinuales impropias, con una importante cantidad que reclamó por resultados decepcionantes, que derivaron en varias denuncias realizadas por un considerable número de pacientes y médicos, que constataron los daños iatrogénicos ocasionados, por procedimientos quirúrgicos que fueron indebidamente planificados, innecesarios y deficientes. Las averiguaciones también señalaron además que Weinberger en 2003, tuvo ingresos brutos de casi 14 millones de dólares que le permitieron vivir una vida de lujos y excentricidades, circunstancia que le permitió además comprobar que se sobrefacturaron intervenciones que nunca fueron realizadas.

Después de las varias acusaciones judiciales presentadas por varios de sus pacientes, la Junta de Licencias Médicas del estado de Indiana le revocó de manera definitiva su licencia para ejercer la medicina. En 2004, después de haber realizado un viaje con su esposa a las islas griegas huyó sin dejar ningún rastro, declarándose una búsqueda internacional por la justicia norteamericana, siendo capturado por las autoridades policiales cinco años después en los Alpes italianos (diciembre 2009), en un paraje en el cual vivía en una tienda de campaña con una nueva pareja

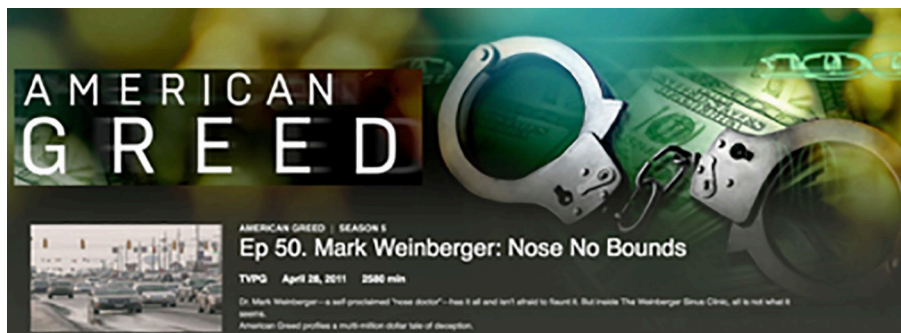


Figura 1.

de género transexual. Su extradición se realizó inmediatamente a Indiana-USA y fue juzgado por 22 cargos de negligencia y fraude sanitario en 2012, declarándose penalmente culpable de conformidad a la negociación propuesta por el fiscal acusador, recibiendo una sentencia a siete años en una prisión federal, aceptando además responder a 350 demandas civiles por negligencia médica, por un monto de 55 millones de dólares en 2013.

Este patético personaje, cuya siniestra historia también fue objeto de diversas crónicas en varios noticieros y un series televisivas norteamericanas como: America's Most Wanted-Fox televisión, Vanity Fair Confidential, Real Truth Crime, NBC5 Investigates, Secrets Uncovered en Dateline-MSNBC breaking news, Larry King Live CNN e Investigation Discovery, entre otras; quienes también lo apodaron como el "Doctor Nariz" (Nose Doctor) y el "Médico fugitivo" (Runaway Doctor), cumplió su condena en prisión saliendo en libertad en 2019.

En la actualidad intenta sacar provecho de su nueva vida en West Palm Beach, Florida-USA, donde se dedica a través de sus redes sociales a dar recomendaciones de como invertir exitosamente en inversiones en criptomonedas y se promociona a sí mismo como un "médico" e "influencer" que vende sus videos online en los que, para lucir bien, recomienda practicar yoga y meditación.

CONCLUSIONES

El síndrome de la nariz sin límites, es una entidad con un conjunto de características distintivas que se presentan juntas, que derivan en problemas y complicaciones serias en los individuos agraviados, que usualmente pueden ser irreversibles e irreparables, provocadas como consecuencia de la indicación y aplicación de tratamientos o procedimientos intervencionistas (funcionales y/o cosméticos) en la nariz, los cuales generalmente son realizados por charlatanes (el que actúa como de médico sin serlo), intrusistas (profesionales de otras áreas de la salud que actúa como de médico especialista sin serlo) o médicos especialistas desactualizados o que ejercen su profesión sin escrúpulos. La nomenclatura de este síndrome en la que los autores de esta reseña

nos hemos basado, se inspiró en un sonado caso de la vida real ocurrido en Norteamérica, protagonizado por un otorrinolaringólogo que ejerció su profesión de manera incorrecta y deshonesto, cuya práctica codiciosa ocasionó graves consecuencias en muchos de sus pacientes y sirvió de referencia a un capítulo titulado: "Nariz sin límites", de una serie de televisión de historias de la vida real, fundamentada en las actuaciones retorcidas de algunos individuos que hacen cualquier cosa por el dinero (American Greed «Codicia americana» de CNBC).

El síndrome de la nariz sin límites representa una amenaza encubierta de iatrogenesis y malapraxis realizados por médicos o no médicos que ejercen la piratería profesional al ofrecer tratamientos inescrupulosos, indebidos y potencialmente dañinos, que solo buscan beneficiarse económicamente sin importar sus consecuencias, las cuales pueden ser graves y a menudo irreparables. La colectividad debe ser advertida sobre las ofertas de tratamientos que se promocionan como efectivos, garantizados y rutinarios, los cuales pueden potencialmente convertirse en una amenaza "sin límites" para la salud y la economía de las personas que se someten a los mismos.

REFERENCIAS

1. Karadaghy OA, Vukas RR, Villwock JA. Evaluation of the literature surrounding shared decision-making in elective rhinological surgery: A scoping review. *Auris Nasus Larynx*. 2021;48(5):922-927.
2. Blomgren K, Aaltonen LM, Lehtonen L, Helmiö P. Patient injuries in operative rhinology during a ten-year period: Review of national patient insurance charts. *Clin Otolaryngol*. 2018;43(1):7-12.
3. Luong A, Marple BF. Sinus surgery: indications and techniques. *Clin Rev Allergy Immunol*. 2006;30(3):217-222.
4. Baban MIA, Castelnuovo P, Hadi M, Karligkiotis A, Battaglia P, Shawkat A. Surgical Instructions in Revision Endoscopic Sinus Surgery: Pearls and Pitfalls. *Indian J Otolaryngol Head Neck Surg*. 2022;74(Suppl 2):813-820.
5. Jones G, Hemmerich C, Rucker B, Wise A, Kee M, Johnson A, et al. Harms reporting by systematic reviews for functional endoscopic sinus surgery: A cross-sectional analysis. *Eur Arch Otorhinolaryngol*. 2023;280(6):2805-2819.

SÍNDROME DE LA NARIZ SIN LÍMITES

6. Ikeda AK, Hong P, Ishman SL, Joe SA, Randolph GW, Shin JJ. Evidence-Based Medicine in Otolaryngology Part 7: Introduction to Shared Decision Making. *Otolaryngol Head Neck Surg.* 2018;158(4):586-593.
7. Millman B, Smith R. The potential pitfalls of concurrent rhinoplasty and endoscopic sinus surgery. *Laryngoscope.* 2002;112(7 Pt 1):1193-1196.
8. Rohrich RJ. Streamlining cosmetic surgery patient selection - just say no!. *Plast Reconstr Surg.* 1999;104(1):220-221.
9. Huang CC, Wu PW, Lee CC, Chang PH, Huang CC, Lee TJ. Suicidal thoughts in patients with empty nose syndrome. *Laryngoscope Investig Otolaryngol.* 2022;7(1):22-28.
10. Clemente Heimerdinger A. Intrusismo y ejercicio de la medicina. *Gac Méd Caracas.* 2001;109(4):541-545.

Aspectos Bioéticos de la Publicidad Médica en Medios Digitales y Redes Sociales

Bioethical Aspects of Medical Publicity in Digital Media and Social Networks

José Ramón Urdaneta¹, Nasser Baabel Zambrano²

RESUMEN

La publicidad médica en medios digitales y redes sociales es una realidad cada vez más prominente en la sociedad actual y si bien esta forma de publicidad puede tener ventajas en términos de accesibilidad y alcance, también plantea importantes desafíos y cuestiones éticas que merecen reflexión. Por tanto, la presente revisión narrativa pretende caracterizar la publicidad médica en medios digitales y redes sociales, analizando los principales aspectos éticos que involucra la propaganda y publicidad de los médicos en estos nuevos escenarios; con el propósito de propiciar una reflexión en la comunidad médica para el uso óptimo de estas nuevas herramientas sin caer en dilemas éticos ni en acciones que propicien la deshumanización de la medicina.

Palabras clave: *Bioética, Publicidad Médica, Medicina, Medios Digitales, Redes Sociales.*

SUMMARY

Medical advertising in digital media and social networks is an increasingly prominent reality in the actual society and while this form of advertising may have advantages in terms of accessibility and reach, it also raises important challenges and ethical questions that deserve reflection. Therefore, the present narrative review aims to characterize medical advertising in digital media and social networks, analyzing the main ethical aspects involved in the propaganda and advertising of doctors in these new scenarios; to promote reflection in the medical community for the optimal use of these new tools without falling into ethical dilemmas or actions that promote the dehumanization of medicine.

Keywords: *Bioethics, Medical Publicity, Medicine, Digital Media, Social Networks.*

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INTRODUCCIÓN

Si bien la publicidad tiene como fin al ser humano, tanto con un propósito informativo como con una intención instrumental de tipo comercial; en el caso de la publicidad médica, su magnitud sublime y técnica, deben estar siempre sujetas al marco legal y ético-moral. A pesar de ello, existe un tipo de publicidad médica engañosa y/o ilícita, la cual incita o puede instigar al error a sus receptores que son los pacientes, pudiendo afectar a su comportamiento económico, o perjudicar su salud e inclusive a otro colega médico (1).

Para la American Marketing Association (2), el marketing comprende la actividad, instituciones y trámites dirigidos a crear, comunicar, entregar e intercambiar ofertas que representan valor para los clientes, socios y la sociedad en general; en tanto que el marketing digital se refiere al empleo de medios virtuales para promover marcas y llegar a los consumidores mediante internet, plataformas asociadas a redes sociales, dispositivos y otros conductos.

Sin embargo, aunque las palabras clientes y pacientes pudiesen parecer sinónimos, en realidad no significan lo mismo; según la Real Academia Española (3) la palabra “paciente” significa “persona que padece física y corporalmente”, y especialmente quien se halla bajo atención médica, “persona que tiene paciencia”, mientras que la palabra “cliente” significa “persona que utiliza con asiduidad los servicios de un profesional o empresa”. La educación médica tradicional ha inculcado a los médicos que los pacientes no son considerados clientes; por el contrario, el paciente es un ser humano sagrado al que se le debe ofrecer lo mejor de la preparación profesional y moral para lograr su recuperación (4); la mercantilización de la salud comienza desde el primer momento en que al paciente dejó de llamarse paciente para ser nombrado cliente (5).

Por otra parte, es importante conocer la ética publicitaria como el conjunto de principios y normas que guían la práctica de la publicidad de manera moral y responsable, lo cual implica la promoción de la honestidad, integridad, equidad y transparencia en la comunicación con los consumidores; buscando equilibrar los objetivos

comerciales con el respeto por la verdad y el bienestar de la sociedad a la que se dirige (6). Aunque en el área médica se ha considerado que no era ético promover la “venta” de un servicio médico, no debe olvidarse que, en realidad, la atención a la salud se desarrolla en un ámbito económico y de mercado; por tanto, las técnicas de marketing digital pretenden justamente dar a conocer el valor diferencial de cada servicio médico a sus pacientes potenciales, y, en consecuencia, el prestigio y la profesionalidad de los médicos y personal sanitario que les atenderán (7).

Dentro de la medicina, tradicionalmente la única estrategia ética y válida para mercadear el servicio profesional era una excelente experiencia de servicio por parte de los pacientes; por lo que el mercadeo en salud debería estar dirigido a optimizar la calidad del servicio prestado, para lo cual debe comprenderse que los servicios de salud son productos más intangibles que tangibles, así como considerar la responsabilidad médica y la incertidumbre del paciente que tiene la opción de tomar o no dicho servicio. Frente a la digitalización y la emergencia de nuevas formas de interacción, los medios digitales se han convertido en una herramienta de bajo costo y con un alto alcance e impacto para comunicarse con todos los públicos; lo cual ha conllevado a repensar los modelos de comunicación publicitaria bajo los entornos mediáticos actuales (8).

Actualmente, con el intenso desarrollo y expansión de las tecnologías de la comunicación y la información, los profesionales se dan cuenta de que, si no buscan alternativas para dar a conocer sus servicios, estarán en desventaja competitiva en el mundo globalizado del trabajo (9). Además de medios tradicionales como la radio y la televisión, los médicos pueden disponer de instrumentos como sitios web, blogs, e-mails, Facebook, Twitter, Instagram, YouTube y WhatsApp; para atraer pacientes a sus consultorios (10); estos medios digitales aglutinan a todos los potenciales “clientes”, sin embargo, en el sector salud, deberían centrarse en la mejora de la eficiencia de procesos y en la búsqueda de mecanismos para reforzar la visibilidad, notoriedad o reputación (7).

La presente revisión persigue caracterizar la publicidad médica en medios digitales y redes

sociales, analizando los principales aspectos éticos que involucra la propaganda y publicidad de los médicos en estos nuevos escenarios.

Marco Biojurídico

La publicidad se abordó inicialmente en la 3.^a Asamblea General de la Asociación Médica Mundial en 1949, celebrada en Inglaterra, desde entonces, la comunidad médica y la sociedad en general han cuestionado cómo el médico puede ejercer su derecho a revelar sus conocimientos sin herir los valores éticos; así pues, en su Código Internacional de Ética Médica se establece que el médico debe abstenerse de publicidad y comercialización intrusivas o de otro modo inadecuadas y asegurarse de que toda la información utilizada por él en publicidad y comercialización sea objetiva y no engañosa. Asimismo, los médicos tienen deberes para con la sociedad, desempeñando un papel importante en asuntos relacionados con la salud, la educación y la formación sanitarias; en el cumplimiento de esta responsabilidad, deben ser prudentes al discutir nuevos descubrimientos, tecnologías o tratamientos en lugares públicos no profesionales, incluidas las redes sociales y deben asegurarse de que sus declaraciones sean científicamente precisas y comprensibles (11).

La Asociación Americana de Marketing capítulo México, recomienda seguir una serie de normas de buenas prácticas del marketing médico para el aprovechamiento óptimo de las redes sociales, entre las que destacan: todas las publicaciones deben contar con la autorización del ente competente, incluir las referencias bibliográficas de toda la información que se utiliza, no mostrar los productos médicos, sus cajas o presentaciones, no hablar directamente del producto y mucho menos invitar a consumirlo, e incluir la leyenda obligatoria “consulta a un profesional de la salud”, para acercar al paciente a un diagnóstico profesional (12).

En Brasil el Consejo Federal de Medicina enfatiza que el médico debe evitar la autopromoción, el sensacionalismo y la comercialización del acto médico, en virtud de la profesión que ejerce y por tanto, ha regulado la publicidad que puede efectuar el médico en sus redes sociales a fin de evitar abusos en los mensajes publicitarios que

puedan derivar en procesos éticos con sanciones disciplinarias o judiciales; estando prohibido publicar autorretratos (*selfies*), imágenes y/o audios que caractericen sensacionalismo, autopromoción o competencia desleal, así como la necesidad de resguardar el sigilo y la imagen del paciente (incluso si el paciente autoriza la divulgación). En este sentido, también se prohíben los anuncios que difundan el “antes y el después” de los procedimientos, así como la publicación por parte de terceros de reiterados elogios a las técnicas y resultados obtenidos; de manera de garantizar que no se utilicen de forma abusiva, engañosa o seductora representaciones visuales e información que pueda inducir a promesas de resultados (13,14).

En Venezuela, la regulación de la publicidad y la propaganda está sujeta a diversas leyes y regulaciones emitidas por el gobierno venezolano, las cuales establecen los parámetros legales y éticos que rigen la publicidad y la propaganda en el país. En primer término, la Constitución de la República Bolivariana de Venezuela (15) establece no sólo el derecho a la libertad de expresión y de información (artículos 57 y 58), sino también que estos derechos deben ejercerse respetando otros derechos y valores constitucionales, como el respeto a la moral, la ética y el orden público (artículos 46, 60 y 61).

Por su parte, la Ley de Responsabilidad Social en Radio, Televisión y Medios Electrónicos (16) regula la transmisión de mensajes publicitarios en radio, televisión y medios electrónicos; estableciendo tanto pautas sobre el contenido de los mensajes publicitarios (artículo 10), como la protección del honor, vida privada, intimidad, propia imagen, confidencialidad, reputación y al acceso a una información oportuna, veraz e imparcial, sin censura, la protección de los niños y adolescentes, y la promoción de valores culturales y éticos (artículo 4). En tanto que Ley Orgánica de Telecomunicaciones (17) controla la transmisión y distribución de contenidos a través de medios electrónicos y telecomunicaciones, lo que incluye aspectos relacionados con la publicidad en línea.

De igual manera, la Ley de Defensa de las Personas en el Acceso a los Bienes y Servicios (18) regula la publicidad y promoción de bienes y servicios (artículo 7), prevención

en la publicidad dirigida a grupos susceptibles (artículo 34), prohíbe la publicidad engañosa o que induce a error (artículo 57), y establece sanciones por prácticas publicitarias desleales, engañosas o abusivas (artículo 58). A su vez, la Ley de Propiedad Industrial (19) controla los aspectos relacionados con las marcas comerciales y otros derechos de propiedad intelectual, incluida la publicidad de marcas y productos.

En lo referente a grupos poblacionales específicos, la Ley Orgánica sobre el Derecho de las Mujeres a una Vida Libre de Violencia (20) en su artículo 15, numeral 15 define el término “violencia mediática”, entendiéndose como “la exposición, a través de cualquier medio de difusión, de la mujer, niña o adolescente, que de manera directa o indirecta explote, discrimine, deshonre, humille o que atente contra su dignidad con fines económicos, sociales o de dominación”. Asimismo, la Ley Orgánica de Protección a Niños y Adolescentes (21) en su artículo 32 establece el derecho a la integridad personal de los niños y adolescentes por lo que queda prohibida cualquier publicidad y promoción de productos o servicios que puedan ser perjudiciales para la salud, la seguridad o el bienestar de los niños y adolescentes; en tanto que el artículo 65 obliga a proteger la privacidad y la información personal de los niños y adolescentes, por lo que en su parágrafo primero prohíbe exponer o divulgar, a través de cualquier medio, la imagen de los niños, niñas y adolescentes contra su voluntad o la de su padres y/o representantes.

En el marco de las ciencias de la salud, específicamente la Ley Orgánica de Salud (22) señala que el ejercicio de estas disciplinas deberá estar a cargo de las personas idóneas, con reconocida moral y provistas de sus respectivos títulos profesionales (artículo 58); en tanto que el artículo 69 señala como derechos de los pacientes tanto recibir información veraz y comprensible que les permita otorgar su consentimiento informado, como a que se les respete dignidad e intimidad. Por su parte, la Ley del Ejercicio de la Medicina (23) establece disposiciones relacionadas con la publicidad y la promoción de servicios médicos en Venezuela, tales como el derecho de los médicos a anunciarse previa aprobación de la respectiva asociación gremial y con restricciones de la publicidad (artículo 14), prohibición de publicidad a

medicamentos (artículos 19 y 102), promoción ética y confidencialidad de la información de los pacientes (artículo 46).

El Código de Deontología Médica (24) sancionan y regulan la práctica de la publicidad, determinando que sólo se pueden dar a conocer datos generales, lugares y horarios de consulta. Sin embargo, es un hecho evidente que en el último tiempo han aparecido con frecuencia en las redes sociales, mensajes que promocionan en forma explícita o encubierta tratamientos médicos o quirúrgicos realizados por ciertos médicos, o que destacan características personales de algunos de ellos, con el objeto evidente de atraer pacientes (1).

Este código deontológico limita la publicidad, cohibiendo abusos, engaños y la competencia desleal entre sus agremiados; así pues en el artículo 20 establece que es contrario a la moral médica cualquier publicidad encaminada a atraer la atención del público profano hacia la acción profesional, salvo aquellos avisos en la prensa autorizados por el respectivo Colegio de Médicos; mientras que en el artículo 27 dispone las reglas para la publicidad y oferta de sus servicios profesionales tanto en prensa como avisos y placas exteriores para consultorios y/o clínicas. Asimismo, el médico tiene prohibido publicitar condiciones privilegiadas para tratamientos o procedimientos, además de métodos o técnicas que no estén científicamente reconocidos; el artículo 28 de este código señala algunas características de los anuncios que están expresamente reñidas con las normas de ética (24).

De igual manera, aquellos médicos que participen en campañas públicas de carácter preventivo o curativo y la utilicen en sus redes sociales, como medio de propaganda para incrementar su clientela privada, estarían inmerso en una violación al artículo 94 de este código. Igualmente, si los médicos son entrevistados en medios de comunicación escrita o audiovisual y posteriormente utilicen fragmentos de la entrevista audiovisual o fotografías de la entrevista en prensa escrita este tipo de publicaciones, se consideran una falta a la ética médica dado a que son violatorias a lo expuesto en los artículos 27, 28 y 29 del Código de Deontología Médica (24).

A pesar de todo este marco biojurídico tanto nacional como internacional, al revisar en las

redes sociales cualquier cuenta profesional de médicos venezolanos pueden observarse publicaciones que serían transgresoras de esta normativa, como aquellas que informan sobre la asistencia a congresos médicos o sus viajes al exterior vinculados a funciones profesionales, que involucren directa o indirectamente propaganda al realzar ante el público su prestigio profesional; o aquellas donde se ofrezca o garantice la curación de enfermedades, o llamen la atención de procedimientos especiales, o simplemente publicaciones que resultan ambiguas o confusas para los pacientes. Por otra parte, es común observar como el médico que es entrevistado en medios de comunicaciones audiovisuales o escritos utilice fragmentos de la entrevista audiovisual o fotografías de la entrevista en prensa escrita, los cuales son expuestos al público en sus redes sociales profesionales como propagandas o referencias de carácter individual sobre la especialidad del entrevistado, con miras a su beneficio profesional.

No obstante, se observa como la norma deontológica deja un vacío en cuanto a la realidad actual y al desarrollo de las nuevas formas de comunicarse y mercadear presentes en la sociedad moderna; hoy día en Venezuela es casi inexistente la prensa escrita, lo cual si se quiere puede propiciar que el profesional de la medicina deba recurrir a las redes sociales como única alternativa accesible, con relativo bajo costo y al alcance de la mayoría de sus pacientes y potenciales pacientes.

Es esencial que las normas relativas a la publicidad médica sigan la transformación constante de las tecnologías y, en consecuencia, de las relaciones, dando al médico la oportunidad de difundir su conocimiento sin el riesgo de herir ningún precepto ético (9). Asimismo, es fundamental que los profesionales de la salud venezolanos se familiaricen con las regulaciones vigentes en relación con la publicidad y promoción de los servicios médicos para así no caer en infracciones a las mismas y falta bioéticas.

Consideraciones bioéticas

El médico, es libre de producir su marketing a través de la publicidad, no obstante, esta libertad no es tan amplia como puede parecer. Tanto

la digitalización como la globalización, asoma nuevas dimensiones a los cuestionamientos éticos, entrando en una ética que ya no solo afecta a la esfera pública offline, sino al ciberespacio público y privado online; la libertad de expresión es compatible con el respeto a los derechos individuales y colectivos, con el ejercicio de esos mismos derechos y el cumplimiento de las obligaciones fuera y dentro de Internet, por lo que se debe aprender a ser persona y un agente moral en una comunidad (25).

a) Veracidad

La información publicada debe ser precisa, basada en evidencia y no engañosa, dado a que las afirmaciones exageradas o falsas pueden llevar a decisiones médicas inadecuadas por parte de los pacientes; por tanto, es deber moral del médico garantizar que sus contenidos sean reales, sin caer en sensacionalismo ni crear falsas expectativas en los receptores de sus mensajes publicitarios. Asimismo, en caso de delegar el diseño de su publicidad a terceros, es su deber vigilar la calidad y el tipo de contenido que se transmitirá bajo su nombre.

El mensaje publicitario tiene importancia mercadológica para el profesional en el sentido de reforzar su marca, pero debe transmitirse con mucho cuidado, en la medida en que una publicidad tergiversada (publicidad engañosa) o abusiva puede generar expectativas inalcanzables en los potenciales pacientes, y, por supuesto, atraerlos por la “promesa” que ofrece el médico en su difusión. Por tanto, el médico debe estar atento al contenido transmitido en sus mensajes publicitarios en las redes sociales, pues ante tal escenario no dejará dudas en cuanto al carácter engañoso o abusivo del contenido publicado, surgiendo de ahí la potencial responsabilidad del médico (26).

Debe tenerse en consideración que el acto médico además de individual es un acto moral, es por ello que muchos profesionales médicos cada vez se muestran más preocupados por el creciente número de publlirreportajes engañosos, confusos de actos médicos quirúrgicos que pueden crear falsas expectativas, por parte de estos profesionales médicos; estos anuncios, que tienen la intención de publicitar servicios, prestaciones e inclusive resultados, van en contra de la deontología profesional son allí los verdadero

riesgos de ese tipo de publicidad que puede considerarse como engañosa, la banalización de la salud, la indefensión del paciente y el mercantilismo que se está realizando con el acto médico (1). Los anuncios de servicios médicos no están prohibidos ni son ilícitos, el problema radica en su contenido, que estará expuesto a la sociedad laica, que no tiene los conocimientos técnicos suficientes sobre medicina; por lo que la publicidad debe tener una información clara, objetiva, transparente y veraz, que será determinante para que el paciente acuda o no al profesional presentado (26).

b) Respeto por la Autonomía del Paciente y Consentimiento informado

La publicidad no debe presionar ni manipular a los pacientes para que tomen decisiones médicas; los pacientes deben tener la libertad de tomar decisiones informadas y basadas en sus necesidades y valores personales. Por tanto, a pesar de presentar resultados formidables en su anuncio publicitario profesional, el médico tiene aún la oportunidad de hablar con el paciente e informarle sobre los detalles de los resultados presentados en las publicaciones; permitiéndole que acepte o no, los riesgos del procedimiento de manera libre y autodeterminada, traducido en su consentimiento informado (27).

El médico debe presentar tanto en sus anuncios publicitarios todos los beneficios y riesgos de las prácticas utilizadas, como también en la consulta en la que el paciente contrata el servicio, ya que allí ya se establece el objeto de la relación legal obligatoria; siendo evidente que sólo se reconocerá el consentimiento informado cuando la información proporcionada por el médico sea clara y precisa, por lo que, de no hacerlo, correrá el riesgo de responder por la omisión de datos considerados esenciales (26).

c) Beneficencia y No Maleficencia

Estos principios bioéticos obligan a los médicos a no realizar terapias no comprobadas científicamente, a indicar lo eficaz y a no exponer a riesgos innecesarios a sus pacientes; por tanto, la publicidad médica no debe promover tratamientos médicos que carezcan de respaldo científico sólido o que puedan causar daño a los pacientes. Deben priorizarse las intervenciones que tengan beneficios reales y minimicen riesgos,

sin utilizarse contenido gráfico o sensacionalista para atraer la atención de los usuarios, que puedan explotar el miedo de los pacientes y que se constituya este temor en barreras para acceder a los servicios sanitarios o que pueda socavar su capacidad de tomar decisiones informadas.

De acuerdo a la regulación brasilera, en la publicidad de servicios médicos, está prohibido utilizar expresiones tales como “el mejor”, “el más eficiente”, “el único capaz”, “resultado garantizado” u otras con significado similar, así como sugerir que el servicio médico o el profesional es el único capaz de tratar el problema de salud; prohibiéndose además, asegurar resultados al paciente o sus familiares, mostrar de manera abusiva, engañosa o seductora imágenes de cambios corporales causados por supuestos tratamientos e incluso usar celebridades para publicitar su servicio e influir en las personas laicas (13).

d) Confidencialidad y Privacidad

El derecho de imagen del individuo está protegido por los códigos deontológicos de cada profesión, por legislaciones específicas y por el Derecho del Consumidor; así, además de causar daños irreversibles y gran constreñimiento al paciente, la exposición indebida de su imagen compromete ética y jurídicamente al profesional involucrado, pudiendo incluso generarse multas o indemnizaciones (28). Por tanto, debe respetarse la privacidad de los pacientes y sus datos médicos, por lo que no deben ser compartidos datos clínicos sin el consentimiento explícito de los pacientes involucrados; de modo, que el uso inadecuado de imágenes clínicas puede generar problemas éticos, disciplinarios y legales a los miembros de la profesión, incluyendo a los estudiantes de medicina (29)

e) Justicia y Equidad

El principio de justicia es uno de los aspectos que se debe considerar en la publicidad médica, por tanto al momento de diseñar un mensaje publicitario, el mismo debe tener un público objetivo y usar los canales más idóneos para llegar a ese nicho de mercado; por tanto, la publicidad médica en línea abierta al no poder controlar quienes serán los receptores de dichos mensajes, no debería promover tratamientos inaccesibles para ciertos grupos demográficos debido a

limitaciones financieras u otras barreras, por lo que lo más recomendable sería apalancar los mensajes en sitios web o aplicaciones dirigidos al mercado particular que se desee acceder o que utilicen algoritmos para que el mensaje llegue al público objetivo.

Por otra parte, cuando la publicidad se hace con fines educativos, el principio de justicia viene a ser un aspecto por considerar, dado que al ser salud un derecho universal de todos los ciudadanos, las actividades de promoción en salud deberían dirigirse a toda la población; por lo que la reducción de la brecha digital y el acceso al internet como un derecho son algunos de los desafíos que tiene la ética digital (30).

f) Responsabilidad Médica

Los médicos pueden ser eventualmente responsabilizados por el uso abusivo de la publicidad con fines comerciales, en desacuerdo con la sobriedad exigida al profesional. Por regla general, su obligación es de medio, es decir, se obliga a proporcionar los recursos necesarios para la consecución de un fin, sin ser responsable del resultado dado a que no puede tener la obligación de resultado debido a que no trabaja con promesas, en la medida en que innumerables factores externos repercuten en materia de salud; por lo que surge el dilema de si el profesional que induce la garantía de resultados con su publicidad podrá responder por el desenlace no alcanzado, aunque se haya utilizado de todos los recursos que la medicina ofrece (26). Por tanto, aunque existe una tendencia cada vez más significativa de los profesionales de orientarse y valerse de las diversas técnicas que ofrece el marketing digital para atraer clientes, se deben respetar las reglas establecidas en las normativas que rigen el actuar profesional (31).

g) Honorarios médicos

En la actualidad muchos pacientes perciben que el interés primario de la atención de la salud no es su persona, sino un interés económico, en parte debido a la comercialización de la salud, con el uso de publicidad extensa dentro de la economía de mercado que prevalece en la sociedad. Se habla de justicia conmutativa cuando en las relaciones, en especial las de naturaleza contractual, las partes acuerdan retribuirse lo que intercambian en forma proporcional y apropiada;

en tal sentido, los honorarios médicos son una forma de denominar una compensación que, debido a la naturaleza impagable del servicio prestado (restaurar la salud o salvar la vida), no solo se hace con dinero, sino también con honor y aprecio (32).

Los médicos están sujetos a normas dispuestas en sus códigos profesionales que regulan la difusión pública que pueden hacer de sus competencias y que proponen que los honorarios médicos sean proporcionados a la solvencia económica del paciente; la publicación de honorarios es otra cuestión no solo disruptiva de las normas, sino que además de traspasar cualquier arancel mínimo ético, establecido por las instituciones colegiadoras, mercantiliza la práctica médica en tenores como promociones (31).

La mención explícita de honorarios en la publicidad de algunos médicos en las redes sociales es un grave problema moral que afecta tanto a la profesión médica como a los pacientes; la conducta es moralmente inaceptable para el médico y en la misma se identifica el valor negativo del desconocimiento de la norma, la naturaleza del acto médico y la ética publicitaria aplicada a la medicina, lo cual no exime de culpa al profesional. Aunque en Venezuela, no exista legislación para este tipo de conductas, al igual que numerosos otros aspectos de la praxis médica, no por ello pierden relevancia ya que constituyen un comportamiento impropio merecedor de la desaprobación del gremio médico (33).

h) Mala Praxis Médica

La mala formación, la improvisación, la charlatanería, la negligencia, la impericia o la irresponsabilidad como profesional tanto en el ejercicio como en el ofrecimiento de sus servicios a través de técnicas publicitarias, son algunas de las formas de proceder con significativas y dañinas repercusiones; pues son las comunicaciones públicas y la mala praxis uno de los pilares centrales en la formación y reproducción de representaciones sociales, muchas de ellas distorsionadas y con un profundo efecto deslegitimador de la profesión (31).

Las recomendaciones de los *influencers* en plataformas digitales y redes sociales como Instagram se han vuelto algo cotidiano, incluso en el ámbito de los medicamentos, sin considerarse

los riesgos que esto puede suponer para la salud de los usuarios. El *influencer* no sanitario no tiene la capacidad legal, de prescribir medicamento, mediante receta, ningún producto sanitario; no obstante, desde el ámbito del marketing se hace uso del concepto de prescripción cuando una figura mediática, normalmente una *celebrity*, tiene el suficiente poder para recomendar o aconsejar su uso, convirtiéndose en un prescriptor de marca. Es esencial crear conciencia en la sociedad para que cada individuo se centre en su ámbito profesional, de manera que no haya espacio para el intrusismo (34).

i) Transparencia y Conflictos de intereses

Los profesionales médicos y las organizaciones deben identificarse claramente en sus publicidades, antes de publicar contenido publicitario en línea, se debe someter a una revisión ética que evalúe la precisión, el tono, el enfoque y el impacto potencial en los pacientes, cumpliendo con todas las leyes y regulaciones pertinentes en el ámbito médico y publicitario. Asimismo, los conflictos de interés deben divulgarse de manera transparente para evitar sesgos o percepciones erróneas.

Aunque los médicos tienen el interés legítimo de obtener mediante el ejercicio profesional un medio de vida digno, el mismo debe supeditarse a un interés superior que debe primar, ante todo, que es el de mirar por el mejor bien o interés de sus pacientes; por tanto, tienen las obligaciones morales hacia sus pacientes de tener un nivel de conocimientos adecuado y actualizado, una competencia técnica suficiente, además de condiciones de honradez e integridad intelectual. Sin embargo, pueden surgir eventuales conflictos de intereses, como por ejemplo en la relación médico-industria farmacéutica, los que pueden conducir a un accionar incorrecto (35).

Reflexiones finales

La publicidad médica en internet y redes sociales debe estar centrada en principios éticos fundamentales que guíen la promoción de servicios y productos médicos en entornos digitales; principios que persigan garantizar que la publicidad sea precisa, transparente, respetuosa y beneficiosa para los consumidores de atención médica. En este sentido, las consideraciones

éticas son esenciales para garantizar que la información médica compartida en línea sea confiable y beneficiosa para todos los usuarios.

El profesional de la medicina debe ser sumamente cuidadoso con la propaganda y publicidad médica, ya que estas a menudo promueven una visión simplificada y comercializada de la atención médica; deben esforzarse por mantener la empatía y la atención personalizada en su práctica, mientras que los pacientes deben buscar una atención médica basada en la evidencia y la relación médico-paciente en lugar de depender exclusivamente de la publicidad para tomar decisiones de atención médica. Por tanto, es importante que tanto médico como pacientes y la sociedad en general sean críticos con los mensajes publicitarios.

Asimismo, se deben implementar regulaciones y estándares éticos sólidos en la publicidad médica para proteger la integridad de la atención médica, de manera que al garantizar el cumplimiento de los códigos profesionales y del marco regulatorio de la publicidad médica, se contribuirá a luchar contra el flagelo de la deshumanización de la medicina y que los pacientes puedan recuperar la confianza en sus médicos; de modo, que la relación médico-paciente se establezca con base a la confianza y no como una mera relación contractual entre las partes involucradas. Así pues, para mantener una relación médico-paciente ética y centrada en el bienestar del paciente, es fundamental que tanto los médicos como los pacientes sean críticos con la información que reciben de la publicidad médica y busquen una toma de decisiones informada y basada en la evidencia científica; además, es importante que los profesionales médicos se adhieran a estándares éticos sólidos y eviten cualquier conflicto de intereses que pueda comprometer la atención al paciente.

Por tanto, la publicidad médica en medios digitales y redes sociales no debe ser satanizada dado a que pudiese tener un impacto significativo en la sociedad y la toma de decisiones de los pacientes, de modo que desde una perspectiva social, sería importante analizar desde una visión transdisciplinar cómo esta publicidad afectaría a diferentes segmentos de la población y cómo influye en la salud pública; sin olvidarse, abordar la misma desde una perspectiva filosófica, que permita tener siempre presente las cuestiones

éticas y morales asociadas con la promoción de la salud en un entorno digital en constante evolución.

En virtud de ello, es fundamental que los colegios médicos venezolanos a través de sus tribunales disciplinarios por una parte reeduchen a sus afiliados y refresquen sus conocimientos en el marco ético y deontológico de la práctica médica en relación con el tema de la publicidad y propaganda médica; y por otro lado, a través de la Federación Médica Venezolana se debe propiciar una revisión al Código de Deontología Médica, el cual sin lugar a dudas requiere una actualización y ajuste a los tiempos modernos. Ni la Medicina ni las nuevas generaciones tanto de médicos como pacientes son los mismos que en el siglo pasado cuando este fue promulgado; por tanto, no puede seguir manteniéndose esta significativa brecha entre el marco deontológico vigente y los adelantos tecnológico de los tiempos modernos. En este sentido, el mundo digital cada vez crecerá más y los médicos sí o sí accederán en mayor medida al Internet y redes sociales, por lo que la publicidad en estos medios digitales es una realidad que requiere su revisión y regularización bajo una mirada actualizada y amplia; en la cual converjan diferentes puntos de vistas y perspectiva, que abarquen desde las concepciones filosóficas y éticas hasta los aspectos sociales inherentes a la publicidad médica.

Así pues, la publicidad médica en medios digitales y redes sociales es una realidad cada vez más prominente en la sociedad actual y si bien esta forma de publicidad puede tener ventajas en términos de accesibilidad y alcance, también plantea importantes desafíos y cuestiones éticas que merecen reflexión. Es esencial que la publicidad médica en línea esté regulada de manera adecuada y que tanto los profesionales de la salud como los consumidores sean críticos y responsables al interactuar con información médica en línea.

REFERENCIAS

1. Araujo JC. Publicidad médica maliciosa y desleal en el ejercicio profesional de la medicina. Su problemática ética, moral y jurídica actual en Venezuela. *Gac Int Cienc Forense*. 2022;45:29-53.
2. American Marketing Association. *Definitions of Marketing*. 2017. Disponible en: <https://www.ama.org/the-definition-of-marketing-what-is-marketing/> Fecha de consulta: 8 de mayo de 2023.
3. Real Academia Española, *Diccionario de la lengua española*. 23ª edición. Madrid, España; 2014.
4. Rincón PG. *¿Salud y mercadeo: amigos o enemigos?*. Universidad Militar Nueva Granada. 2011. Disponible en: <https://core.ac.uk/download/pdf/143447134.pdf>
5. Araujo JC. La salud ¿cómo derecho o cómo mercancía? Mercantilización de la relación médico-paciente y su correlación ética-bioética profesional. *Gac Int Cienc Forense*. 2023;43:20-33.
6. Reid GS, Reid MS. Ethical issues in advertising: perceptions of actual and expected ethical standards. *J Business Ethics*. 2016;136(2):227-240.
7. Sánchez J, Coello MF, Manosalvas JC, Miranda MF. El marketing digital y su potencial aporte para el posicionamiento de marca. *Rev Caribeña Ciencias Sociales*. 2019;8(6).
8. Ortiz H. Comunicación publicitaria en medios digitales. La gestión de la responsabilidad social en las Organizaciones del Tercer Sector. *Inmediaciones de la Comunicación*. 2020;15(1):109-131.
9. Schmidt ACFD de A, Manfredini GB, Brito LC de, Penido M de S, Buch PH, Purim KSM. Publicidade médica em tempos de medicina em rede. *Rev Bioét*. 2021;29(1):115-127.
10. Souza E da S, Lorena SB de, Ferreira CCG, Amorim AFC, Peter JVS. Ética e Profissionalismo nas Redes Sociais: Comportamentos On-Line de Estudantes de Medicina. *Rev Bras Educ Med*. 2017;41(4):564-575.
11. Asociación Médica Mundial. *Código Internacional de Ética Médica*. 73ª Asamblea General de la AMM. Berlín, Alemania, octubre 2022. Disponible: <https://www.wma.net/es/policias-post/codigo-internacional-de-etica-medica/>
12. Rivera G. *Redes sociales: aprovechamiento y restricciones en el sector salud*. Expomed. 2020. Disponible en: <https://www.conexiones365.com/nota/expo-med/regulacion/redes-sociales-salud> Fecha de consulta: 24 de abril de 2023.
13. Conselho Federal de Medicina. Resolução nº 1.974, de 14 de julho de 2011. Estabelece os critérios norteadores da propaganda em medicina, conceituando os anúncios, a divulgação de assuntos médicos, o sensacionalismo, a autopromoção e as proibições referentes à matéria. *Diário Oficial da União*. Brasília, 19 ago 2011. Disponible: <https://bit.ly/3q2wgoU>
14. Conselho Federal de Medicina. Resolução nº 2.126, de 16 de julho de 2015. Altera as alíneas “c” e “f” do art. 3º, o art. 13 e o anexo II da Resolução CFM nº 1.974/2011, que estabelece os critérios norteadores da propaganda em medicina, conceituando os anúncios,

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- a divulgação de assuntos médicos, o sensacionalismo, a autopromoção e as proibições referentes à matéria. *Diário Oficial da União*. Brasília, 1º out 2015. Disponible: <https://bit.ly/3t91bBW>
15. Asamblea Nacional Constituyente. Constitución de la República Bolivariana de Venezuela (1999). *Gaceta Oficial de la República Bolivariana de Venezuela*, No. 5.908 (Extraordinario) del 19 de febrero de 2009. Ediciones de la Asamblea Nacional: Caracas, Venezuela. Disponible en: <http://www.minci.gob.ve/wp-content/uploads/2011/04/CONSTITUCION.pdf>.
 16. Asamblea Nacional de Venezuela. República Bolivariana de Venezuela. Ley de Responsabilidad Social en Radio Televisión y Medios Electrónicos. *Gaceta Oficial No 39.610 del 7 de febrero de 2011*. Disponible en: <http://www.conatel.gob.ve/files/lehrs06022014.pdf>
 17. Asamblea Nacional de Venezuela. República Bolivariana de Venezuela. Ley Orgánica de Telecomunicaciones. *Gaceta Oficial N° 39.610 del 7 de febrero de 2011*. Disponible en: <http://www.conatel.gob.ve/ley-organica-de-telecomunicaciones-2/>
 18. Asamblea Nacional de Venezuela. República Bolivariana de Venezuela. Ley de Defensa de las Personas en el Acceso a los Bienes y Servicios. *Gaceta Oficial N° 39.165 del 24 de abril de 2009*. Disponible en: http://portal.ucv.ve/fileadmin/user_upload/auditoria_interna/Archivos/Material_de_Descarga/Ley_para_la_Defensa_de_las_Personas_en_el_Acceso_a_los_Bienes_y_Servicios_-_39.165.pdf
 19. Congreso de la República de Venezuela. Ley de Propiedad Intelectual. *Gaceta Oficial N.º 25.227 del 10 de diciembre de 1956*. Disponible en: https://sapi.gob.ve/wp-content/uploads/2020/09/ley_propiedad_intelectual.pdf
 20. Asamblea Nacional de Venezuela. República Bolivariana de Venezuela. Ley Orgánica sobre el derecho de las mujeres a una vida libre de violencia. *Gaceta Oficial No 38.668 del 25 de noviembre de 2014*. Disponible en: <http://www.minmujer.gob.ve/?q=descargas%2Fleyes%2Fley-organica-sobre-el-derechos-de-las-mujeres-una-vida-libre-de-violencia>
 21. Asamblea Nacional de Venezuela. República Bolivariana de Venezuela. Ley orgánica para la protección de niños, niñas y adolescentes. *Gaceta Oficial No 5.859 (Extraordinaria) del 10 de diciembre de 2007*. Disponible en: https://www.oas.org/juridico/PDFs/mesicic4_ven_ley_org_prot_ninos_adolc.pdf
 22. Congreso de la República de Venezuela. Ley Orgánica de Salud. *Gaceta Oficial N.º 36.579 del 11 de noviembre de 1998*. Disponible en: http://www.fenasinpres.org/documentos/l_o_salud.pdf
 23. Asamblea Nacional de Venezuela. República Bolivariana de Venezuela. Ley del Ejercicio de la Medicina. *Gaceta Oficial N° 39.823 del 19 de diciembre de 2011*. Disponible en: <https://alc.com.ve/wp-content/uploads/2013/10/Ley-del-Ejercicio-de-la-Medicina.pdf>
 24. Federación Médica Venezolana. Código de Deontología Médica. LXXVI Reunión Extraordinaria de la Asamblea de la Federación Médica Venezolana, realizada en Caracas el 20 de Marzo de 1985. Disponible en: <https://docs.venezuela.justia.com/federales/codigos/codigo-de-deontologia-medica.pdf>
 25. González R, Bernal C, Palomero I. Uso de las redes sociales entre los jóvenes y ciudadanía digital: análisis tras la COVID-19. *REIDICS. Rev Investig Didáct Cienc Soc*. 2020;(7):64-81.
 26. Romeiro DA, Mascarenhas I de L, Godinho AM. Descumprimento da ética médica em publicidade: impactos na responsabilidade civil. *Rev Bioét*. 2022;30(1):27-35.
 27. Maluf CAD, Maluf ACRFD. A responsabilidade civil na relação dos profissionais da área da saúde e paciente. In: Azevedo ÁV, Ligiera WR, coordenadores. *Direitos do paciente*. São Paulo: Saraiva; 2012:511-551.
 28. Leal MCB, Barreto FSC, Flizikowski EB da S, Nascimento WR. O conhecimento dos estudantes sobre direito de imagem do paciente. *Rev Bioét*. 2018;26(4):597-605.
 29. Torregrosa L, Sotomayor J, Jssir MP, Barriga S. La realidad del uso actual de imágenes clínicas. En: Torregrosa L, Gempeler FE, editores. *Ética en el uso de imágenes clínicas*. Bogotá: Editorial Pontificia Universidad Javeriana; 2020.
 30. Beever J, McDaniel R, Stanlick NA. *Understanding Digital Ethics: Cases and Contexts*. Routledge. 2019.
 31. Degiorgi G, Colombero ML, Revol J. Publicidad y ejercicio profesional en contexto de pandemia: una lectura deontológica y legal. *An Investig Fac Psicol*. 2020;5(1):22-36.
 32. Lolas F, Rodríguez E. *Bioética y humanidades médicas: lecturas complementarias*. Ciudad Autónoma de Buenos Aires: Hygea Ediciones; 2020;138.
 33. Rojas G. Hablemos de honorarios médicos en la publicidad de las redes sociales. *Gac Méd Caracas*. 2023;131(3):722-732.
 34. Jiménez-Marín G, Bellido-Pérez E, Trujillo M. Publicidad en Instagram y riesgos para la salud pública: el influencer no sanitario como prescriptor de medicamentos, a propósito de un caso. *Rev Esp Comun Salud*. 2021;12(1):43-57.
 35. Rotondo MT. Relaciones profesionales: conflictos de intereses. *Rev Méd Urug*. 2006;22(2):88-99.

Amanecer de la Anatomía Patológica Venezolana y de su Primer Instituto Universitario

Dawn of Venezuelan Pathological Anatomy and its First University Institute

Claudia Antonieta Blandenier Bosson de Suárez Rengifo

RESUMEN

En esta narración histórica, se hace un recorrido acerca del desarrollo de la Anatomía Patológica en Venezuela, comenzado por el conocimiento de la Anatomía Humana y luego por el establecimiento de la histopatología en el primer laboratorio científico fundado por el Dr. José Gregorio Hernández. Se narra la institucionalización de la Patología en Venezuela por el Dr. O'Daly, la fundación del primer instituto Anatomopatológico universitario, donde se inició el primer posgrado de esta especialidad y la fundación de la Sociedad de Anatomía Patológica. Se hace un recordatorio de las etapas de la fundación del Instituto y de la evolución de las funciones docentes, asistenciales y de investigación durante varias direcciones del Instituto Anatomopatológico entre los años 1949 y 2006.

Palabras clave: Anatomía Patológica, patología, Instituto Anatomopatológico, O'Daly.

SUMMARY

In this historical narrative, a journey is made through the development of Pathological Anatomy in Venezuela, beginning with the knowledge of Anatomy and then with the establishment of histopathology in the first scientific laboratory founded by Dr. José Gregorio Hernández. It narrates the institutionalization of Pathology in Venezuela by Dr. O'Daly, the foundation of the first university Anatomopathological Institute where the first postgraduate course in this specialty was initiated, and the foundation of the Society of Pathological Anatomy. A reminder is made of the stages of the foundation of the Institute and the evolution of the teaching, care, and research functions during various directions of the Anatomopathological Institute between 1949 and 2006.

Keywords: Pathological anatomy, Pathology, Anatomopathological Institute, O'Daly.

INTRODUCCIÓN

En Venezuela, la Anatomía Patológica como especialidad médica, tardó en institucionalizarse y definirse ya que, las guerras de independencia y las civiles retrasaron su desarrollo como sucede en estados políticos y civiles caóticos. Sin embargo, esta especialidad médica comenzó muchos años antes a desarrollarse parcialmente, con los conocimientos adquiridos en las autopsias practicadas en forma esporádica. De tal manera que el desarrollo de la especialidad de la Anatomía Patológica propiamente

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dicha en nuestro país fue progresivo y parcial. Comenzó con los conocimientos macroscópicos de los órganos y tejidos mediante la instalación del estudio de la Anatomía Humana, con la disección anatómica y con las autopsias realizadas desde el siglo XVI. Luego estos conocimientos se afianzaron con el estudio formal de esta materia en las Cátedras de Anatomía en las Universidades de Caracas y en las del interior del país.

Posteriormente, la Anatomía Patológica propiamente dicha, fue introducida en Venezuela, bajo el nombre de “Histología Patológica” por el Dr. José Gregorio Hernández Cisneros, hoy beato de la Iglesia Católica y Apostólica. El Dr. Hernández en el mes de noviembre de 1891, instaló y/o fundó el primer laboratorio de Técnica Histológica y de Patología en Venezuela, en la Universidad de Caracas, donde se realizaron por primera vez los estudios histopatológicos. De esta manera, el estudio macroscópico adquirido mediante autopsias y disecciones quedó completo con el estudio histopatológico realizado en el laboratorio del Dr. Hernández. Consideramos que no se puede hablar de Anatomía Patológica, sin mencionar la Técnica Histológica, ciencia del tratamiento de los tejidos a examinar, cuyos instrumentos y equipos trajo el Dr. Hernández y quien, además, enseñó su funcionamiento. Por esta razón, históricamente, también, se considera al Dr. José Gregorio Hernández como el primer Técnico Histólogo y Anatomopatólogo venezolano. Su laboratorio fue la primera institución concebida y destinada para su funcionamiento en el Hospital Nacional de Caracas, posteriormente llamado Hospital José María Vargas. Lamentablemente, este laboratorio tuvo que ubicarse en la Universidad Central, donde el Dr. Hernández formó los primeros técnicos histólogos y a varios estudiantes de medicina entre ellos, al Br. Rafael Rangel Estrada. Años después, el laboratorio del Hospital Vargas fue reinaugurado, donde se formaron los primeros anatomopatólogos venezolanos. Sería el Dr. José Antonio O’Daly Seraille discípulo de Jesús Rísquez Iribarren, quien, en la década del 30, institucionalizó y le dio formalidad a la Anatomía Patológica venezolana. Acompañado del patólogo alemán Rudolf Jaffé, el Dr. O’Daly, instruyó a un grupo de jóvenes médicos en esta disciplina, quienes, en el devenir, serían los que constituyeron la plataforma de la Anatomía Patológica nacional. No podemos desestimar la labor de un pequeño grupo de patólogos europeos que llegaron a Venezuela en las décadas del 40 al 50, quienes fundaron varios

servicios de Anatomía Patológica en los Hospitales de las principales ciudades del interior del país.

En 1949, se inaugura en la Universidad Central, el Instituto Anatomopatológico “Dr. José Antonio O’Daly”, el primero de esta naturaleza en Venezuela, fundado por el mismo Dr. José Antonio O’Daly y sus colaboradores. Enseguida, en su sede, se iniciaron las actividades propias de esta institución: docencia de pregrado en la Cátedra de Anatomía Patológica (1949), investigaciones propias del organismo Instituto de Anatomía Patológica (IAP) (1954), labores asistenciales (citología, biopsias y autopsias) (1956) y docencia de posgrado (1959). La institución del primer posgrado de Anatomía Patológica en el país sirvió de base para la formación de la mayoría de los anatomopatólogos venezolanos hasta el año 2018. Los siguientes años de la fundación del IAP, fueron de establecimiento y de asentamiento de los organismos internos, los cuales se fueron poco a poco desarrollando. Para la década del 60, ya se contaba con los Departamentos: Técnico, Administrativo, Docente, de Especialización de Anatomía Patológica y el de Patología Experimental. El Departamento Técnico comprendía las secciones de biopsias, autopsias, laboratorio de rutina, fotografías, archivo, biblioteca y habían surgido las primeras secciones especializadas: Citología, Neuropatología, Cardiopatología, Oftalmopatología y Dermatopatología entre 1958 y 1959. Poco a poco, nacieron las otras subespecialidades de la Patología, consolidadas en secciones, de las cuales surgieron numerosos trabajos científicos, libros y pautas que rigieron otras instituciones semejantes en todo el ancho de Venezuela. Posteriormente fue muy importante la labor de continuación de las generaciones “intermedias” de patólogos en estas funciones inclusive en la dirección del instituto.

Desde 1949, hasta el cierre del Instituto Anatomopatológico en el año 2018, su organismo desempeñó un gran papel en la sociedad venezolana prestando servicios asistenciales, docentes y de investigación, sobre todo, constituyéndose en el Centro de Referencia en Patología del país. A partir del año 2015, lentamente el ocaso cayó sobre sus predios, hasta oscurecer completamente en el año 2022, situación que permanece hasta nuestros días (2023).

El objetivo de este trabajo histórico descriptivo es realzar el papel que los pioneros de la Patología nacional ejercieron en nuestro país y dejar una

memoria de estos hechos para las futuras generaciones de patólogos. Describir un breve recorrido de las etapas del desarrollo de la Anatomía Patológica y de las primeras etapas del Instituto Anatomopatológico de la Universidad Central de Venezuela (UCV).

METODOLOGÍA

La metodología siguió los pasos del método descriptivo que se aplica en el diagnóstico de las muestras anatómicas tanto en autopsias como de biopsias, es decir, la descripción macroscópica seguida de la histopatológica. La evolución e instalación de la Anatomía Patológica en Venezuela, siguió esta evolución: el conocimiento anatómico macroscópico precedió al conocimiento histológico y/o histopatológico. Para estos objetivos, se realizó una investigación bibliográfica en fuentes primarias y secundarias de documentos archivados, registros y algunas entrevistas sobre los aspectos históricos de la época. Se escogieron los más importantes acontecimientos relativos al desarrollo inicial de la Patología nacional, en el hospital Vargas y en el Instituto Anatomopatológico de la Universidad Central de Venezuela.

1. Inicio del estudio de la Anatomía Humana en Venezuela. Disección de cadáveres. Importancia de la observación macroscópica

La enseñanza formal de la Anatomía

El estudio de la Anatomía Humana mediante la disección de cadáveres y autopsias es el comienzo científico y parcial de la Anatomía Patológica, la cual comprende, no solo el estudio de la Anatomía de los órganos y sistemas, sino de su constitución histológica normal y patológica, así como de su correlación clínico-patológica.

Durante la colonización del país, los primeros pasos dados hacia el conocimiento de la Anatomía Patológica fueron las observaciones macroscópicas de órganos y tejidos disecados en las autopsias. Según varios historiadores la primera autopsia fue practicada en 1696, por un cirujano llamado Francisco Guerra Méndez, obligado por el gobernador, durante una epidemia de fiebre amarilla. En general, las autopsias se realizaban en forma esporádica como la hecha por el Dr. Luis Mario Montero en 1874, en un hombre

a quien se le encontró un tumor laríngeo. Sanabria en su libro Historia de la Medicina y la Semiotecnia en Venezuela y el Mundo, relata que el Dr. Gaspar Juliac, francés en Puerto Cabello, hizo la autopsia de un soldado que había fallecido de fiebre amarilla. El Dr. Plácido Daniel Rodríguez Rivero, en su trabajo: "Las autopsias en nuestra época colonial", menciona que desde 1661, cuando se realizó la primera autopsia hasta la última en 1779, por el Dr. Bartolomé Ballester, nunca se empleó el término de autopsia sino el de Anatomía, como era empleado en España (1). Sin embargo, estos hechos son anecdóticos, ya que el estudio formal de la Anatomía Humana se inició un siglo después.

El estudio universitario de la Anatomía Humana en nuestro país se inició con la fundación de la Prima de Medicina por el protomédico canario Lorenzo Campins y Ballester, donde él dictó el primer curso de medicina el 10 de octubre de 1763, en la Universidad Real y Pontificia de Caracas. El curso duraba tres años de lecturas teóricas dictadas por el Dr. José Joaquín Hernández y la Medicina práctica a cargo del Dr. Santiago Bonneaud. El curso se complementaba por estudios prácticos en hospitales civiles y militares de la ciudad. Dentro de las atribuciones del Dr. Campins y Ballester estaba todo lo relacionado con salud pública: médicos, cirujanos, boticarios, algebristas, destiladores etc., hasta 1789. Durante ocho años fue el primer administrador del Tribunal del Protomedicato, establecido en Venezuela en 1777. En la Prima de Medicina, estaba contemplada la enseñanza formal de la Anatomía Humana. Los estudiantes no contaban con modelos o dibujos anatómicos, no se hacían disecciones, no había bibliotecas ni libros de texto. Tampoco se dispuso de ninguna imprenta en Caracas para usos docentes. Al no existir libros en esa época, el estudio se basaba en los apuntes que tomaban los alumnos, situación que duró los 22 años de la enseñanza de Campins y Ballester, quien utilizó el idioma español en vez del latín. Los estudiantes debían copiar los apuntes dictados por Campins y los otros profesores, para luego memorizar y recitar lo aprendido. De esta forma se demostraba el aprendizaje de la materia. En 1789 se solicitó la fundación de la Cátedra de Anatomía, la cual se gestionó años después en 1802. Posteriormente, fue Federico Meyer quien, en 1811, inició unas clases de Anatomía Quirúrgica, las cuales fueron interrumpidas por el terremoto de 1812. Las clases se reiniciaron sin programación formal en 1823, encargándose del curso el Dr. Santiago Bonneaud (2).

Introducción de los libros de texto de Anatomía en Medicina. Fundación de la Facultad de Medicina reformada

El tercer protomédico de Venezuela, Felipe Tamariz (1759-1814), caraqueño, fue profesor en la cátedra Prima de Medicina de la Universidad de Caracas, por un período de 26 años. Este protomédico, introdujo reformas docentes: adoptó las obras de los españoles Bartolomé Serena y Antonio Medina para la docencia anatómico-quirúrgica y la obra del escocés William Cullen, *First fines of the practice of Physic*. Después del fallecimiento de Tamariz, en 1815, lo sucede el Dr. José Joaquín Hernández, quien quedó con el cargo como protomédico (último en ejercer dicho cargo colonial en Venezuela). Hernández, introdujo el importante y moderno texto de Anatomía General aplicada a la Fisiología y a la Medicina de Xavier Bichat, muy en boga en Francia. Es de hacer notar que la labor docente en la cátedra Prima de Medicina por parte de José Joaquín Hernández, se vio muy restringida por la larga y sangrienta guerra de Independencia venezolana. Dicha guerra interrumpió la educación en todos sus niveles durante varios periodos comprendidos entre 1811 y 1821.

Posteriormente, en el Congreso de Cundinamarca, el 18 de marzo de 1826, el Libertador Simón Bolívar consolidó la enseñanza de la Medicina, promulgando la Ley General sobre Educación Pública en la cual, en su Capítulo Séptimo, artículo 42, se dispuso que: “En las capitales de los Departamentos de Cundinamarca, Venezuela y Quito, se establecían las Universidades Centrales que abarcarían con más extensión, la enseñanza de las materias entre ellas : la Anatomía General y Anatomía Patológica, Terapéutica y Materia Médica, Clínica Médica, Cirugía y Clínica Quirúrgica, Farmacia experimental y Medicina Legal y Pública”. El protomédico José Joaquín Hernández, sería uno de los redactores de los estatutos republicanos de la Universidad sancionados por el Libertador Simón Bolívar al año siguiente, el 24 de junio de 1827. En esta sanción, se estableció un nuevo pensum de estudios con las materias mencionadas y al día siguiente, se fundó la Facultad de Medicina de Caracas. En esta instancia, se ejercían las funciones jurisdiccionales que tenía el antiguo Protomedicato (enseñanza académica, otorgación de títulos y ejercicio profesional). El encargado de la Cátedra de Medicina reformada fue el Dr. José María Vargas Ponce.

En otras regiones de Venezuela también se inició la docencia en Medicina. En 1810 se fundó

la Universidad de Mérida de los Caballeros, donde se emprendió la enseñanza de la Medicina en esta región. Sin embargo, fue solo después de 1860, a raíz de la labor de Eloy Paredes, rector de la Universidad de Mérida, que los estudios médicos en esta región se fueron estableciendo lentamente. Sin embargo, la expansión de la enseñanza de la medicina en el interior del país solo comenzó con la fundación de las Universidades del Zulia (1891) y la de Carabobo (1892).

Importancia del papel que jugó el Dr. José María Vargas Ponce, en la enseñanza de la Anatomía. Comienzo del estudio completo de autopsias

El desarrollo de los estudios anatómicos se debe en gran parte al Dr. José María Vargas Ponce, quien, desde 1826 hasta 1853, se dedicó a la labor docente, como catedrático de la asignatura Anatomía, primero en clases dictadas a *motu proprio* en su casa y luego en la Universidad (3). También, el Dr. Vargas, propulsó el ejercicio de la Medicina, al iniciar su laboriosa práctica médico-quirúrgica en los hospitales: Hospital Militar de Caracas, Hospital de la Caridad para Hombres y en el medio privado. Las clases de Anatomía General y Descriptiva, previstas en el Artículo 88 de la Ley, estuvieron en sus manos, acompañado por el Dr. Antonio José Rodríguez. El Dr. Vargas no sólo disecó cadáveres, sino que practicó autopsias, de las cuales se conservan documentos de 55 protocolos de estas, lo cual demuestra su aprecio y conocimiento de Anatomía Patológica adquiridos en Europa. El Dr. Vargas tenía un microscopio traído de Edimburgo, pero no tenemos noticias que hiciera sistemáticamente estudios histopatológicos. También sus discípulos practicaron autopsias siendo el más importante de ellos, el Dr. Eliseo Acosta, quien le hizo la autopsia a su maestro fallecido en Nueva York en 1854. La labor del Dr. Vargas fue más lejos, reformó e introdujo cambios en los estudios de Medicina, en las especialidades de Cirugía, Anatomía y Química, e impulsó el desarrollo otras disciplinas en la Universidad. Una vez concluido su período como rector de la Universidad en 1832, Vargas se dedicó a la docencia en la Facultad de Medicina, aceptó el nombramiento de bibliotecario con el objetivo de formar una buena colección de libros, periódicos y folletos de ciencias y artes, y de vincular a la Universidad de Caracas con sus análogos en Europa y en América con muchas sociedades científicas. José María Vargas escribió un libro intitulado “Curso de

Lecciones y demostraciones Anatómicas”, primer libro sobre el tema, escrito e impreso en Venezuela en 1838, el cual se utilizó como texto oficial durante unos 37 años en la cátedra de Anatomía. En 1840, Vargas, inauguró la cátedra de Cirugía y no solo fue su docente por muchos años, sino que publicó un “Manual de Cirugía” en 1841. También fue docente de la cátedra de Química (como parte de los estudios médicos de la época) destacándose cuando en 1842, publicó su libro sobre “Curso de Lecciones de Química”. Después del fallecimiento del Dr. Vargas en 1854, le sucedió en el cargo, el maracaibero Dr. José Briceño Carmona, quien utilizó el libro de Vargas y sus métodos de enseñanza e introdujo el texto de Fort y el de Anatomía Descriptiva de Jean Cruveilhier. El Dr. José de Briceño, fue el sustituto más destacado del Dr. Vargas, siendo profesor de esta asignatura durante 30 años (1853-1883).

A partir de 1875, se reorganizaron los colegios de la República y se crearon otros en cada capital de los estados de la república. En 1876, por Decreto del presidente constitucional, Antonio José Ramón de la Trinidad y María Guzmán Blanco, se funda una sala de autopsias en la Universidad Central de Venezuela (antes Convento de San Francisco), la cual ocupó un local meridional del edificio de la Facultad de Ciencias Médicas. En esta sala se dictaban las clases de Anatomía con las autopsias practicadas por los catedráticos de Anatomía y de Cirugía. En este decreto también, se emitieron artículos que reglamentaban el traslado de cadáveres.

En 1883, después del retiro del Dr. Briceño, se encargó de la cátedra, el cumanés, Dr. Alejandro Frías Sucre, maestro de Razetti, quien ejerció este cargo entre 1883 y 1893. La enseñanza de Frías fue teórica, adaptada al tratado de Anatomía Humana de Marie PSappey, ayudado gráficamente con maniqués e ilustraciones, porque las disecciones cadavéricas habían sido prohibidas por razones de salubridad. Ese mismo año, se emitió un reglamento del anfiteatro de Anatomía Patológica. Vemos con este hecho, que se consideraba el estudio de las autopsias como la especialidad en su totalidad. También funcionaban tres cátedras: Anatomía Descriptiva III, Técnica de Anatomía-Topográfica y Medicina Operatoria. En 1893, se encargó de esta cátedra el Dr. Pablo Acosta Ortiz quien utilizó el tratado de Anatomía Humana de Leo Testut, el cual era utilizado en Francia, país, donde el obtuvo el título de Doctor en Medicina. En 1896, el Dr. Luis Razetti Martínez introdujo en el

pensum de Anatomía, los conceptos de la teoría de la evolución de Darwin.

El 19 de abril de 1910, el General Gómez, decretó la creación del Instituto Anatómico inaugurado el 25 de julio de 1911, ubicado sobre el antiguo Cementerio de Las Mercedes, situado al norte de la esquina de San Lorenzo, adyacente al Hospital Vargas (4). En aquella época, la cátedra de Anatomía y Medicina Operatoria era ejercida por el Dr. Luis Razetti, quien consideró la disección como el principal elemento para objetivizar la enseñanza de la Anatomía e inclusive dictó una materia denominada “Disección”, la cual, según Plaza Izquierdo, sólo existió en esa época. Lamentablemente, el año siguiente, la universidad fue cerrada durante varios años y hubo una ausencia de conocimientos de Anatomía (5,6). Para ese entonces, ya podemos decir que la Anatomía Patológica se había iniciado con el estudio microscópico introducido por el Dr. José Gregorio Hernández, quien tenía en ese instituto, su laboratorio trasladado desde la Universidad Central, donde enseñaba esa materia (7-9).

2. Pasos previos a la fundación del Instituto Anatomopatológico

Algunos aspectos históricos previos al inicio de la fundación del primer laboratorio de Patología en 1891. Ambiente cultural, educativo y científico de la época

Según los historiadores ya para mediados del siglo XIX, había una tendencia a la cultura y a la educación superior. Entre 1839 y 1884, se crearon los Colegios nacionales en las capitales y ciudades más importantes del país, tales como: Cumaná, Maracaibo, Barcelona, así como en pueblos del interior como Calabozo del estado Guárico, Guayana, El Tocuyo en el estado Lara y en Margarita en el estado Nueva Esparta. En estas ciudades se impartía los estudios del Trienio Filosófico, establecido por la Universidad Central. Para esa época, los Colegios de la República se dividieron en tres categorías: los Colegios Federales donde solo se enseñaban estudios secundarios, los Colegios Seccionales y los de Primera Categoría, donde no solo se impartía la enseñanza secundaria sino también la superior. Entre los Colegios de primera categoría con escuelas de Medicina, estaban el de Falcón-Zulia creado en 1881, el de Calabozo, Estado

Guárico en 1883 y Barquisimeto, Edo. Lara, en 1884. En estos Colegios, los programas de las escuelas de Medicina contemplaban el estudio de Anatomía General e Higiene y Anatomía Descriptiva, entre otras materias dictadas en seis años. En el Colegio de Cumaná se destacó un investigador de origen francés, Luis Daniel Beauperthuy, quien descubrió el vector, el mosquito transmisor de la fiebre amarilla, trabajo que publicó en la revista de la Academia de Ciencias de París en 1866 (10). En Maracaibo, existía el mismo ambiente progresista, en 1884 fue instalado el Anfiteatro Anatómico, el cual contaba con el primer microscopio binocular traído a Venezuela y con el que se realizaron investigaciones en Fisiología y Anatomía mediante la disección de cadáveres, e inclusive estudios de laboratorio. Se destacó en estas funciones el profesor Manuel Dagnino, emigrante italiano oriundo de Génova, quien le dio impulso a las reformas de la medicina zuliana, practicó autopsias e inclusive el estudio histológico de los hallazgos (11). Algunos historiadores consideraron que la influencia de Guzmán Blanco fue importante para el ambiente cultural, educativo y científico de esa época, cuando se fundan y construyen: el Teatro Municipal de Caracas (1881), la Academia Nacional de La Lengua (1883), la Academia de Bellas Artes (1887), entre otras obras como el Panteón Nacional y el Palacio Federal Legislativo.

A partir del año 1888, fue el primer, presidente civil de la República, Juan Pablo Rojas Paúl (1888-1890), quien, el mismo año de la posesión de la presidencia, decretó la construcción del acueducto de Barquisimeto y la construcción de un hospital nuevo moderno, el Hospital Nacional de Caracas (16-8-1888), futuro hospital José María Vargas. Concedió una beca al recién graduado de médico, el Dr. José Gregorio Hernández Cisneros, para realizar estudios de posgrado en Francia con el fin de fundar y dirigir el laboratorio de este nuevo hospital. Rojas Paúl, sin duda fue uno de los presidentes más progresistas del período posguzmancista. También decretó obras importantes tales como: la fundación del Observatorio Cajigal y la fundación de la Academia Nacional de la Historia. Contrario a la política anticlerical de Antonio Guzmán Blanco, autorizó la fundación de las Facultades de Ciencias Eclesiásticas con los Colegios nacionales de Maracaibo y Barquisimeto, trajo a Venezuela a las monjas de San José de Tarbes y las Hermanitas de los Pobres para la labor hospitalaria. En 1990, Rojas Paúl, decretó el establecimiento del Laboratorio Nacional de Química, fundado por el químico Vicente Marcano. En este laboratorio

se realizaban diversas investigaciones sobre los productos naturales de Venezuela, las cuales fueron publicadas en la Academia de Ciencias de París. Es importante recordar que el presidente Juan Pablo Rojas Paúl pudo realizar todas estas obras, ya que existía en esa época en Venezuela una bonanza económica debido particularmente al auge de los precios del café en los mercados internacionales (12,13).

3. Nacimiento de la Anatomía Patológica en Venezuela. Fundación del primer laboratorio de Patología. Dr. (beato) José Gregorio Hernández Cisneros. Los primeros pasos de la Técnica Histológica en el país.

El presidente Juan Pablo Rojas Paúl, en 1888, decretó la construcción de un hospital moderno que no existía en Caracas. Para ello, varios de sus consejeros viajaron a París y escogieron el modelo del Hospital Lariboisiere para la construcción del hospital Nacional de Caracas que se llamaría posteriormente, “José María Vargas”, en honor a este eminente reformador de los estudios médicos en Venezuela. En el plan de la construcción de este nuevo hospital estaba contemplado el levantamiento de un laboratorio moderno en toda su extensión y modernidad. Para este fin, era necesario formar el personal adecuado para estas funciones. El Dr. José Gregorio Hernández fue escogido entre los médicos recién graduados, para realizar estudios de posgrado en las especialidades médicas de Histología Normal, Histología Patológica (Anatomía Patológica), Bacteriología y Fisiología Experimental, en la Universidad de París. En los años siguientes, el Hospital Vargas, se transformaría en el centro de la reforma de los estudios en Medicina, liderada por médicos venezolanos que habían completado su formación en Europa especialmente en Francia, meca de la Medicina internacional, tales como Luis Razetti Martínez, Pablo Acosta Ortiz, José Gregorio Hernández Cisneros y Santos Aníbal Domínic Otero.

El 5 de julio de 1891, el presidente Raimundo Andueza Palacio, sucesor legítimo del presidente Rojas Paúl, inauguró el flamante hospital “José María Vargas de Caracas”. Aún no estaban completamente equipadas varias estancias del hospital ni tampoco el laboratorio. De tal manera que el presidente ordenó la construcción de una modesta edificación para instalar el laboratorio del Dr. Hernández, ubicada en el terreno de la Universidad de Caracas, que había sido el corral de los animales del convento de los

franciscanos. Según los planos examinados de 1911, el área del laboratorio era de forma rectangular y limitaba al oeste con el jardín de la Universidad, resto del antiguo corral, el cual se observaba por las ventanas aparentemente en número de tres. Al este las paredes del laboratorio colindaban con los salones de clases de la Universidad. Al norte, el laboratorio limitaba con otro grupo de salones de clases y dependencias universitarias no identificadas o no construidas para la época (futura biblioteca Nacional) y al sur con espacios no construidos ni identificados en el plano. La puerta de acceso al laboratorio estaba ubicada en el corredor suroeste de la sede de la Universidad que colindaba con el Patio Cajigal de la Universidad, actual Palacio de las Academias. Esta puerta separada de la escalera por un arco de mampostería es lateral a la escalera que comunicaba con el segundo piso. Para entrar al laboratorio había que recorrer un corto trayecto por un pasillo angosto (Hoy clausurado) (14). De acuerdo con la organización de las funciones docentes descritas por los biógrafos del Dr. Hernández, el laboratorio constaba de dos ambientes. Se entraba en el primer ambiente por la puerta principal y se comunicaba con el segundo ambiente por una puerta interna. En el primer ambiente, se impartían las clases de Técnica Histológica, de exámenes de laboratorio funcional y Bacteriología. El segundo ambiente, estaba dedicado

a la Fisiología Experimental, el cual comunicaba con un pequeño bioterio construido en el jardín. Lamentablemente, este espacio no disponía de un vivisectorium ni de un espacio para el laboratorio de Electrofisiología. Presumimos que todas las actividades de diferente naturaleza se hacían en el mismo ambiente. Igualmente, no había una Biblioteca propiamente dicha, sino un estante con los 30 libros que trajo el Dr. Hernández. Un hecho de extrañar es que, en ningún trabajo de los últimos años, realizado por varios autores, encontramos una sola fotografía del interior de este laboratorio, tan importante, por ser el primero de esta naturaleza instalado en Venezuela (Figura 1).

En noviembre de 1891, el Dr. Hernández regresa a Venezuela, después de haber realizado dichos estudios con honores en Francia e instala el laboratorio en el sitio asignado para tal fin. Traía consigo el cargamento de muebles, equipos y aparatos para introducir por primera vez en nuestro país la Técnica histológica, la Histología normal y Patológica, la Bacteriología y la Fisiología Experimental. Desde ese momento, el Dr. José Gregorio Hernández Cisneros, comienza en su cátedra a formar a los de estudiantes de medicina con la Técnica Histológica, mediante el uso del microtomo, la tinción de las secciones histológicas, así como la observación y diagnóstico al microscopio fotónico.

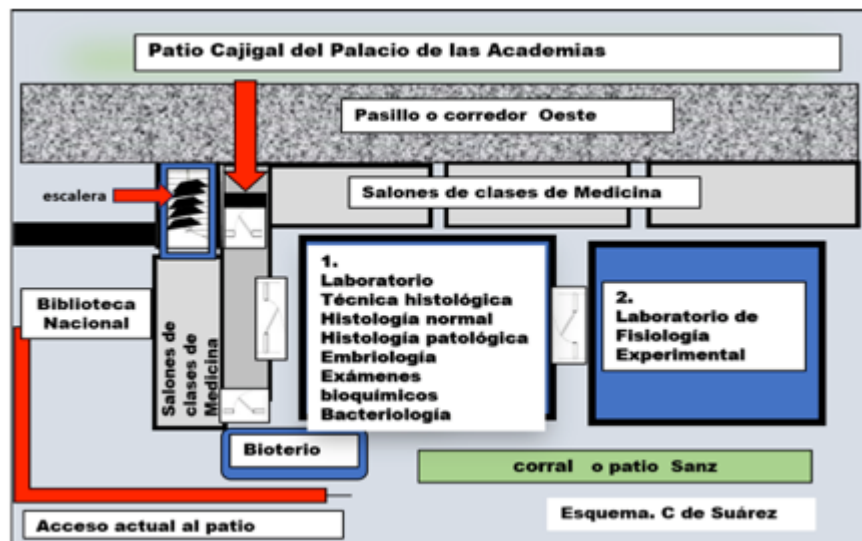


Figura 1. Plano que ilustra la situación y constitución física del primer laboratorio de técnica histológica, de Histología patológica, Bacteriológica y Fisiología Experimental fundado por el Dr. José Gregorio Hernández en 1891 en la Universidad Central de Venezuela (Convento de San Francisco, actual Palacio de las Academias).

Organización del laboratorio del Dr. Hernández. Dotación de muebles, equipos, reactivos, insumos de laboratorio entre otros

En ese precario local, el Dr. Hernández tuvo que organizar el gran arsenal del moderno laboratorio que traía personalmente desde París. El Dr. Hernández tuvo la precaución de traer a Caracas todo lo indispensable para el funcionamiento de su laboratorio. Sumamente previsivo y conociendo el medio a dónde iba llegar, sabía que era importante traer hasta los muebles indispensables para instalar de inmediato su laboratorio, como lo hizo. Es importante destacar que ese laboratorio poseía los cinco primeros microtomos llegados a Venezuela: tres de tipo Ranvier, un microtomo de marca Reichert, otro de marca Cambridge y un microtomo de Thomas-Jung. José Gregorio Hernández también trajo cuatro microscopios de marca Zeiss, verticales, monoculares, con un diafragma y un condensador que permitía iluminar, controlar el brillo de la preparación y evitar la dispersión de la luz. La iluminación se hacía por reflexión, poseían un espejo que recogía la luz natural o artificial. Los microscopios no poseían revólver y por lo tanto estaban provistos de un solo objetivo. Dos de estos microscopios estaban cubiertos por campanas de vidrio. Lo más importante era, que todos los objetivos eran apocromáticos. Estos modernos lentes era una novedad, ya que los microscopios de los profesores de la Facultad como Guillermo Morales, Calixto González y en los otros microscopios existentes en país, tenían lentes cromáticos. De tal manera que históricamente, el modelo de microscopio que trajo el Dr. Hernández no podía ser antes del período 1878-1886, porque en ese período de tiempo fue cuando Abbe introdujo los cambios más importantes en la fabricación de los microscopios. En la lista del inventario de instrumentos y libros que constaba en el laboratorio adquirido por el Dr. Hernández, se comprueba que los cuatro microscopios tenían cada uno aumentos diferentes: de 420X, 865X, 1250X y 1500X. No hay datos sobre la resolución de los mismos ni sobre los aumentos de los objetivos y oculares (15,16) (Figura 2).

En ese pequeño Laboratorio, el Dr. Hernández enseñó personalmente a todos los estudiantes de medicina las materias mencionadas contenidas en 79 temas y 2311 prácticas. Además, adiestró personalmente a sus discípulos en el manejo de todos los aparatos referentes a la Técnica Histológica y aplicar más de 13 métodos de tinciones o coloraciones

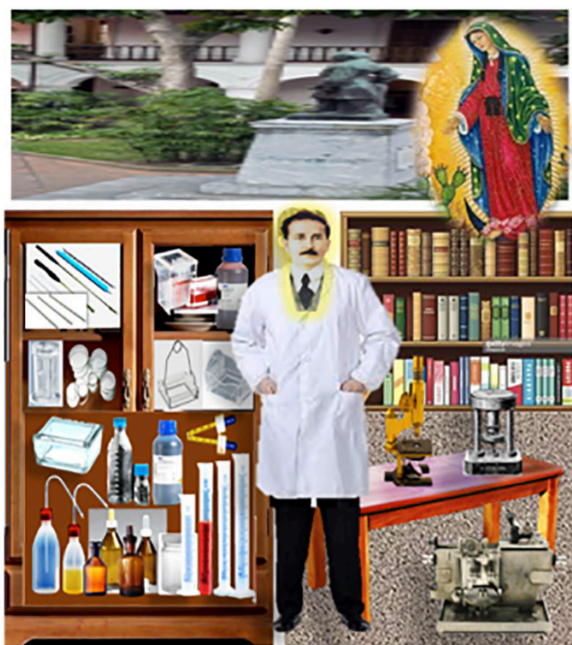


Figura 2. Dr. José Gregorio Hernández Cisneros. Su laboratorio (ficción). Patio Cajigal. Composición Dra. Suárez (7,15,16).

histológicas. Algunos estudiantes destacaron por su capacidad y diligencia, quienes fueron nombrados preparadores de la Cátedra: Felipe Guevara Rojas, Rafael Rangel Estrada, Rafael Pino Pou, Jesús Rísquez Iribaren, Temístocles e Inocente Carvalho Hernández (sobrinos del beato), entre otros, quienes posteriormente destacaron como científicos como Alberto Fernández, Leopoldo Aguerrevere, Martín Vegas, Andrés Herrera Vegas, entre otros discípulos. De esta manera surgieron los primeros técnicos histólogos y los tres primeros anatomopatólogos quienes ejercieron sucesivamente la Anatomía Patológica en el laboratorio del Hospital Vargas: Rafael Rangel Estrada, Inocente Carvalho y Jesús Rísquez Iribaren (17-19). Cuando se inauguró el Instituto Anatómico en 1911, el Dr. José Gregorio Hernández dejó el laboratorio de la Universidad, después de casi 20 años de permanencia, para impartir sus clases en un local ubicado al norte de la edificación donde, además, dirigía las prácticas de Histopatología, Química Médica, Bacteriología y Parasitología. También, disponía de un bioterio para las prácticas de Fisiología Experimental.

La Cátedra de Anatomía Patológica en la Universidad Central de Venezuela. Su evolución

El Dr. Santos Aníbal Dominici Otero, a su regreso de Francia, después de haber realizado estudios especializados como lo hizo su amigo, José Gregorio Hernández, fue el primero en ser nombrado profesor titular de la primera Cátedra de Anatomía Patológica en la Facultad de Medicina, de la Universidad Central de Venezuela, con el inconveniente de que esta cátedra funcionó unida a la Cátedra de Clínica Médica, según el decreto del año 1895. Para ese momento se consideraba suficiente que los profesores de Clínica practicasen sus autopsias ellos mismos y participaran sus resultados a los estudiantes. La inauguración de la Cátedra de Clínica Médica y de Anatomía Patológica se efectuó el 6 de marzo de 1895. Para la misma época Dominici conjuntamente con Enrique Meier Flegel, Pablo Acosta Ortiz, Elías Rodríguez hijo y Nicomer Guardia funda el Instituto Pasteur de Caracas (1894-1895). En ese laboratorio se realizaban exámenes bacteriológicos, histológicos y químicos que servían de ayuda para un diagnóstico más preciso de diversas enfermedades que afectaban a los pobladores de Caracas. Nos llama la atención que Dominici, siendo amigo de Hernández, no lo incluyera en el personal de la Cátedra ni en el Instituto Pasteur (20,21). Los mismos profesores que habían realizado estudios en Francia y EE.UU, consideraron llevar la Anatomía Patológica a la altura de una Ciencia moderna. Para este fin, fue enviado a estudiar esta materia a un alumno del Dr. Hernández, el Dr. Felipe Guevara Rojas, quien tenía bases de Histopatología normal y patológica entre otros materiales afines para realizar estudios en Alemania. El 14 de septiembre de 1909, la Cátedra de Anatomía Patológica fue separada de la Catedra de Clínica Médica de tal manera que se hizo “independiente”, 18 años después de haberse instalado el laboratorio de Histología Normal y Patológica por el Dr. José Gregorio Hernández. Esta cátedra funcionaba anexa al laboratorio del Hospital Vargas y la regentó durante dos años el Dr. José Gregorio Hernández hasta su fallecimiento, en junio de 1919.

El 16 de setiembre de 1911, se refunda la Cátedra de Anatomía Patológica, encargándose de la misma el Dr. Felipe Guevara Rojas, quien había regresado a Venezuela después de 10 años de estudios en Europa con el diploma de Anatomopatólogo. Guevara también se encargó de la dirección del recién inaugurado Instituto Anatómico. Lamentablemente, el Dr. Guevara, el único anatomopatólogo graduado en esta especialidad, falleció prematuramente de

fiebre tifoidea después de haber ocupado el Rectorado y el Ministerio de Educación. Después de su fallecimiento, nuevamente, la materia queda en manos de profesionales con grandes méritos científicos, pero sin conocimientos básicos de Anatomía Patológica. De tal manera que la muerte prematura de Guevara Rojas conllevó al Dr. Jesús Rafael Rísquez, discípulo de José Gregorio Hernández, a encargarse de la Cátedra de Anatomía Patológica secundado por Aníbal Santos Domínici, Jesús Romero Sierra, entre otros.

4. El laboratorio del hospital Vargas, cuna de la Anatomía Patológica formal e/o institucionalizada en Venezuela

En 1892, fue inaugurado el Laboratorio del Hospital Vargas dentro del contexto del Hospital, sin embargo, no estaba acondicionado para iniciar sus funciones. Después de 10 años, se reinaugura el laboratorio propiamente dicho y funcionante, el 18 de febrero de 1902, por iniciativa de la Junta de los Hospitales constituida por los Drs. Miguel Ruiz, Emilio Conde Flores, Juan Pablo Tamayo y Martín Herrera. Se encargó de su dirección, el Br. Rafael Rangel Estrada, expreparador del Dr. Hernández. Se estaba cumpliendo con el propósito original de establecer un laboratorio moderno como el de los hospitales de Francia, sin embargo, todo el material que había traído de Francia el Dr. Hernández, para este fin, quedó en el laboratorio de la Universidad y luego en el laboratorio del Instituto Anatómico. El laboratorio del hospital estaba localizado en la parte noreste del edificio, cerca de la sala de enfermos y al principio, el laboratorio carecía de aparatos, pero poco a poco con ayuda del material que poseía el Dr. Juan Pablo Tamayo en el laboratorio de su casa y otros insumos conseguidos con varias instituciones, el trabajo se puso en marcha. Durante 7 años, Rangel realizó una importante labor no solo asistencial sino también científica. En esta sede puso en práctica los conocimientos adquiridos de su maestro, el Dr. Hernández, durante más de cuatro años de preparaduría. Realizó autopsias y biopsias, montó un museo de Anatomía Patológica, dirigió más de treinta tesis de estudiantes de medicina y describió, por primera vez, el Necátor americano (22).

Los sucesores del Br. Rafael Rangel en el laboratorio del Hospital Vargas

Si recordamos la secuencia de los médicos quienes ejercieron no solo la Anatomía Patológica, sino que

también fueron técnicos histólogos, vemos que todos ellos, fueron directa o indirectamente instruidos por el Dr. Hernández. Hubo una transmisión directa de estos conocimientos de uno a uno a varios directores del Laboratorio. Al fallecer, el Br. Rangel en 1909, le sucedió su maestro, el beato Dr. José Gregorio Hernández. La divina providencia quiso que, por fin, el Dr. Hernández ocupara su sitio en el laboratorio del Hospital Vargas, originalmente planificado para que él lo instalara y dirigiera. En ese laboratorio, el Dr. Hernández, no solo se dedicó a realizar un número creciente de exámenes de todo tipo, incluyendo exámenes histopatológicos, sino también contribuyó a la formación de un cuerpo de “preparadores de laboratorio” (¿Asistentes o técnicos histólogos?), lo que consideramos de suma importancia. Cuidó y aumentó el museo de piezas anatómicas que dejara el Br. Rangel. Al fallecer trágicamente, diez años después, en 1919, el laboratorio quedó en manos de su sobrino y exdiscípulo, Inocente Carvallo Hernández, quien, a su vez, instruyó al Dr. Jesús Rafael Rísquez, uno de los más destacados alumnos del Dr. Hernández. Rísquez ocupó la jefatura del laboratorio al retirarse Carvallo. Además, Rísquez dirigió la Cátedra de Anatomía Patológica de la Escuela de Medicina donde dictó la Lección inaugural en 1922 (23).

En realidad, Rísquez Iribaren y Romero Sierra, ambos microbiólogos, surgen después de un nuevo decaimiento de la ciencia médica venezolana con el cierre de la Universidad. Como siempre la política rompe los hilos del seguimiento científico y ambos destacan como los pioneros del nuevo resurgimiento. El Dr. Rísquez siguiendo la tradición, se rodeó de estudiantes de medicina para inculcarles el amor por la Patología e inclusive publicó un folleto para instruir a los alumnos sobre algunos aspectos de la Anatomía Patológica y publicó trabajos de patología basados en su experiencia como patólogo quirúrgico (24-27). Atraído por la personalidad estudiosa y docente del Dr. Rísquez, el joven estudiante de medicina, José Antonio O’Daly Serraille, se formó con él en esta materia. Al jubilarse el Dr. Rísquez en 1934, el ya graduado de médico, Dr. O’Daly ocupó la jefatura del laboratorio. El Dr. O’Daly siguió los pasos de su maestro, se rodeó de estudiantes de medicina interesados en la Anatomía Patológica de tal manera que formó un grupo alrededor de su personalidad científica y con carisma docente. Fue el grupo que lo siguió cuando en 1949, el Dr. O’Daly se trasladó al Instituto Anatomopatológico que él fundó en la Ciudad Universitaria de Caracas. En ese entonces, dejó el

Laboratorio y la Cátedra de Anatomía Patológica en manos de su dilecto discípulo, el Dr. Blas Bruni Celli.

5. Institucionalización de la Anatomía Patológica venezolana. Su pionero: el Dr. José Antonio O’Daly Serraille

Desde un principio el Dr. O’Daly luchó por desarrollar esta especialidad en el Hospital Vargas como él mismo lo expresaba, mediante prácticas y procedimientos y convertirla en una especialidad médica permanente en la palestra médica venezolana. El Dr. O’Daly se dedicó a reestructurar las actividades del laboratorio dotándolo de una Sección de Microscopía, de un museo nuevo y de una Sección de Autopsia. Refiere el Dr. O’Daly en unas notas autobiográficas donde textualmente relataba: “en enero de 1931 fundé en el laboratorio del Hospital Vargas de Caracas, la Sección de Histología microscópica, siendo aún estudiante bajo la dirección de mi maestro, el Dr. Jesús Rafael Rísquez”. En dicha Sección, que fue el germen del actual servicio de Anatomía Patológica, se hicieron estudios microscópicos de biopsias y de piezas operatorias con muy escasos recursos y sin remuneración alguna, debido a la precaria situación económica del hospital en ese tiempo” (28). En 1932, la Sección de Histología microscópica se transformó en el llamado Departamento Anatomopatológico, donde se comenzó a recolectar piezas para un museo. El Dr. O’Daly quedó en la dirección el servicio de Laboratorio y en la del Departamento Anatomopatológico. Según el Dr. O’Daly, el servicio de Anatomía Patológica del Hospital Vargas había sido un organismo que representaba la evolución de la Anatomía Patológica en esa época de transformación del Hospital Vargas, la cual comenzó en 1930 y culminó con la creación de la Junta Directiva del Hospital Vargas en 1936-1937. Hay que mencionar dentro de la labor asistencial realizada en este período, el hecho de haberse podido realizar la autopsia en el 17,0 % de los cadáveres del Hospital. Este logro se debió en gran parte a la incorporación de un patólogo alemán, quien traía en su haber una gran experiencia, el Dr. Rudolf Jaffé. Contratado como técnico, desde Alemania, el Dr. O’Daly enseguida lo introdujo en la dinámica del laboratorio como patólogo, donde su aporte fue importantísimo para el desarrollo de este. En 1937, Dr. O’Daly fue nombrado jefe titular del servicio de Anatomía Patológica después de haber presentado un brillante concurso. Durante su mandato se realizaron

mejoras del local del laboratorio, decía el Dr. O'Daly": propendiendo a un mejor trato y más humana consideración de los cadáveres de compatriotas en el hospital, de mayores seguridades sanitarias para el personal y de mayor comodidad de trabajo, a veces luchando contra opiniones y posiciones adversas, pero con la convicción de que era bien para el Hospital". Según el propio O'Daly en el Servicio de Patología, a pesar de las dificultades del medio en aquella época, se habían realizado más de 6 000 autopsias y cerca de 20.000 biopsias, material que representaba un trabajo fortalecido con las publicaciones de índole científica.

Importancia de las primeras publicaciones sobre Anatomía Patológica en Venezuela

Fue el Dr. O'Daly quien insistía que había que reforzar el trabajo asistencial con publicaciones de índole científica, que él valoraba como de importancia capital para el país. Se lamentaba que no era la posición de los anatomopatólogos formados por él, con honrosas excepciones. No aceptaba que el trabajo del patólogo se valorara solo como un medio de ganancias monetarias o como la obtención de un escalafón en los estamentos sociales. Se lamentaba que no se tenía un sentido trascendente que le dejaría a las futuras generaciones, los puntos de referencia para apoyar sus investigaciones y a su vez, dejar un legado científico a nuestro país.

Formación del grupo de jóvenes patólogos y de histotecnólogos en el laboratorio del Hospital Vargas, quienes constituyeron la base de la patología nacional hasta nuestros días

Para el año 1936, el Dr. O'Daly y su adjunto el Dr. Rudolf Jaffé, comprobaron que el trabajo había aumentado mucho. El laboratorio funcionaba muy bien, de tal manera que una de las primeras tareas que se impuso el Dr. O'Daly fue formar un grupo de jóvenes estudiantes y médicos, quienes se sintieran atraídos por las labores que se realizaban en el Laboratorio. Al servicio, comenzaron a llegar y a formarse en Técnica Histológica y Anatomía Patológica los jóvenes doctores Leandro Potenza Michelena, Alberto Angulo Ortega tachirense, Armando Domínguez Capdevielle yaracuyano, Darío Lozano, Rubén Calderón tachirense, Luis Manuel Carbonell Parra, Salvador Mijares, Blas Bruni Celli larense, Jack Castro, Miguel Lairisse

y la primera anatomopatóloga venezolana, María Rivas Roz. Varios de ellos, después de su iniciación, completaron su formación en el extranjero en varias subespecialidades tales como Neuropatología, Neumopatología, Patología Ginecológica, Patología Forense, entre otras especialidades patológicas.

Formación de los primeros técnicos histólogos como profesionales

La primera técnica históloga que laboró en ese laboratorio fue Ilse, la propia hija del Dr. Jaffé, quien fue sustituida por la sobrina del doctor, Heimilinde Klanke a partir de 1955. Siendo insuficiente una sola técnica para todo el trabajo que había, el Dr. O'Daly comenzó a desarrollar otra labor importantísima en ese ámbito, formar un grupo de técnicos histólogos durante la década del 40 al 50. El Dr. O'Daly, desplegando una gran paciencia y dedicación, enseñó los procesos de la Técnica Histológica a jóvenes empleadas, asistentes de laboratorio que desconocían por completo esta disciplina. De esta manera, se mencionan las primeras histotecnólogas formadas por el Dr. O'Daly: Lourdes Urpin, Antonieta Rodríguez, Ildelfonsa Colina, Corina Rodríguez Brito, Lula Drayer y más tarde, a América Fernández (1943 a 1948) y a Gloria Mosqueda de Stoyanovich (1950-1952). También se recuerda a la Srta. García Maldonado quien laboraba en el Departamento de Investigaciones Clínicas" Alberto Fernández" del mismo hospital Vargas, fundado por el Dr. Fernández, expreparador del Dr. José Gregorio Hernández. El Dr. O'Daly haciendo varias disertaciones sobre los métodos de impregnación al nitrato de plata reducido para el estudio del tejido nervioso decía: "a mí me tocó divulgar en este país algunas de esas técnicas como también los métodos de Río Hortega al carbonato de plata entre los años 1933 y 1950, con poca suerte, por cierto, porque siempre encontré la renuencia de los médicos a aplicarlas personalmente. En efecto, son los mismos investigadores los que tienen que ajustar los reactivos y tiempos de actuación al fin perseguido" (29,30).

6. Contribución de los patólogos extranjeros al establecimiento primario de la Anatomía Patológica en Venezuela. Resumen de sus aportes

Desde el siglo XVII ya había ingresado al país un médico austriaco y en el siglo XVIII tres médicos de

origen alemán. Fue en el siglo XIX cuando ingresaron 14 médicos alemanes, pero entre ellos no se menciona ningún patólogo. Muchos de ellos fueron boticarios. En el siglo XX, después de cada una de las dos guerras mundiales llegaron médicos y técnicos. La mayoría de ellos ejercieron en la provincia como médicos generales o especializados. Pero como se mencionó anteriormente, el primer anatomopatólogo extranjero que llegó a nuestro país en 1936 fue el alemán hebreo, Dr. Rudolf Jaffé, quien se integró en el Laboratorio del Hospital Vargas. Posteriormente entre los años 1940 y 1967, llegaron nueve anatomopatólogos extranjeros, quienes fueron ubicados por las autoridades del Ministerio de Sanidad en diferentes ciudades del país. La labor prestada por estos patólogos en las décadas del 40 y 50 fue muy importante ya que ellos fundaron los primeros servicios de Anatomía Patológica en las ciudades más grandes del país, mientras que, en Caracas, se consolidaba la formación de un gran grupo de patólogos venezolanos quienes serían los herederos de todos estos servicios en el futuro.

El primer anatomopatólogo de formación germano-suiza que llegó a Caracas después del Dr. Jaffé fue el Dr. Gerardo Will, anatomopatólogo alemán que se viene a Venezuela en plena Segunda Guerra Mundial (1940), por sugerencia del Dr. O'Daly. Gerardo Will, jefe de Servicio de Anatomía Patológica del Hospital Vargas de Caracas, también alemán con una excelente hoja de trabajo en el país. El Dr. Will se había formado durante cinco años en el Instituto de Anatomía Patológica de Ginebra, Suiza, bajo la guía del Profesor M. Askanazi. El Dr. Will, comenzó a trabajar en el laboratorio del Hospital Vargas, pero no se entendió con el Dr. Jaffé y en julio de 1943 fue contratado para reorganizar del servicio del Hospital de la Maternidad Concepción Palacios, donde se destacó por su labor no solo asistencial, sino también científica. Era un extraordinario fotógrafo, todo lo cual contribuyó a que organizara la preparación de un archivo de macro y microfotografías de piezas diagnosticadas por él. Publicó el primer libro de patología gineco-obstétrica y dejó un interesante museo de piezas anatómicas patológicas. Además, publicó su experiencia en patologías, por primera vez, en el país tales como: fetos acardio amorfos, ausencia de una arteria umbilical, rotura de aneurismas aórticos, mioma uterino en un útero doble, entre otras anormalidades. Una vez retirado de este hospital, se trasladó a Mérida donde fundó el segundo servicio de Anatomía Patológica en el antiguo Hospital "Los Andes". Actuó como profesor de Anatomía

Patológica de la Universidad de los Andes (1951). Regresó a Caracas donde actuó en la Medicatura Forense y nuevamente en el hospital Vargas (31). El segundo patólogo extranjero, fue el Dr. Bela von Gavnall, húngaro, quien se integró en el laboratorio de investigación del Instituto Anatomopatológico en 1954. Allí, conjuntamente con el Dr. Jaffé, se dedicó a la investigación de la miocarditis Chagásica experimental. Al mismo tiempo se desempeñó en el servicio de Anatomía Patológica de la Maternidad Concepción Palacios con el Dr. Will. El Dr. De Gavnall fue el primer anatomopatólogo que autopsió un caso de Miocarditis Chagásica aguda congénita. Algunos bloques de parafina que contienen fragmentos de placenta infectada con *Tripnozoma cruzi*, reposan en el museo de la Academia Nacional de Medicina. (Donación de la Dra. Claudia de Suárez). Posteriormente, en la década del 70, el Dr. Gavnall emigró a EE.UU.

En las ciudades del interior del país se mencionan a el Dr. Franz Wenger Roth austríaco, fue el primer patólogo que llegó al interior del país (1946). El Dr. Wenger tenía en su haber una gran experiencia en el campo de la Patología en Europa, pero su condición de hebreo como el Dr. Jaffé, lo obligó a salir de Europa y aceptar un trabajo como Técnico del laboratorio de Anatomía Patológica en Bolivia, donde en realidad, se destacó como patólogo y músico, ya que era un consumado pianista. Posteriormente, fue contratado por el Club Rotario de Maracaibo donde comenzó a trabajar en el Hospital Central con las tareas del Laboratorio de Patología y como patólogo forense. En 1948, fue nombrado profesor de Anatomía Patológica hasta 1952, cuando pasó a encargarse de la Cátedra de Histología y Embriología de la misma Facultad y posteriormente, se encargó de la Cátedra de Anatomía Patológica de la Universidad del Zulia. La actuación del Dr. Wenger en Maracaibo fue muy importante desde el punto de vista científico y cultural (32).

El Dr. Baer Von Schilling Cannstut, se estableció primeramente en la ciudad de Cumaná (1949) donde fundó el servicio de Anatomía Patológica del Sanatorio Antituberculoso. Posteriormente, se trasladó a Caracas, donde se encargó del Departamento de fotografía científica en el Instituto de Oncología Luis Razetti. En 1951, fue contratado por el Dr. Alberto Rivero para integrarse como profesor de Histología de la Facultad de Medicina de la UCV hasta 1958. Ese año, fue contratado como patólogo del Instituto de Medicina Experimental de la UCV y del Instituto Anatomopatológico del Hospital Vargas bajo la

dirección del Dr. Bruni Celli. En 1963, fue nombrado monitor del posgrado de Anatomía Patológica en el Instituto Anatomopatológico por un año.

El Dr. Karl Hans Salferder, comenzó su ejercicio como patólogo en Venezuela, en la ciudad de Cumaná (1950), donde fundó los servicios de Patología del Hospital General de Cumaná y del Hospital Antituberculosos de Oriente. Posteriormente, se radicó en la ciudad de Mérida, al año siguiente, donde fundó los servicios de Patología en el Hospital de Los Andes y en el Sanatorio Antituberculoso de esta ciudad.

El Dr. Karl Brass, en 1950, por disposición del Ministerio de Salud, se encargó de la institución de la Anatomía Patológica en la ciudad de Valencia, estado Carabobo, donde fundó los servicios de Anatomía Patológica del Instituto Oncológico (1951) y del Sanatorio Antituberculoso.

El Dr. J Romanovich de origen ruso. Fue profesor de Anatomía Patológica en la Universidad de Los Andes, en Mérida, desde 1950 hasta su jubilación en 1976 y el Dr. E Kleiss profesor de Anatomía y Embriología en la Facultad de Medicina de la Universidad de los Andes, Mérida (1951-1977). El Dr. Philip Herman Hartz fue un patólogo alemán quien se estableció en 1951 en la ciudad de San Cristóbal, donde trabajó hasta 1956. El Dr. Hartz falleció en esa ciudad.

El Dr. Gerhard Franz llegó a Maracaibo en 1952, contratado por el Ministerio de Sanidad y Asistencia Social para encargarse del servicio de Anatomía Patológica del Sanatorio Antituberculosos de Maracaibo hasta 1962. Trabajó como anatomopatólogo en varios hospitales de esta ciudad: Hospital de Niños, Hospital Central (Urquinaona), Hospital Psiquiátrico, Hospital Chiquinquirá, Leprocomio del Lago de Maracaibo, Hospital Nuestra Señora de Coromoto e inclusive en otros sitios como en la compañía Shell, y en las clínicas D'Empaire y Amado. Fue jefe de la Cátedra de Anatomía Patológica en las Facultades de Medicina y de Odontología.

El Dr. Hans Rudolf Doehnert se estableció en Barquisimeto en 1953, donde fundó el servicio de patología del Hospital Antonio María Pineda y luego en el Hospital Central. También llegó a ocupar la jefatura de la Cátedra de Anatomía Patológica de la Universidad Centro-Occidental en 1965.

El Dr. Eberhard Sauerteig llegó en 1957 contratado por el Ministerio de Sanidad y Asistencia Social para

desempeñarse en Ciudad Bolívar, donde fundó el servicio de Anatomía Patológica del Hospital Ruiz y Páez, para luego radicarse en la ciudad de Barinas, diez años después (1967) donde fundó el servicio de Anatomía Patológica del Hospital Luis Razetti de Barinas (33).

7. Fundación del primer instituto de Anatomía Patológica (IAP), en la Ciudad Universitaria de la Universidad Central de Venezuela. Su amanecer

La fundación de la Ciudad Universitaria, y del Hospital Universitario de Caracas, fue acompañada del nacimiento de varios Institutos docentes y asistenciales, así como de investigación. Se menciona el Instituto Anatómico, el Instituto de Medicina Experimental, el Instituto de Higiene y el Instituto Anatomopatológico (IAP). Durante el mandato de la Junta Militar (Delgado Chalbaud, Marcos Pérez Jiménez, Luis Llovera Páez), el Dr. O'Daly Serraille, fue llamado para establecer todas las bases para la fundación del IAP de la Facultad de Medicina de la Universidad Central de Venezuela. El Dr. O' Daly consultó a sus colegas, el Dr. Alberto Rivero, el Dr. Luis Manuel Carbonell Parra y el Dr. Rudolf Jaffé, para diseñar la estructura interna del instituto (34). El 21 de junio de 1949, el Dr. O' Daly fue notificado por la División de Salud que se le entregaría el edificio el día 5 de julio de ese año. De tal manera que la obra magistral del Dr. O'Daly, en el campo de la Anatomía Patológica, se hizo realidad ese día, cuando recibió de manos del Rector Julio de Armas y del ministro de Sanidad, Dr. González Gómez, la edificación que sería la Sede del IAP de la Universidad Central de Venezuela hasta nuestros días. El Dr. O'Daly había suscrito todos los documentos concernientes al funcionamiento y organización del IAP, especificados en el "Proyecto de la instalación general y funcionamiento del Instituto Anatomopatológico de la Ciudad Universitaria", aprobado por la Facultad de Medicina, el 15 de junio de 1949. En el diario El Universal del domingo 3 de julio se lee textualmente "El Instituto Autónomo de la Ciudad Universitaria hace entrega hoy, al Ejecutivo Federal, de un conjunto de importantes obras e inicia un vasto programa de nuevas construcciones de innegable función social, asistencial y docente". Sus fines y funciones principales se publicaron en el diario La Esfera, bajo el título de "Instituto de la Ciudad Universitaria", con el programa de las nuevas obras para el año económico 1949-1950. En ese periódico se definió "El Instituto Anatomopatológico

es una entidad docente y de investigación destinada al servicio de la república y orientada hacia el estudio de los grandes problemas nacionales relacionados con la especialidad.” Dentro de sus funciones más importantes señaladas el día de su inauguración, se leía:

1. Enseñanza por medio de las Cátedras que en él funcionan.
2. Preparación de personal especializado para la docencia y la investigación. Trabajos de investigación en relación con los grandes problemas nacionales de la patología.
3. Contribuirá por todos los medios posibles a suministrar apoyo y ayuda técnica a todos los Institutos, hospitales y laboratorios nacionales o municipales que lo soliciten, siempre dentro del marco que limiten el Estatuto Orgánico de las Universidades Nacionales y sus Reglamentos.
4. Realizará labores de naturaleza diagnóstica sobre el material que le sea suministrado por los organismos oficiales llevando esta labor a una escala nacional de acuerdo con al Art. 1º Parágrafo Único del Estatuto Orgánico de las Universidades nacionales.
5. Organizará conferencias, demostraciones, actos científicos, relacionados con su campo de acción, con un amplio criterio de colaboración interinstitucional.

Se afirma que el IAP fue fundado por el Dr. José Antonio O’Daly Seraille (†) ya que el suscribió todos los documentos relativos a la organización consolidación de las funciones del IAP hasta 1968, fecha cuando se retira definitivamente de la vida universitaria. Fue secundado en su plan por un pequeño grupo de patólogos considerados como los cofundadores, Luís Manuel Carbonell Parra (†), Rudolf Jaffé (†), Leandro Potenza Michelena (†), Alberto Angulo Ortega (†), Armando Domínguez Capdevielle (†), María Rivas Roz (†) y Blas Bruni Celli (†). Es de recordar que tanto el Dr. Rudolf Jaffé como el Dr. Alberto Rivero Vásquez fueron consultados por los constructores para emitir ideas sobre las instalaciones definitivas del edificio (36). En una carta dirigida a la Dra. Claudia Blandenier de Suárez (1999), el Dr. Rivero le recordó que fue testigo en calidad de jefe de la Cátedra de Histología,

“de la aprobación de los planos elaborados por los arquitectos de la obra”. Señaló que “el salón de necropsias, gigante, se recortó para incluir dos pequeñas salas de necropsias, una para los casos privados y otra para casos de enfermedades infecciosas delicadas”. También recordó que “se construyó un túnel entre el hospital y el instituto para el transporte discreto de los enfermos fallecidos”.

Al principio solo se planificó el traslado de la Cátedra de Anatomía Patológica desde el Hospital Vargas a la nueva edificación. El Dr. O’Daly entregó la dirección del servicio de Patología del Hospital Vargas a su discípulo, el Dr. Blas Bruni Celli (35). El traslado de la Cátedra de Anatomía Patológica no fue fácil. El Dr. O’Daly tuvo que solicitar la instalación del agua y del alumbrado en la sede del IAP, así como la realización del aseo del edificio, la dotación de muebles, aunque el mismo, trajo varios de ellos para la cátedra. En diciembre de ese año aún no se había instalado la línea telefónica y el Dr. O’Daly se trasladó al nuevo instituto, cuando todavía estaban por terminar muchas infraestructuras del edificio y de sus alrededores como el garaje y las entradas al edificio las cuales aún no estaban asfaltadas. Acompañado del grupo de sus colaboradores los Drs. Leandro Potenza, Rubén Calderón, Darío Lozano, Luis Manuel Carbonell, Salvador Mijares, Jack Casto, María Rivas Roz y Alberto Angulo, comenzaron a dictar las clases de pregrado de Anatomía Patológica, encargándose de la dirección de la Cátedra, el Dr. Potenza (Figura 3). Desde ese momento hubo una separación de la Cátedra con el instituto como organismo, dirigido por su fundador, el Dr. O’Daly *ad honorem*, acompañado del subdirector, el Dr. Luis Manuel Carbonell Parra (Figura 1). Es de hacer notar que en ese mismo año comenzó a funcionar en el IAP la Cátedra de Histología Normal de la Facultad de Odontología, situación que duró poco tiempo. El 1ro de octubre de 1954, comenzó su funcionamiento el Departamento de Investigaciones dirigido por el Dr. Jaffé y su adjunto el Dr. Bela von Gavaller, patólogo del Servicio de Patología del Hospital Materno Infantil Concepción Palacios. Para este departamento de Investigaciones, fue contratado en 1957, el profesor Carlos Kosma, quien también colaboraba con clases en el Posgrado de Patología del IAP. Después de varias ausencias para realizar varios cursos, entre ellos métodos electroforéticos en papel, el Dr. Kosma salió del IAP en 1960, para realizar investigaciones en la Facultad de Farmacia hasta 1963.



Figura 3. Vista panorámica actual del Instituto Anatomopatológico. Fotografía. Cortesía de la Dra. Victoria G de Barriola (2023). Aspecto del recién inaugurado Instituto en 1949. Fotografía de los jóvenes patólogos cofundadores: izquierda a derecha: Drs. Alberto Angulo, Armando Domínguez, Darío Lozano, Luis Manuel Carbonel y Salvador Mijares. La técnica Marta Leal.

El establecimiento de las funciones asistenciales y científicas propias del instituto fue lento, pero seguro. En 1956, el director del IAP, Dr. José A O'Daly, fue nombrado decano de la Facultad de Medicina, circunstancia favorable para el establecimiento de las actividades asistenciales que se prestarían al recién inaugurado Hospital Universitario de Caracas, en mayo de 1956. De esta manera el IAP quedó consolidado como organismo universitario con todas las funciones previstas (35,36). Durante este período de establecimiento destacaron en las labores asistenciales de los jóvenes patólogos, la Dra. María Rivas Roz y el Dr. Jack Castro Rodríguez (†). También fueron importantes en el desempeño de las labores docentes y asistenciales, las tres primeras técnicas histólogas: Corina Rodríguez, Ildefonsa Colina y Clory Velásquez, la primera secretaria, Luz María Sarabia y el primer residente, Francisco Dulcey, quien al retirarse fue sustituido por el Dr. Ilderín Domínguez Cedeño. En 1957 fue aceptado el Dr. Walter Wessenberg como el primer becario para realizar una pasantía de Anatomía Patológica durante tres años (1957-1960). Los Drs. Angulo y Carbonell se ocuparon de las labores asistenciales, y docentes fomentando reuniones anatomoclínicas y seminarios con los docentes del recién abierto Hospital Universitario de Caracas (HUC). Fue muy importante la gestión del Dr. Luis Manuel Carbonell Parra, subdirector quien inició una “campana de

reclutamiento” de jóvenes estudiantes de medicina quienes, en sus horas libres, venían a la institución a colaborar con las autopsias y biopsias. De esta manera el Dr. Carbonell abrió las puertas del IAP a los estudiantes a quienes denominó “estudiantes asistentes”. En menos de dos años, habían entrado varios estudiantes al IAP. Uno de ellos fue el Br. José Ángel Suárez Rengifo (1957) y luego los bachilleres: María Orlandi, Claudia Blandenier, Eduardo Viso, los hermanos Franco Guida, Edgar Rivas Acuña y Alejandro Guida (1958). También se recuerdan a Anastasio Cabrera Santos y Cándido Muñoz Cegarra. De esta experiencia, Carbonell publicó varios trabajos sobre la formación del personal y su captación para la especialidad (37-39).

8. Período de consolidación del Instituto Anatomopatológico (IAP). Instalación del primer posgrado de Anatomía Patológica en Venezuela. Comienzo de la Patología especializada y de los trabajos de investigación (1960-1972). La Sociedad de Anatomía Patológica (1952)

A partir del año 1958 nacieron las primeras subespecialidades de la Anatomía Patológica organizadas en las primeras secciones del IAP. En 1958 fue creado el Departamento de Patología Experimental y las Secciones de Neuropatología y

de Patología Cardiovascular, esta última, en conjunto con la División de Enfermedades Cardiovascular del Ministerio de Salud. En marzo de ese mismo año, el Dr. Luis Carbonell propuso la fundación de un laboratorio de Patología Ocular en el IAP el cual sería el primer laboratorio de esta naturaleza en el país. De tal manera que el Dr. Rafael Cordero Moreno oftalmólogo, con un posgrado en esta disciplina en EE.UU, profesor Asociado de la Cátedra de Oftalmología del Hospital Universitario, acompañado de su esposa, la Dra. Malaquita de Cordero, fundan el laboratorio propuesto. La Dra. Cordero, farmacéutica, había recibido un entrenamiento en Técnicas Histológicas con especialización en Patología ocular, y se encargó *ad honorem* de estas tareas en el recién laboratorio. Los esposos Cordero, trajeron los equipos que habían adquirido en EE.UU con sus propios recursos, tales como: microtomo, cuchillas, cristalería, etc. En el mes de julio de ese año (1959), se procesó la primera biopsia de un globo ocular con el diagnóstico de *Ptisis bulbi*. Más tarde constituido en sección, se consolidaron las labores asistenciales, docentes y de investigación. Fue el comienzo de un importante centro de formación de médicos de posgrado de Oftalmología y de Patología. De esta sección, salieron muchos trabajos científicos y su conducción fue ejercida por las exalumnas del Dr. Cordero cuando se jubiló muchos años después (40). A partir de ese año, comenzaron las reuniones anatomoclínicas con los diversos servicios del Hospital Universitario de Caracas, los sábados una vez al mes en el auditorio del hospital. Esta actividad fue muy importante como instrumento de interrelación y control de los casos fallecidos en el Hospital (41).

En 1959, la instalación del primer posgrado formal de Anatomía Patológica en esta sede sería el organismo formador de patólogos, quienes ejercieron esta especialidad médica en todo el país hasta nuestros días y los que sustituyeron a los cofundadores en las secciones del IAP e inclusive en la dirección del IAP. El primer posgrado (1960-63) constó de 12 becarios (Amelia de Serpa, Carlos Aizpurua, Corzo Romero, Carlino Solarte, José Ángel Suárez R, José R Becker, José L Yáñez, Rafael Elías Pérez y Alcides Larez G) y el monitor de este curso fue el Dr. Von Shilling, quien la ejerció por poco tiempo y que fue sustituido por el Dr. Jack Castro (Figura 4). El segundo curso de posgrado (1963-66) constó solo de seis becarios (Jesús Morales Nieto, José Ramírez, Luis Brito, José Silverio Villarroel, Tito Zerpa y Claudia de Suárez). Hasta el año 2015, se contaron 47 promociones de



Figura 4. Arriba: Integrantes del primer posgrado de Anatomía Patológica Nacional en el IAP. Con el Dr. Manuel Carbonel Parra. Abajo: Integrantes de tres posgrados con los profesores: Drs. Atahualpa Pinto P, José Ángel Suárez R, Jorge García Tamayo, María Rivas Roz, Aldo Gozález, Blanca de Rodríguez y Jesús González Alfonzo (1977-1988).

anatomopatólogos en esta institución. Aparte de los médicos que se formaron en el posgrado de patología, también se comenzaron a recibir jóvenes médicos para entrenamiento en Patología especializada. En 1967 entró al IAP una joven médica, la Dra. Ghislaine Céspedes Caravaca, para realizar una pasantía de posgrado en neuropatología bajo la tutela del Dr. Domínguez, hasta 1971.

Durante este período de consolidación del IAP, hubo un importante movimiento de personal técnico y otorgamiento de varias becas para estudiar en el exterior no solo de profesores como el Dr. Pedro Grases y Luis Alezard, sino también de algunos técnicos histólogos. Para el año 1960, el subdirector Dr. Luis Carbonell envió una relación al director del Hospital Universitario, donde le expresaba que había un aumento progresivo del trabajo asistencial, y que habían empezado regularmente a funcionar los laboratorios de Histopatología de la piel y de Oftalmopatología, razón por la cual requería más recursos económicos. En ese mismo año, por orden del Decano, se instaló el 2^{do} Consejo Técnico y se redactó un Proyecto de Reglamento General de los institutos universitarios. En 1962, desde el punto administrativo se organizó el servicio de fotografía

y una sección audiovisual que prestaría servicio a todos los profesores del IAP y a los de la cátedra. También comenzó a funcionar el Departamento de Medicina Forense. El Dr. O'Daly a su vez, inició los diagnósticos de las biopsias renales secundado por la Dra. Amelia Campos de Serpa, su exalumna del primer posgrado. Fue relevante la instalación del primer curso de Citología dirigido por la Dra. María Rivas Roz con doce integrantes (42). En el espacio utilizado como bioterio por los patólogos, anteriormente proyectado como el Instituto de Medicina Legal, fue inaugurado como la capilla del HUC, el 25 de marzo de 1963.

En 1965, El Dr. Rivero, subdirector, terminó la organización de la Biblioteca del IAP de una manera ejemplar, consultando con varios organismos internacionales, recibiendo libros y artículos extranjeros, así como colecciones de los Archivos de Patología. Ese mismo año, el Dr. O'Daly, comenzó a gestionar la instalación del Departamento de Microscopía Electrónica en el IAP, especialmente requerido el neuropatólogo, Dr. Armando Domínguez, quien realizaba una investigación sobre las formas evolutivas del *Schyzotrypanum cruzi* en la Encefalitis Chagásica experimental. Con el fin de entrenarse en el manejo y en técnica básica de la ultraestructura, fue enviado al IVIC el Dr. José Antonio O'Daly Carbonell instructor de la Sección de Neuropatología, por 6 meses. También recibieron entrenamiento en técnica ultraestructural, los Drs. Suárez y Alezard, quienes asistieron al curso organizado por el Dr. Ogura de la Facultad de Ciencias. Es de hacer notar, que, para esa época, ya se habían publicado varios trabajos con medios de investigación histológicos instalados por el Dr. Carbonell como la Histoquímica y las coloraciones especiales para hongos (43). Fueron importantes los trabajos de patología pulmonar implementados por el Dr. Alberto Angulo Ortega, formado en Alemania en esta especialidad patológica y quien fue el iniciador de esta patología en el Instituto de Tuberculosis, el Algodonal y jefe de la Sección de Patología Pulmonar en el IAP (44). Por otro lado, se proyectaba un trabajo de investigación sobre el estudio histopatológico del hueso temporal, el cual se consideraba importante para el avance de la Otolología, debido a que, en el país, había un ritmo creciente industrial y esta situación podía ocasionar mayores problemas otológicos.

La implementación de numerosos cursos y seminarios para la formación y el mejoramiento profesional de técnicos histólogos, personal administrativo y de servicios diversos, fue prioritario. En todas estas actividades se establecieron nexos con

otras dependencias de la Facultad de Medicina y se realizaron trabajos de extensión universitarios y de cooperación con los organismos oficiales de salud. A fines de 1968, el Dr. Pedro Grases Galofré fue nombrado jefe de la Sección de Patología del Aparato Digestivo. Para el año 1970, el Dr. Domínguez entregó la jefatura de la sección de Neuropatología al joven patólogo formado en los EE.UU., el Dr. Jesús Enrique González Alfonso quien la ejerció hasta 1995 y le sucedió en ese cargo la Dra. Céspedes.

9. La fundación de la Sociedad De Anatomía Patológica

La Sociedad Venezolana de Anatomía Patológica (SVAP) fue fundada en noviembre de 1952, según testigos fundacionales presenciales de prestigio como los Drs. Blas Bruni Celli y Alberto Angulo Ortega y de acuerdo con varios documentos históricos. Dicha fecha, ha sido controversial, porque el Acta Constitutiva original está aparentemente extraviada, hecho que se interpreta como la consecuencia de los numerosos cambios de sede de las juntas directivas. Las fuentes históricas señalan que, a principios del año de 1952 la cantidad de especialistas en Anatomía Patológica (venezolanos y extranjeros) era suficiente para constituirse en sociedad y por esta razón tres jefes de servicio, los Doctores José Antonio O'Daly, Serafino Lamanna y Bela de Gavalier invitaron mediante una comunicación a los patólogos venezolanos a "constituir una Sociedad Científica de Anatomía Patológica". Posteriormente, formaron un "Comité provisional de la Sociedad Venezolana de Anatomía Patológica", enviaron un proyecto de estatutos a todos los patólogos y solicitaron las opiniones de cada uno de ellos. De tal manera que, para fines de noviembre de 1952, con el visto bueno de la mayoría de los patólogos, con 15 miembros en Caracas y varios de los servicios de Anatomía Patológica del interior del país, se constituyó dicha sociedad. Primero se eligió la Junta directiva formada por el presidente Dr. José Antonio O'Daly Serraille; el secretario, Dr. Alberto Rivero Vásquez; el tesorero, Dr. Leandro Potenza y el vocal, Dr. Darío Lozano. En un solo día, los integrantes de la Junta directiva elaboraron el Acta constitutiva y se adoptaron los estatutos (45). La Sociedad era de índole exclusivamente científica y de carácter nacional. Tenía por objeto exclusivamente, fomentar el adelanto de la Anatomía Patológica en el país y las relaciones e intercambios científicos entre sus miembros. Caracas fue su ciudad domicilio, donde residían la mayoría de sus miembros y donde ya se

habían iniciado reuniones mensuales ordinarias. En 1953, se realizó la Ira. Jornada de Anatomía patológica y para mediados de ese año, ya se tenía la lista de sus primeros miembros, a saber los integrantes de la Junta Directiva, Rudolf Jaffé, Armando Domínguez, Blas Bruni Celli, María Rivas Roz, Serafino Lamanna, Salvador Mijares, Rubén Calderón, Franco Donadelli, Manuel Henríquez, Baer Von Schilling, José A Mantilla, Ladislao Pollak, Scarovich y Carbo gniani de Caracas; Karl Brass (Valencia), Enrique Merino (Maracay), Mota (Barquisimeto), Guillermo Mújica (Valencia), Gerardo Will (Mérida), Alberto León, Gerard Franz y Franz Wenger (Zulia). Algunos patólogos venezolanos que estaban en el exterior tales como Luis Manuel Carbonell Parra, José Antonio Estévez, María Cristina Marantes y Modesto Scharvy, fueron también nombrados miembros de la sociedad. La Sociedad de Patología se organizó en comisiones, las cuales se ocuparon de diversos asuntos científicos y gremiales, tales como el fomento de reuniones científicas y cursos sobre tópicos de patología especial y general y apoyó a la publicación de libros. Sus miembros intervinieron activamente como participantes y conferencistas en numerosos eventos científicos nacionales e internacionales, conjuntamente con la Sociedad Latinoamericana de Patología y otras Sociedades Científicas. Una de las notas más importantes de la nueva Sociedad de Anatomía Patológica, era que varios de sus miembros eran subespecialistas destacados en patología Linfohematopoyética, Neuropatología, Patología Digestiva, Cardiovascular, Osteo-muscular, Pulmonar, Nefropatología, Oftalmopatología, Inmunohistoquímica y Ultraestructura, no solo en Venezuela sino también en el exterior.

10. Instituto Anatomopatológico. Cambio de directores (1968-1971)

A partir de 1968, cuando se jubiló el Dr. O'Daly, transcurrió un corto período de tiempo de transición, donde la labor comenzada en el IAP, continuó con el nombramiento de dos de sus discípulos y cofundadores.

Direcciones de los Drs. Alberto Angulo Ortega (1968-1971) y Armando Domínguez Capdevielle (1971)

El primero en ocupar la dirección fue el Dr. Alberto Angulo Ortega, neumopatólogo (1-9-

1968 al 16-3-1971) y luego el neuropatólogo Armando Domínguez Capdevielle (16-3-1971 al 30-11-1971), ambos exalumnos del Dr. José Antonio O'Daly. Durante estas cortas direcciones se tomaron decisiones importantes en la organización funcional de la institución. Se oficializaron ante la Facultad de Medicina, las secciones existentes en el IAP, Neuropatología, Patología Pulmonar, Cardiopatología, Ginecopatología, Patología del Aparato digestivo, Oftalmopatología, Citopatología, Patología de autopsias y quirúrgica. Desde el punto de vista administrativo, se realizó la fusión de la Cátedra con el IAP, de tal manera que los docentes de la cátedra y los del IAP formaron un solo cuerpo laboral. Desde el punto científico comenzaron a realizarse los trabajos con ultraestructura en el primer Microscopio Electrónico de transmisión alemán, marca Carl Zeiss, instalado por el Dr. Domínguez, fundador de la Sección de Microscopía Electrónica del IAP (42,43). Para su funcionamiento, dos jóvenes patólogos, los Drs. José Ángel Suárez y Luis Alezard fueron enviados a la Escuela de Ciencias con el Dr. Ogura, para realizar un curso sobre el manejo del microscopio. Posteriormente, el uso del microscopio quedó solo en manos del Dr. Domínguez y del Dr. Alemán, patólogo del servicio de Patología del Hospital Vargas.

Dirección del Dr. Alberto Rivero Vásquez (noviembre de 1971- febrero de 1977)

A partir del 24 de noviembre 1971 se inició la dirección del Dr. Alberto Rivero Vásquez, patólogo contemporáneo del Dr. O'Daly desde 1932, formado en EE.UU y quien había ejercido la subdirección del IAP en 1964, al retirarse el Dr. Luis Manuel Carbonell Parra al Instituto Venezolano de Investigaciones Científicas (IVIC). En el campo de la Anatomía Patológica venezolana, la actuación del Dr. Rivero había sido muy importante como fundador de los servicios de Patología de otros hospitales como en el Hospital Oncológico "Luis Razetti", en la Maternidad "Concepción Palacios" y en el Hospital de los Seguros Sociales. Durante su dirección en el IAP, el Dr. Rivero, cambió la orientación operativa, aunque manteniendo sus objetivos generales. En 1975, el Dr. Rivero impulsó la introducción de nuevos docentes especialmente investigadores, como fue la incorporación al IAP del profesor Agregado Dr. José Atahualpa Pinto, exdiscípulo del Dr. Blas Bruni Celli en el Hospital Vargas de Caracas, quien

se desempeñaba como docente de la Universidad de Oriente. El Dr. Pinto fue nombrado para ocupar la jefatura de la Sección de Nefropatología que dejara la Dra. Amelia de Serpa, fallecida accidentalmente. Igualmente, el Dr. Rivero tramitó la incorporación del Dr. Alfredo Suárez como hematopatólogo graduado en Estados Unidos para desarrollar la sección de Hematopatología. El Dr. Rivero se jubiló en 1977, después de 36 años de actuación universitaria y de 8 años de dirección del Instituto Anatomopatológico y de la Cátedra de Anatomía Patológica (45).

Primera intervención de la Facultad de Medicina en la Reorganización del Instituto Anatomopatológico a raíz de una crisis institucional. Período de transición

A partir de 1975/76, los estudiantes de pregrado y un grupo de profesores del IAP comenzaron a presentar varias protestas verbales y por escrito acerca de irregularidades en el funcionamiento de la Cátedra de Anatomía Patológica y del Instituto. Dichas protestas se hicieron continuas, situación que ocasionó una crisis institucional. La crisis se hizo aguda con reuniones de protesta que solicitaban el retiro del director, quien en ese momento era el Dr. Alberto Rivero Vásquez. A raíz de estos hechos, las autoridades de la Facultad de Medicina consideraron conveniente realizar una intervención técnica en dicho conflicto. Después de un acuerdo, un grupo de profesores de la Facultad de Medicina realizaron un trabajo de averiguación de los hechos mediante entrevistas a los profesores de la cátedra y del IAP, después de la cual entregaron un informe al Consejo de Facultad. Una de las consecuencias de esta intervención de la Facultad fue la separación del IAP propiamente dicho con sus actividades asistenciales, docentes de posgrado y de investigación, de la Cátedra de Anatomía Patológica, tal como había funcionado desde la fundación de la Sede en 1949. Otra consecuencia de esta intervención fue la jubilación del Dr. Rivero en 1977 y el nombramiento de un nuevo director.

11. Segunda etapa de transición (1977-1984). Reorganización del Instituto Anatomopatológico

Esta etapa se caracterizó por dos direcciones cortas, de tres a cuatro años de duración, caracterizadas por una reorganización parcial administrativa y

docente de posgrado del Instituto Anatomopatológico. Igualmente, se prestó ayuda administrativa a la Cátedra de Anatomía Patológica ya separada del IAP. En el mes de febrero de 1977, es nombrado director del IAP el Dr. Pedro Grases Galofré (1977-1981), seguido por el Dr. José Ángel Suárez Rengifo, exdiscípulo de O'Daly (1981-1984). A partir del año 1977 comenzó lentamente un desarrollo favorable de las funciones del IAP, especialmente relacionadas con la aparición de nuevas secciones de subespecialidades patológicas, la incorporación de nuevas iniciativas y proyectos de investigación que le dieron realce a la institución desde varios puntos de vista.

Comienzo de la etapa de oro del Instituto Anatomopatológico. Dirección del Dr. Pedro Grases Galofré (1977-1981)

Durante la corta dirección del Dr. Grases, la investigación recibió un trato preferencial. A su favor, sucedió un acontecimiento que fue a la postre una gran adquisición para el IAP, la contratación a dedicación exclusiva del Dr. Jorge García Tamayo en agosto de 1976. El Dr. Jorge García Tamayo era un patólogo reconocido como un experimentado y competente investigador, formado como patólogo y en Ultraestructura en las Universidades de Wisconsin y de Pennsylvania, así como en la Universidad de California-Berkeley en EE.UU. Desde 1968, el Dr. García Tamayo había ocupado el cargo de exdirector del Laboratorio de Microscopía Electrónica del Hospital General del Sur del MSAS, siendo patólogo Adjunto, Especialista II del mismo servicio en Maracaibo y docente de la Cátedra de Histología y Embriología en la Facultad de Ciencias Veterinarias de la misma Universidad del Zulia. En 1975, durante su año sabático, el Dr. García Tamayo se había desplazado a la ciudad de Caracas donde ocupó el cargo de Neuropatólogo, Médico Adjunto en el Instituto de Patología, Hospital Vargas de Caracas. En esta institución, el Dr. García Tamayo logró conseguir un Microscopio Electrónico Hitachi H-500 a través del CONICIT, y desarrollar una gran actividad en Neuropatología y Ultraestructura. Sin embargo, en 1975, de manera inconsulta fue conminado por la jefatura a regresar a Maracaibo. El Dr. Pedro Grases director del IAP en esos momentos, en conocimiento de esta situación lo invitó a trabajar en el IAP. Inmediatamente, el Dr. García Tamayo se encargó de la Sección de Microscopía Electrónica en calidad de jefe de la misma, trayendo

el Microscopio Hitachi otorgado por el CONICIT a través de sus proyectos de investigación. Allí, este científico logró reestructurar físicamente la Sección de Microscopía Electrónica y entrenar el personal técnico adecuado. Enseguida, las diversas secciones del IAP presentaron proyectos de investigación que requerían ultraestructura, lo cual apoyó la adquisición de dos ultra-microtomos. También fue muy valiosa la incorporación de dos patólogos experimentados. El joven patólogo, Aldo González Serva, formado en los EE.UU, doctor y Board de Patología, quien fue designado para desempeñarse como profesor y Coordinador del posgrado de patología (1977-1981). En 1978, ingresó el Dr. Arturo Rosas Uribe como profesor contratado, experimentado hematólogo, Board de patología, graduado en los EE.UU, para suplir el retiro del Dr. Alfredo Suárez de la jefatura de la Sección de Linfohematopoyético. En ese mismo año, se gestionó formalmente la transformación de la sección de Inmunopatología en Unidad, dirigida por el Dr. Nicolás Bianco Colmenares, acompañado de los Drs. Gloria Pérez de Rojas, Raúl Suárez Chacón y Dieter Zscheck. Posteriormente, esta unidad se transformaría en el Instituto de Inmunopatología ubicado en el 1^{er} piso del bloque noreste del IAP.

También durante esta dirección, hubo algunos cambios operacionales para la renovación y actualización de la Biblioteca, así como directrices acerca de los informes de las gestiones realizadas, reestructuración del programa de posgrado, entre otras reformas menores. Lo más importante, fue el notable crecimiento de la producción científica en el instituto, especialmente los dirigidos por el Dr. García Tamayo, quien refería en sus memorias que la "Sección de Microscopía Electrónica comenzó a desarrollarse rápidamente apoyado por los directores, Drs. Grases y Suárez". La investigación se consideró como una actividad preferencial, a través de proyectos científicos financiados por Instituciones como el CONICIT, el CDCH-UCV y de la Fundación José María Vargas. En la Sección de Microscopía Electrónica, el Dr. García Tamayo estaba acompañado por excelentes colaboradores, como el personal técnico integrado por los Licenciados Saudy Escorihuela de García, Abilio Briceño, Teresa Cabañas entre otros, quienes se integraron posteriormente al trabajo ultraestructural. Una de las principales actividades dirigidas por el Dr. García Tamayo fue el examen ultraestructural de los tumores, así como el estudio de algunas enfermedades virales siendo el primer investigador del IAP que se dedicó al estudio de la patología del Síndrome

de Inmuno Deficiencia Adquirida (SIDA) durante la pandemia y de algunas parasitosis y micosis. La Sección de Microscopía Electrónica, promovió programas de Educación Continua en Patología y durante estos ciclos de conferencias se invitaron a patólogos de renombre latinoamericanos, de EE.UU y España, expertos en las diversas áreas de este tipo de patología. En general, todas las secciones publicaron numerosos trabajos científicos nacionales e internacionales, así como libros. Había en el IAP un renacer de actividades científicas que involucraron a los residentes de posgrado, quienes realizaron sus tesis de grado y participaron en muchos trabajos de Patología especializada, formándose de esta manera una pléyade de jóvenes patólogos investigadores y subespecialidades. Fueron muy importantes las investigaciones realizadas por la Sección de Microscopía Electrónica como la investigación sobre el virus de la Encefalitis EV, financiado por el CONICIT. Lamentablemente, no le fue renovado el contrato al Dr. Rosas Uribe para seguir sus funciones como especialista en el IAP. Inmediatamente después, fue contratado en la Unidad de Hematopatología de la UCV y como jefe de Hematopatología en el Hospital Militar de Caracas.

Dirección del Dr. José Ángel Suárez Rengifo (1981-1984)

La gestión del Dr. Suárez fue corta (1981-1984), y una de las primeras decisiones que tomó fue nombrar director adjunto (subdirector) (1982-1983) al Dr. Jorge García Tamayo quien, además, se encargó de los Cursos de posgrado de Especialización, Maestría y Doctorado en Anatomía Patológica (1984-1994). También fue muy importante la decisión de reintegrar al Dr. Arturo Rosas Uribe como profesor a dedicación exclusiva, designado como jefe de la sección de Patología Linfohematopoyética. El Dr. Rosas era un hematólogo de gran experiencia, exprofesor de Patología en la Universidad Stanford-California USA. En general, el Dr. Suárez continuó con la organización del Dr. Grases, dejando la autonomía de la Sección de Microscopía Electrónica y apoyando los proyectos de investigación propuestos que eran los más importantes del IAP. El Dr. Suárez se enfocó en reorganizar con el Consejo Técnico, la administración general de la institución, de tal manera que se realizó la planificación financiera con el presupuesto general y las partidas de las secciones e implementó la creación de ingresos propios. El director, se dedicó

al mejoramiento de la planta física que adolecía de defectos desde su inauguración, de tal manera que la infraestructura tuviese un mejor aspecto. Se reubicaron varios locales en algunas secciones, especialmente la del departamento de Archivo General del material de biopsias y autopsias y el local de la sección de Ginecopatología. Continuando la labor del Dr. Grases, se le dio apoyo al nuevo Instituto de Inmunopatología, instalado en la parte baja, al este del IAP y a la Comisión de posgrado de la Facultad de Medicina. Se fomentó la interrelación con los docentes de la Cátedra de Anatomía Patológica remodelando el local ocupado el cual era insuficiente y dotándolo de una sala de reunión de profesores.

12. Etapa de estabilidad del instituto anatomopatológico (1984-2006)

Durante 22 años, el IAP, dos direcciones largas favorecieron el florecimiento de la formación de numerosos patólogos y de la investigación dándole a la institución una fama internacional. Dos hechos importantes para la institución se dieron durante este largo período llamado por algunos como la etapa de oro: darle a su sede física el nombre de su fundador, “Dr. José Antonio O’Daly”, y el nombramiento del Instituto Anatomopatológico como Centro Nacional de Referencia. Los nuevos patólogos fueron y son los que sucedieron a sus profesores en los cargos desempeñados en clínicas, universidades y en los servicios de patología nacional. Igualmente, todas las secciones especializadas se desarrollaron especialmente en las investigaciones y publicaciones. De estas secciones también salieron patólogos especializados.

Dirección del Dr. Jorge García Tamayo (1984-1994)

A partir de 1984, asumió la dirección del Dr. Jorge García Tamayo. Durante su larga dirección de 10 años, el Dr. García Tamayo continuó con las directrices generales del funcionamiento del IAP, y se tomaron decisiones trascendentes para el IAP. En el área de la Anatomía Patológica, la aplicación diagnóstica del Microscopio Electrónico, particularmente para los tumores malignos y la incorporación de conceptos ultraestructurales a la docencia del postgrado para los patólogos, modificaría el ejercicio de la especialidad en la formación de patólogos desde finales de los 70, hasta la década de los años noventa. La productividad

medida en publicaciones con aportes ultraestructurales estableció cifras tope para el IAP, entre los Institutos de la UCV. A través de una labor de educación continuada en Patología, el Dr. García Tamayo recordaba que de esta manera se prepararon la mayoría de los patólogos que actualmente ejercían en el país. Los Cursos y Talleres fueron dictados por los mejores patólogos internacionales. Esta labor no se limitó a los patólogos del IAP, sino a todos los especialistas, lo que se pudo implementar gracias a la comunicación constante con la Sociedad Venezolana de Anatomía Patológica. El IAP pasó a ser una institución de referencia en Latinoamérica. La implementación de la inmunohistoquímica introducida por la Licenciada Saudy Escorihuela de García en la década de los 80, acompañada por el Dr. Jesús González, dieron origen a la Sección de Inmunohistoquímica dirigida por el Dr. García Tamayo desde 1998. La labor de este laboratorio no solo se circunscribió a Caracas sino en todo el país. En esta sección se realizaron trabajos científicos e inmunoreacciones para el diagnóstico rutinario de tumores y otras entidades patológicas que se diagnosticaban en todas las secciones del IAP. El Dr. García Tamayo por esta labor a la cual dedicó más de seis décadas, es considerado como el Pionero en Venezuela en el uso de la inmunohistoquímica para el diagnóstico de tumores. En 1992, la dirección del Dr. García Tamayo fundó el Centro Nacional de Referencia del IAP, a través de un convenio con el Ministerio de la Salud y Desarrollo Social, acción trascendental para la institución, cuya función se expandió en todo el país. Desde el año 1993, el IAP, fue objeto de una activa colaboración de la Fundación Gipuzkoa a través del Dr. Eduardo Blasco, así como del MD del Hospital Anderson de Houston (EE.UU), gracias a la colaboración continua del Dr. Mario Armando Luna. La institución de una Maestría en Microscopía Electrónica fue básica para el trabajo de la Sección y para la implementación de los Cursos de Maestría y Doctorado en Anatomía Patológica, mención “Patología Ultraestructural” iniciados en 1994. Fueron siete los trabajos de Especialización en Anatomía Patológica que el Dr. García dirigió. Desde diciembre de ese mismo año se nombró al Dr. García Tamayo jefe de la Unidad de Investigación en Patología Ultraestructural y Biología Molecular, así como director del Curso de Maestría y Doctorado en Anatomía Patológica, mención Patología Ultraestructural cargo que ejerció hasta 1998 y 1999, respectivamente. Se recuerda que 7 patólogos especialistas en Anatomía Patológica se graduaron también como Magíster en la mención

“Patología Ultraestructural” y dos de ellos culminaron el Doctorado en dicha mención. Es de recordar que el Dr. García Tamayo había sido el jefe de la sección de Microscopía Electrónica desde el año 1976, cuando ingresó al IAP, hasta el año 1998, cuando se cambió el nombre de la sección (46). De tal manera que podemos asegurar que el Dr. García Tamayo fue quien le dio un nuevo empuje a la investigación científica en el IAP, en otras palabras, le confirió una vida nueva y fama internacional, mediante la presentación de más de 490 trabajos y la publicación de numerosos trabajos científicos, en revistas nacionales e internacionales, la edición de 4 libros de texto y la formación de numerosos discípulos. Bajo su dirección se desarrolló la Unidad de Inmunología Clínica en nuevos locales y otorgándole autonomía de acción (47,48).

Dirección del Dr. Atahualpa Pinto P (1994- 2006)

La dirección del Dr. Pinto comenzó en 1994. En un principio este director se abocó al mejoramiento de las instalaciones y jardines, para luego dedicarse a la modernización de las secciones y dependencias, mediante la instalación de Internet en cada una de ellas y a la dotación de computadoras en todas las secciones. Al mismo tiempo, se ocupó activamente de la patología renal mediante reuniones periódicas con los nefrólogos, publicando trabajos científicos nacionales e internacionales, así como libros. Uno de los hechos de mayor relevancia, prestancia e importancia de su dirección fue honrar la memoria del fundador del IAP, “Dr. José Antonio O’Daly”, concediéndole a la sede el ilustre nombre. Debemos recordar que el IAP, era el único instituto Universitario que no tenía aún un nombre. Después de sustentar con documentos, la fundación del IAP por el Dr. O’Daly, ante el Consejo de la Facultad de Medicina, este organismo aprobó por unanimidad tal petición (sesión, 6 de febrero de 1996). Antes de presentar esta petición, el Dr. Pinto, con la ayuda especialísima de su esposa Paulina Solís de Pinto, estimuló y ayudó en gran parte a la publicación de un libro documentado en el que se describe los inicios de la institución fundada por el Dr. O’Daly Serraille. Con estos documentos, el Dr. Pinto pudo comprobar que el Dr. José Antonio O’Daly Serraille había suscrito todo lo relacionado con la fundación de esa institución, especialmente el “Proyecto de Instalación General y Funcionamiento del IAP de la Ciudad Universitaria”

presentado al Consejo de la Facultad de Ciencias Médicas el 15 de junio de 1949. En junio de 1996, durante la celebración de los 40 años de la fundación del Instituto, se develó el nombre del “Dr. José Antonio O’Daly” en la fachada Sur de la edificación. Fue una ceremonia emotiva que se realizó en los jardines del Instituto, donde se reunieron los familiares del Dr. José Antonio O’Daly, sus amigos más íntimos, docentes, exdocentes y alumnos, con el director, Dr. Pinto y el personal del Instituto (49,50). Otra de las iniciativas importantes que se desarrolló durante la dirección del Dr. Pinto fue estimular la fundación y publicación mensual de un pequeño periódico institucional que cada integrante del IAP recibía puntualmente, El IAPeriodico. Este pequeño medio de comunicación fue fundado en el año 2004 por el personal del instituto dirigido por la Sra. de Pinto y su hija Mariela, quienes se encargaron de transcribir durante más de 11 años, los numerosos artículos publicados por profesores universitarios, anatomopatólogos profesores, discípulos y empleados. Esta publicación fue un aporte positivo informativo sobre la vida del IAP, y de la cultura en general. La importancia de este medio de comunicación interno se expresó en una mayor comunicación entre el personal del IAP. Permitió conocer el intelecto y la sensibilidad de todos los que laboraban en esa antigua institución universitaria, durante más de 20 años. El Dr. Pinto con la ayuda de su esposa se dedicó a embellecer el aspecto físico del IAP y se logró celebrar los sesenta años de su fundación, en perfectas condiciones físicas y de funcionamiento. El Dr. Pinto dejó la dirección en el año 2006, aunque siguió atendiendo la Sección de Patología Renal hasta el año 2017, cuando ocurrió la trágica muerte de su esposa en los predios del IAP (51).

Epílogo

Con la dirección del Dr. Pinto, comienza una nueva etapa histórica del Instituto Anatomopatológico, caracterizada por el decaimiento de sus funciones especialmente por las investigaciones y las labores docentes de posgrado. Esta situación se dio particularmente por la situación económica, social y política que presentaba el país en los años de la década del 2022. También la salida de varios investigadores importantes y de experiencia dejaron un vacío tanto en la asistencia como en la docencia sin contar en las investigaciones propias de sus especialidades.

REFERENCIAS

1. Rodríguez RPD. Las autopsias en nuestra era colonial. *Arch Hist Med Ven.* 1934;1(3):49-55.
2. Romero Reverón F. La evolución en los Estudios Anatómicos en Venezuela durante el siglo XIX. *Gac Méd Boli.* 2022;45.
3. Bruni B. José María Vargas. Obras Completas. I-VI. Caracas: Talleres Gráficos de Ávila Arte; 1986.
4. Instituto Anatómico. Fundación Arquitectura y Ciudad. *Fundaayc.com.* Disponible en: <https://fundaayc.com> 1911. Instituto Anatómico.
5. Rodríguez RJM, Sánchez BJ, Morillo RJ. Vargas en la Enseñanza Anatómica Venezolana en la primera mitad del siglo XIX. *Rev Soc Ven Hist Med.* 2016;64(2).
6. Alegría C. Los estudios anatómicos en Venezuela. Caracas: Sociedad Venezolana de Salud Pública; 1963:1-94.
7. Suárez C. El Venerable Dr. José Gregorio Hernández, Técnico histólogo por excelencia, en el año jubilar de su Beatificación. Inicio de la Anatomía Patológica y medicina experimental en Venezuela. *Tribuna Invest.* 2014;15:18-31.
8. Perera A. Historia de la medicina en Venezuela. Caracas: Ministerio de Sanidad y Asistencia Social; 1951:129-135,139-148, 155-156.
9. Angulo A. Resumen cronológico de la historia de la medicina en Venezuela. Caracas, Venezuela: Editor Angulo Fontivero; 1979.
10. Freitas Y. Ciencia y Tecnología en Venezuela. Venezuela, Enciclopedia Temática. Caracas: Editorial Paneta Venezolana, S.A.; 2002.p.217-239.
11. Wenger F. Apuntes sobre la historia de la Anatomía Patológica en Venezuela y especialmente en Maracaibo. Discurso de inauguración del VIII Congreso Latinoamericano de Anatomía Patológica, 5 de diciembre de 1971.
12. Corso G. El crecimiento económico de Venezuela desde 1830 hasta el 2009: una historia cuantitativa, con un anexo relativo al periodo 1783-1830. versión preliminar no incluye la nueva serie. Doctorado de teoría económica y doctorado de ciencias sociales. Facultad de ciencias económicas y sociales. Universidad Central de Venezuela. <https://www.mozilla.org/es-ES/firefox/central/>
13. Vallenilla N H. Gobierno de Juan Pablo Rojas Paúl. Disponible en: <https://bibliofep.fundacionempresaspolarg.org> > entradas.
14. Clemente H A. Prólogo en: Yáber M. José Gregorio Hernández. Académico-Científico, Apóstol de la justicia social, misionero de la esperanza. 140 aniversarios de su nacimiento. (26-octubre-1864) Ediciones OPSU. Consejo Nacional de Universidades. Caracas, 2004.
15. Suárez B C, López-Loyo ES, López J D. José Gregorio Hernández, la epopeya de su Laboratorio. Análisis descriptivo del primer laboratorio científico venezolano. Ed. Floricanto Press and Berkeley Press. 2019;93021.
16. Inventario del laboratorio adquirido por el Doctor José Gregorio Hernández para la Universidad Central de Venezuela, tomando por modelo el de la Facultad de Medicina de París. *Rev An UCV.* 1990;1(3):637-640.
17. Vélez-Boza F. José Gregorio Hernández, maestro. Aporte al conocimiento de su labor docente en la Facultad de Medicina de la Universidad Central de Venezuela, de 1891 a 1919. *Separata Rev Ven San Asist Soc.* Caracas: Ed Fundaciencia; 1977;42(3-4):423.
18. Vélez Boza F. La docencia médica del Dr. José G Hernández. *Rev Soc Ven Hist Med.* 1995;45(69):288-308.
19. Memoria de Instrucción Pública. I. Caracas; 1892:416. Referido por: Vélez-Boza F. Fundación Cátedras de Histología normal y patológica, Fisiología Experimental y Bacteriología. Profesor de la Universidad Central de Venezuela. Capítulo VII. n: José Gregorio Hernández, maestro. *Separata Rev Ven San Asis Soc.* 1977;XLII(3-4):424-425.
20. Archila R. Santos A. Dominici, una vida excepcional. No. 45. *Cultura Universitaria.* 1954;18-27.
21. Briceño Iragorry L. Instituto Pasteur de Caracas. *Gaceta Médica de Caracas.* 1980;88:331-335.
22. Bruni Celli B. Comp. Rafael Rangel: trabajos científicos. Caracas: Fundación Vargas de publicaciones Médicas. 1960. Edición Especial. Homenaje a Rafael Rangel. Instituto Nacional de Higiene "Rafael Rangel". *Rev Inst Nac Hg Rafael Rangel.* 2006;37.
23. Rísquez JR. Lección inaugural de la Cátedra de Anatomía Patológica de la Escuela de Medicina. *Rev Vargas.* 1922;XII:17-21.
24. Rísquez JR. Apuntes de Anatomía Patológica. Caracas: Tip Americana; 1924:32.
25. Rísquez JR. Lesiones anatomopatológicas en caso de apendicitis. *Bol Hosp.* 1917;XIV(10):477.
26. Rísquez JR. Apendicitis parasitarias. *Bol Hosp.* 1928;XVII(II):477-48.
27. Rísquez JR. Nota sobre la parasitología apendicular. *Gac Med Caracas.* 1917;XXIV;9:71.
28. Suárez BC. Comunicación personal.
29. Suárez BC. Notas sobre el origen de la técnica histológica en Venezuela: con especial referencia a

- su desarrollo en el Instituto Anatomopatológico” Dr. José Antonio O’Daly”. Colección Razetti. Volumen VII. Caracas. En: Heimerdinger A, Briceno Iragorry L, editores. Caracas: Editorial Ateproca; 2009.p.433-465.
30. O’Daly JA. Curriculum vitae. Arch. Personal. Dr. José Ángel Suárez Rengifo.
 31. Agüero O. Historia obstétrico-ginecológica venezolana. Médicos destacados en la Maternidad “Concepción Palacios”. Rev Obst Ginecol Venez. 2005;65:1.
 32. García Tamayo J. Franz Wenger, patólogo y músico. La Peste Loca. 2017; 28 de enero.blogspot.com. Disponible en: <http://lapesteloca.blogspot.com>.2017
 33. Salfender K, Novoa MD. Patólogos alemanes en Venezuela. 1936-1981. Universidad de Los Andes. Consejo de publicaciones. Mérida. Venezuela: Talleres Gráficos Universitarios; 1982.
 34. Suárez BC. José Antonio O’Daly Serraille: Un nombre para el Instituto Anatomopatológico de la Universidad Central de Venezuela. Gac Méd Caracas. 1998;106(3):304-305.
 35. Suárez C. Congreso XIII de Anatomía Patológica” Dr. Blas Bruni Celli”. Gac Méd Caracas. 2005; 113:540-543.
 36. Suárez BC. Historia Documentada del Instituto Anatomopatológico “Dr. José Antonio O’Daly”. Proceso Fundacional: 1937-1968. Caracas: Ed. FEPUVA. UCV; 1999.
 37. Suárez C. Comunicación y documento personal.
 38. Suárez C. El Dr. Luís Manuel Carbonell Parra, cofundador del primer Instituto de Anatomía Patológica” Dr. José Antonio O’Daly” y del primer posgrado de esta especialidad en Venezuela. Gac Méd Caracas. 2016;124:35-49.
 39. Carbonell LM. Factores externos al patólogo que pasan sobre el reclutamiento de los mismos. Consejo Venezolano de Médicos Anatomopatólogos. Planes para la formación y mejor utilización de los patólogos venezolanos. Arch Soc An Patol Bd. 1955.
 40. Oficio 186. Dr. Carbonell al Decano. 12-11-58. Arch IAP-UCV.
 41. Arévalo de Pifano I, Orellana de Alonzo ME. Sección de Patología Ocular. Drs. Rafael y Malaquita Cordero Moreno. El IAPeródico. Número 8. Caracas, febrero 2005. Disponible en la biblioteca del Instituto Anatomopatológico.
 42. Suárez C, Ayala N. Semblanza profesoral. Dra. María Rivas Roz. Rev Fac Med. 2002;25:138-139.
 43. Blandenier de Suárez C, Borges Iturriza J, O’Daly Carbonell JA. Un venezolano de excepción: el Dr. Armando Capdevielle, fundador de la neuropatología venezolana. VITAE, Academia Biomédica Digital. 2018;73. Disponible en: vitae.ucv.ve/?module=articulo&rv=138&n=5711&m=3&e=5741Suárez C.
 44. Suárez C. Dr. Alberto Angulo Ortega: un nombre para las XLLVII Jornadas Nacionales de la Sociedad Venezolana de Anatomía Patológica. Gac Méd Caracas. 2004;112:342-344.
 45. Suárez C. Dr. Alberto Rivero Vásquez: Semblanza. Act 2. Anatomopatol. 2000;4(1):3-4.
 46. García Tamayo J, Caleiras E, Blasco-Olaetxea E, Parada D, De García SE. Aplicación de la microscopía electrónica y de la inmunohistoquímica al estudio de los tumores malignos: una revisión de su importancia diagnóstica. Invest Clin. 1997;38(4):227-259.
 47. Suárez BC. Historia documentada del Instituto Anatomopatológico “Dr. José Antonio O’Daly”. Proceso fundacional: 1937-1968. Vicerrectorado Académico. Universidad Central de Venezuela. ED. FEPUVA-UCV. Caracas. 1999.
 48. Curriculum. Dr. Jorge García Tamayo. Actualización: 24 de julio de 2023.
 49. Suárez C. Los sesenta años del Instituto Anatomopatológico “Dr. José Antonio O’Daly” de la Universidad Central de Venezuela. <http://caibco.ucv.ve>. Abril-junio 2009 N° 38.
 50. Suárez C. El Instituto Anatomopatológico Dr. José Antonio O’Daly cumple cincuenta años de funcionamiento. Rev Fac Med. 2006;29:83-87.
 51. Suárez C. Dr. José Atahualpa Pinto Pinto, Padre de la nefropatología venezolana. La Web de la Salud. 2022. Disponible en: <https://lawebdela salud.com>. Blog.

La Gaceta Médica de Caracas hace 100, 50 y 25 años

The Gaceta Medica de Caracas 100, 50, 25 years ago

Enrique Santiago López-Loyo

Individuo de Número Sillón XXXI

Hace 100 años: Octubre – Diciembre 1923

El 15 de octubre de 1923 se publica el número 19 del año. Identificamos una interesante revisión a cargo del Dr. A. Herrera Vegas titulado “La peptonoterapia en la Jaqueca”. Inicia desmitificando la banalidad de la jaqueca como entidad clínica. La divide en jaqueca simple y jaqueca oftálmica u oftalmopléjica. La simple es la de menor intensidad sin ninguna complicación. La oftálmica y más aún la oftalmopléjica son variantes de alta complejidad clínica hasta con aparición de convulsiones. Se puede generar una parálisis facial. Las de reacciones vasomotoras y secretorias se denominan jaquecas blancas y rojas, respectivamente. Igualmente fue descrita una afasia jaquecosa transitoria, la cual se comporta como un ataque isquémico transitorio con manifestaciones de focalizaciones de déficit motor que revierten, relacionadas con vasoconstricción funcional. Describe que los médicos norteamericanos Joseph I Miller y RO Raulston publicaron un artículo donde describen la peptoterapia, que consiste en la aplicación endovenosa de la peptona seca. Esto se basa en la definición según la cual la fisiopatología

de la jaqueca está relacionada con una reacción anafiláctica como detonante y esta terapia atenúa la respuesta inmunológica (1).

El número 20 del año 1923 trae consigo una detallada definición de los adelantos que para la época se convirtieron en definiciones o problemas terapéuticos, así como técnicas de aplicación frecuentes en la medicina de la segunda década del siglo XX, todo bajo la presentación del Dr. Francisco Antonio Rísquez (Figura 1). Describe en ese orden la aplicación del nitrato de aluminio potásico en las infecciones supurantes, el extracto leucocitario en las infecciones generales, el uso de la insulina en la diabetes, los compuestos de bencilio, el helecho de agua contra los mosquitos, el electrodiagnóstico, la leche en la nutrición humana, el alcoholismo y las reacciones electrónicas de Abrams o energía corporal. Sin duda alguna que de estos temas o aplicaciones terapéuticas las que han trascendido con mayor fundamento de utilización hasta nuestros días han sido la utilización de la insulina en la diabetes y la importancia de los registros de electrodiagnósticos. La discusión que planteó la introducción del uso de la insulina es lo relacionado con el ajuste de las dosis de acuerdo con la edad, el ciclo circadiano y la intensidad clínica de la diabetes. Hubo de superarse muchos escollos de comprensión fisiológicos y fisiopatológicos para estandarizar los cánones de utilización de la insulino terapia como tratamiento de alta efectividad contra la diabetes. Por otra parte, el avance en el electrodiagnóstico pudo

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identificar el curso de la patología cardíaca agudas asociadas a isquemias y a fenómenos arrítmicos, categorizando y gradando estas patologías de gran trascendencia en la salud pública mundial (2).



Figura 1. Francisco Antonio Rísquez (1856-1941).

En el número 21 del año 1923 destaca la comunicación del Dr. Enrique Tejera (Figura 2) donde describe el proceso de diagnóstico del llamado “Carbón sintomático” como se conocía el Carbunco. Se identificaron 38 vacunos muertos en una finca cercana de San Mateo, Estado Aragua, con clínica característica y la verificación de pseudotumores con ruptura supurativa. Destaca que fueron inoculados en el muslo un grupo de acures en los cuales se reprodujo la patología y fueron aislados los microorganismos descritos como representativos del Bacilo de Chauvoei, siendo el germen productor del carbón sintomático o “morriña negra”. Se determina de esta forma el primer grupo de casos de esta patología en el país. Manifiesta que esta epizootia iniciada en el Estado Aragua ha matado a más de 100 terneros por lo cual proponen nuevas medidas profilácticas de contención entre las cuales se impone la incineración de los animales afectados (3).



Figura 2. Dr. Enrique Tejera (1889-1980).

Para el 30 de noviembre de 1923 se edita el número 22 de la Gaceta Médica de Caracas. Encontramos en la sección de Prensa Extranjera una reseña de “Indicaciones terapéuticas generales en la amibiasis hepática”. Describen este trabajo de los franceses François Françon y Jean Hutinel. Plantean los procedimientos generales que incluyen la terapéutica específica aislada y el tratamiento mixto con terapéutica específica como la punción evacuadora y la incisión y el drenaje de la bolsa en absceso. Esta presentación clínica de la infección por *Entamoeba histolytica* ha pasado por innumerables controversias a lo largo de los años, sin embargo, la conducta fundamental por lo general implica el drenaje del contenido en paralelo con la terapia médica vigorosa. Fue en San Petersburgo, Rusia, donde en 1873 el Dr. Fedor Aleksandrovich Lesh (Figura 3), al analizar las heces de un paciente, descubrió y describió al causante de este síndrome clínico complejo.

Debemos recordar que la amibiasis como entidad clínica ha sido descrita desde los tiempos de Hipócrates y se ha constituido como una de las más importantes causas de muerte por infecciones parasitarias. Se ha identificado una interacción huésped-parásito con liberación de

mucina de la mucosa intestinal, en presencia de la flora bacteriana residente en el intestino, la activación del sistema de complemento, y una consistente respuesta inmune, que se constituyen como barreras de defensa contra la *E. histolytica*. Sistemas proteicos de proteasas de cisteína y lectinas actúan como moduladoras de la respuesta de las amibas. Esto hace definir que la patogénesis de la enfermedad se produce por la combinación de los condicionantes del hospedero como respuesta de control de la infección y las características propias del parásito (4).



Figura 3. Dr. Fedor Aleksandrovich Lesh (1840-1903).

La publicación del número 23 se realizó el 15 de diciembre de 1923. Se observa en ella una revisión del Académico Dr. Juan de Dios Villegas Ruíz (Figura 4) sobre la “Epilepsia Jacksoniana por traumatismo de cráneo”. Presenta 3 casos clínicos demostrativos, el primero correspondió a un niño de 2 años y medio quien cayó de la ladera de una montaña y presentó signos de fractura de base del cráneo con otorragia, equimosis peri-palpebral, inmovilidad de pupilas, pulso irregular y convulsión de corta duración. A pesar de su inestabilidad se procuraron cuidados muy próximos con evaluación otológica, cesaron las hemorragias de forma espontánea y no se presentaron otras convulsiones. Se indicó adrenalina en ampollas y a los 8 días se mostraba recuperado plenamente, estableciendo que se

trataba de una conmoción cerebral. El segundo caso, que fue mortal, se debió a un atropellamiento por vehículo en movimiento. Mostró contusiones abiertas craneales con deformidad y deterioro cognitivo inmediato y agravamiento progresivo. Presentó una fase inicial convulsiva episódica. El caso final fue un niño de 10 años con traumatismo accidental parietal izquierdo producido por un trabajador en un mercado de mulas. El niño se levantó y fue a su casa en estado inestable. Presentó cefalea, vómitos y desorientación y al cuarto día una importante confusión mental. Se le hicieron medidas generales y regresó a su casa presentando luego convulsiones incoercibles de epilepsia Jacksoniana del lado derecho contralateral al traumatismo, que ameritaron enemas de hidrato de cloral para lograr efecto anestésico.

El Dr. Luis Razetti discutió el tema presentado y emitió su opinión para dar importancia a esta entidad clínica. En su opinión destacó el hecho que la intervención médica debe ser muy tempranamente para asegurar una terapia efectiva, sin olvidar la altísima mortalidad que presentan estos accidentes que comprometen áreas anatómicas muy delicadas (5).

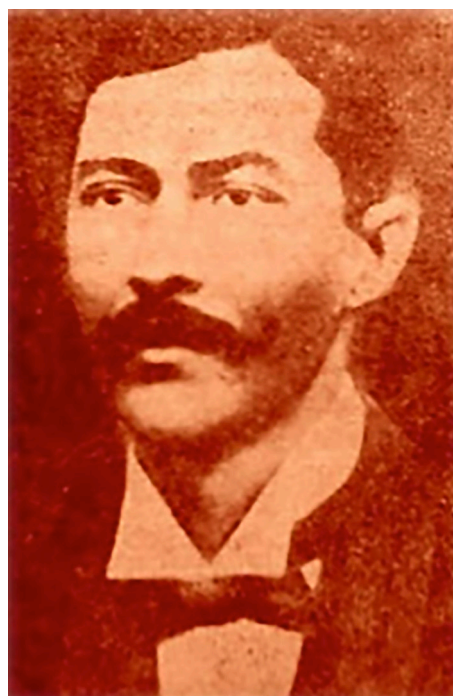


Figura 4. Dr. Juan de Dios Villegas Ruíz (1868 - 1928).

La Gaceta Médica de Caracas cierra el año con el número 24, publicado el 31 de diciembre de 1923, con la presentación de una revisión de Notas breves sobre Paludismo, en la Sección Patología Tropical, escrita por el Dr. Edmundo Chaumer, dedicado a su maestro Dr. Luis Razetti. Describe el paludismo como un síndrome febril inconfundible, con síntomas tan precisos y claros que sería para un médico un fracaso terrible el diagnóstico de otra patología de sus signos y síntomas característicos. También conocida como malaria, es una enfermedad infecciosa producida por parásitos del género Plasmodium, y transmitida por las hembras de varias especies de mosquitos Anopheles. Estudios antropológicos han sugerido que pudo haberse transmitido al humano por los gorilas occidentales. Fue catalogada como la primera enfermedad de importancia entre las patologías debilitantes y hoy mueren más de 400 000 personas por año por su causa, siendo la mayoría de las víctimas unos 240 000 niños. Es importante recordar que los estudios científicos sobre la malaria se completaron en 1880, adelantados por el médico militar francés Charles Louis Alphonse Laveran (Figura 5), a partir de su trabajo en Argelia. Fue el primer investigador que observó los parásitos dentro de los glóbulos rojos al estudiar personas con signos y síntomas de la malaria (6).

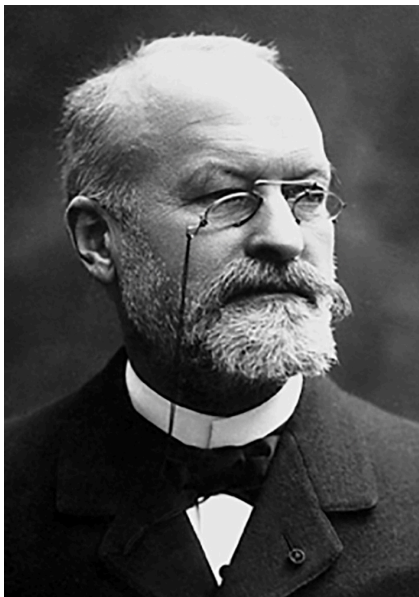


Figura 5. Charles Louis Alphonse Laveran (1845-1942).

Hace 50 años: Octubre – Diciembre 1973

Nos centramos en la reseña de los números 11 y 13 del año 1973. En este número observamos la publicación de “Un caso de Schwannoma de la laringe”. Este trabajo presenta como primer autor al Dr. Franz Conde Jahn. Tomando en cuenta se trata de una rara localización, se recuerda que fue en 1925 cuando se publicó el primer registro a cargo de un Otorrinolaringólogo alemán. Estos tumores se caracterizan por ser generalmente benignos y se manifiestan con crecimiento expansivo, y por ser de naturaleza neural se desarrollan en zonas anatómicas de alta inervación como la cara laríngea de la epiglotis, el espacio inter-aritenoideo, las bandas ventriculares y los repliegues ariteno-epiglóticos. El caso referido se presentó en un niño de 13 años de edad. La tumoración se localizó en el vestíbulo, en la mitad derecha del órgano. En el protocolo operatorio se extirpó el tumor en varios fragmentos, identificando una formación quística superficial. Se pudo controlar fácilmente la hemorragia. El estudio histopatológico estableció el diagnóstico de Schwannoma benigno o Neurilemoma que es su otra acepción terminológica (5).



Figura 6. Dr. Franz Conde Jahn (1901-1977).

Hace 25 años: Octubre – Diciembre 1998

En el volumen 106 de la Gaceta Médica de Caracas de 1998 encontramos una interesante investigación sobre “Infección vaginal por el virus del papiloma humano (VPH)” publicada por los Drs. Rosara Milgrom, Teresa Fuenmayor y Francisco Rincón, entre otros. Estudiaron 25 mujeres con lesiones papilares de la vagina en el Hospital Carlos J. Bello de la Cruz Roja Venezolana entre 1996 y 1997. Tomaron 2 muestras, una para investigación de cepas del VPH 6, 11, 16, 18, 31,33 y 35 a través de la reacción en cadena de polimerasa (PCR) y la otra para procesamiento de anatomía patológica convencional. De todas 11 mostraron cambios histopatológicos sugestivos para VPH y en 8 de las muestras se determinaron secuencias de cepas

virales investigadas. De todas 6 (75 %) resultaron cepas de bajo riesgo, 1 caso (12,5 %) positivo para cepas de riesgo intermedio y 1 (12,5 %) resultó para cepas de alto riesgo oncogénico. En contraste las citologías cérvico-vaginales de las mismas pacientes no mostraron diagnósticos de hallazgos compatibles con VPH (6).

REFERENCIAS

1. Gaceta Médica de Caracas. 1923;30(19):289-304
2. Gaceta Médica de Caracas. 1923;30(20):305-320
3. Gaceta Médica de Caracas. 1923;30(21):321-336
4. Gaceta Médica de Caracas. 1923;30(24):369-384
5. Gaceta Médica de Caracas. 1973;81(11-12):451-552
6. Gaceta Médica de Caracas. 1998;106(4):491-495

Vida de la Academia, Resúmenes de los trabajos presentados y Notas Bibliográficas

Life of the Academy, Summary of the papers presented
and the Bibliographic Notes

Enrique Santiago López-Loyo

Individuo de Número, Sillón XXXI

VIDA DE LA ACADEMIA

CONMEMORACIÓN LX ANIVERSARIO DE LA PROMOCIÓN DE MÉDICOS CIRUJANOS “BICENTENARIO DE ESTUDIOS MÉDICOS” DE LA UNIVERSIDAD CENTRAL DE VENEZUELA 1963

El jueves 14 de septiembre de 2023 en Sesión Extraordinaria se realizó en modalidad mixta, presencial y virtual, el acto por la Conmemoración LX Aniversario de la Promoción de Médicos Cirujanos “Bicentenario de los Estudios Médicos” de la Universidad Central de Venezuela (UCV) 1963.

El Secretario Académico Dr. Marco Sorgi-Venturoni anunció que se ha verificado el cuórum y se inicia el acto con Palabras de la Presidenta Dra. Ysis Nézer de Landaeta, quien agradeció la presencia de la Dra. María Fátima Garcés, Vice Rectora Académica de la UCV y del Dr. Mario Patiño, Decano de la Facultad de Medicina de la UCV.

A continuación la Académica Dra. Claudia Blandenier de Suárez (Figura 1), Individuo de Número Sillón XXI, procedió a presentar el Discurso de Orden en representación de los integrantes de la promoción quien realiza un emotivo análisis histórico acerca de la creación y evolución de la promoción, destaca las elevadas posiciones alcanzadas por los médicos de la promoción y la producción académica, científica, cultural y artística de los mismos y destacó el desarrollo ético y moral de sus compañeros.

Manifestó “Hoy, un grupo representativo de nuestra promoción, aproximadamente el 26,0 %, de los que quedamos vivos, nos hemos congregado esta mañana, en un acto de acción de gracias a Dios y a la Virgen, en la Santa misa, donde elevamos nuestras oraciones por nuestros compañeros fallecidos y por aquellos que no nos pueden acompañar hoy por diversos motivos personales, especialmente por los que están enfermos. Igualmente expresamos nuestros agradecimientos a nuestros padres y maestros que hicieron posible la culminación de nuestros estudios médicos, así como a nuestra Universidad Central de Venezuela, la casa que vence y vencerá la sombra de la ignorancia y protervia. También agradecemos, la generosidad de los Académicos que nos reciben en este vetusto lugar, cuna y representante de la Ciencia médica venezolana”.

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“El día viernes 13 de septiembre de 1963, en el Aula Magna de nuestra Universidad Central de Venezuela, recibimos de manos del Rector Dr. Jesús María Bianco Torres, nuestro Título de Médico-Cirujano. En su discurso, que era su primera actividad como rector, hizo votos para que tuviésemos merecidos triunfos en nuestro ejercicio profesional e hizo alusión a nuestros familiares que este día cosechaban felices, el fruto de sus desvelos y sacrificios. El Rector mencionó a su hijo mayor Jesús, Chucho para nosotros, quien estaba en nuestro grupo. A parte de los cuatro pares de hermanos que se graduaban, es digno de mencionar al señor Ciro Mendoza Torres quien a los 53 años se graduaba con su hijo. El Rector nos dejó un mensaje claro” hagáis ante vuestras conciencias, la promesa formal de “no adulterar los ideales ciudadanos”.

“En este momento, se agolpan en nuestras mentes, los recuerdos de lo que deseábamos realizar y que tal vez no pudimos alcanzar. Nuestros ojos miran al camino recorrido y se juntan los recuerdos de lo que hemos hecho en el campo profesional. Hemos sido testigos de la transformación sustantiva y sintáctica de la Biología, trayendo como consecuencia la formación a nivel mundial, de movimientos Bioéticos, que surgen como una nueva forma de conducta en un mundo posmoderno”.

“Pero no todo termina hoy, cargados de ilusión y esperanza seguiremos luchando por el bienestar de la salud de la población de nuestro país, hasta que Dios nos llame a su seno. Deseamos que nuestra experiencia adquirida, sea útil para la medicina venezolana y estamos convencidos que la sabiduría consiste en aceptar nuestra realidad física actual. Hemos llegado al momento sublime de la paz interior, de las ambiciones abolidas, de los odios perdonados y de las envidias fundidas. Nuestra promoción, se caracteriza por su cohesión, consolidada por el tiempo. Hoy, aprovecharemos cada minuto que respiramos para compartir, porque quizás para algunos de nosotros, será el último encuentro. Para concluir, consideren estas palabras como el grito del cisne cantor, de una generación que ingresó hace 60 años a la palestra del ejercicio médico, llena de entusiasmo y con un gran amor al prójimo, que es la esencia del arte de curar”.

A continuación, la Dra. María Fátima Garcés, Vice Rectora Académica de la UCV dirigió su mensaje destacando el valor institucional de la UCV que trascendió a lo largo de los años y ha dejado un legado imborrable en el país.

Cumplida la agenda del día se clausura esta Sesión extraordinaria.



Figura 1. Dra. Claudia Blandenier de Suárez.

SIMPOSIO SOBRE DIABETES MELLITUS
JUEVES 21 DE SEPTIEMBRE DE 2023
COMISIÓN DE MEDICINA Y ESPECIALIDADES
MÉDICAS
COORDINADOR: DR. JOSÉ LUIS CEVALLOS
GONZÁLEZ, MIEMBRO CORRESPONDIENTE
NACIONAL N° 4

Conferencia 1: Epidemiología Nacional y Mundial de la Diabetes Mellitus

Ponente: Dra. Maritza Duran (Figura 2).

Resumen

En las últimas cuatro décadas el número de personas que vive con diabetes aumentó de 108 millones en 1980 a 463 millones en 2019. Para

2021 la Federación Internacional de Diabetes (IDF) contabilizó 536,6 millones de adultos entre 20 y 79 años con diabetes, 10,5 % de la población mundial, para 2045 se espera un aumento de 51 %, 783,2 millones de personas viviendo con diabetes, 12,2 % de la población mundial. Este aumento será más marcado en los países de medianos y bajos ingresos. La región de mayor prevalencia es Oriente Medio y Norte de África con 16,2 % y la de menor, África con 4,5 %. En Sur y Centro América, la prevalencia es de 9,5 %. 1.1 millones de niños y adolescentes menores de 20 años viven con diabetes tipo 1, no ha sido posible calcular la cantidad de niños y adolescentes con diabetes tipo 2. La carga global de la diabetes aumentó de forma significativa. La diabetes es una de las 10 primeras causas de muerte en el mundo, las personas que viven con diabetes tienen 2 a 3 veces más riesgo de mortalidad por todas las causas, y está asociada a infecciones, enfermedad cardiovascular, ictus, enfermedad renal crónica, hepática y cáncer. Las muertes por diabetes en el mundo entre 1990 y 2017 aumentaron en 125,5 %, de 0,61 millones en 1990 a 1,37 millones en 2017. En el año 2021 la diabetes fue responsable de 6,7 millones de muertes en el mundo. Los años de vida ajustados por discapacidad o DALY's por sus siglas en inglés también aumentaron de 31,3 millones en 1990 a 67,9 en 2017.



Figura 2. Dra. Maritza Durán.

En Venezuela, el Estudio Venezolano de Salud Cardiometabólica (EVESCAM), mostró una prevalencia de diabetes de 12,3 %, mayor en los hombres (14,5 %), que en las mujeres (10,3 %). Las regiones con mayor prevalencia son la Occidental con 14,3 %, la Central (13,9 %) y Capital con 13,5 %. El 34,9 % de la población venezolana tiene prediabetes. Casi 2,5 millones de venezolanos.

Conferencia 2: Fisiopatología de la Diabetes Mellitus

Ponente: Dra. Irene Stulin (Figura 3).

Resumen

La Diabetes mellitus tipo 1 es un desorden complejo autoinmune con múltiples factores implicados en su fisiopatología tales como genéticos, inmunológicos y medio ambientales. La alteración fundamental se expresa en la funcionalidad de las células B y se traducirá en alteración de los valores glicémicos. En individuos genéticamente susceptibles, el proceso autoinmune se desencadena por estímulos infecciosos o ambientales, los cuales pueden ocurrir tanto in útero, como en el primer mes o años de vida, afectando el inicio o la continuación de la autoinmunidad sobre dichas células. En la patogénesis de la Diabetes mellitus tipo 2 involucra la interacción de factores genéticos y ambientales. Los factores medio ambientales como exceso de ingesta calórica, sedentarismo y estilo de vida, juegan un rol crítico en el Desarrollo de la DM tipo 2. Adicionalmente la epigenética, la alteración de los ritmos circadianos y el microbioma son factores ambientales involucrados en la génesis de la misma. La alteración de la glicemia se produce por la resistencia insulínica en los tejidos periféricos, secreción anormal de insulina en respuesta al estímulo de la glicémico e incremento en la producción de glucosa por el hígado. Apesar del debate sobre cuál es el defecto primario, muchos estudios apoyan la hipótesis de que la insulino-resistencia precede el defecto de la secreción de insulina.



Figura 3. Dra. Irene Stulin.



Figura 4. Dra. Gisela Merino.

SIMPOSIO SOBRE DIABETES MELLITUS
JUEVES 28 DE SEPTIEMBRE DE 2023
COMISIÓN DE MEDICINA Y ESPECIALIDADES
MÉDICAS
COORDINADOR: DR. JOSÉ LUIS CEVALLOS
GONZÁLEZ, MIEMBRO CORRESPONDIENTE
NACIONAL N° 4

Conferencia 1: Dispositivos mecánicos y automáticos para el tratamiento de la Diabetes Mellitus

Ponente: Dra. Gisela Merino (Figura 4)

Resumen

Se expuso sobre las nuevas insulinas que existen actualmente en el mercado, sobre el monitoreo continuo de glucosa y sus sensores que se ha sobrepuesto a la glicemia capilar y las bombas de infusión de insulina.

Conferencia 2: Nuevos enfoques terapéuticos de la Diabetes Mellitus

Ponente: Dr. Marcos Lima (Figura 5)

Resumen

La Diabetes Mellitus es una enfermedad heterogénea que se asocia a una elevada morbimortalidad cardiovascular. En el pasado, las Guías de Práctica Clínica para el manejo de la Diabetes se centraban en el cumplimiento de metas de control glucémico; sin embargo, diferentes ensayos clínicos mostraron que el control intensivo de la glucosa si bien es cierto produce una disminución de las complicaciones microvasculares, no se asocia con una reducción en los eventos cardiovasculares. En esta conferencia, se evaluará el enfoque actual en el manejo de la Diabetes Mellitus haciendo una revisión de las diferentes Guías de Práctica

Clínica que postulan un manejo personalizado, centrado en el paciente y sus comorbilidades. De igual forma, revisaremos la evidencia clínica más actualizada y los fármacos que han demostrado no solo mejorar el control metabólico del paciente diabético, sino también una reducción significativa en la tasa de eventos cardiovasculares y en la progresión de la enfermedad renal crónica.



Figura 5. Dr. Marcos Lima.

“FORO SOBRE: SIMPOSIO “INTELIGENCIA ARTIFICIAL EN MEDICINA”

JUEVES 05 DE OCTUBRE DE 2023

Conferencia: Inteligencia Artificial en Medicina. Una introducción para profesionales médicos

Ponente: Pedro Simón Romero Cánovas (Figura 6)

Resumen

La inteligencia artificial (IA) es una rama de las ciencias de la computación que busca crear sistemas capaces de realizar tareas que normalmente requieren inteligencia humana, como el aprendizaje, el razonamiento y la toma de decisiones. La IA tiene múltiples aplicaciones en el campo de la medicina, desde el diagnóstico y tratamiento de enfermedades hasta

la investigación y desarrollo de nuevos fármacos y terapias. En esta presentación se dará una visión general de los conceptos básicos de la IA, su historia y evolución, sus principales técnicas y métodos, y sus ventajas y desafíos. También se mostrarán algunos ejemplos concretos de cómo la IA se está utilizando en la medicina actual y cómo puede contribuir a mejorar la calidad y eficiencia de la atención sanitaria.



Figura 6. Lic. Pedro Simón Romero Cánovas.

ELECCIÓN DE TRES INDIVIDUOS DE NÚMERO PARA OCUPAR LOS SILLONES V, VIII Y XII

JUEVES 26 DE OCTUBRE DE 2023

Se convocan a tres Sesiones Extraordinarias el 26 de octubre de 2023, para elegir a los nuevos Individuos de Número que ocuparan los Sillones V, VIII y XII. La votación se realizó en modalidad mixta presencial y virtual por la plataforma Zoom.

Se procede a nombrar a la Comisión Electoral en la persona de los Académicos Drs. Oscar Beaujon-Rubín y Felipe Martín Piñate, presentes en el Salón de Sesiones.

Primera convocatoria. Elección de Individuo de Número para ocupar el Sillón V, vacante por el fallecimiento del Académico Dr. Miguel González Guerra

Los candidatos a la elección son, el Dr. José Luis Cevallos González, Miembro Correspondiente Nacional Puesto N° 4 y el Dr. José Manuel De Abreu Do Monte. Miembro Correspondiente Nacional Puesto N° 43.

Se indica que pueden ejercer el voto: a) los conectados por Zoom por medio de la Planilla de votación electrónica en pantalla de sus monitores y b) los presentes en sala, por medio de las papeletas que el Dr. Felipe Martín Piñate entrega y son recolectadas. Se habilitan 18 electores totales.

Se procedió al conteo de los votos y el resultado fue el siguiente:

Dr. José Manuel De Abreu Do Monte: 10 votos

Dr. José Luis Cevallos González: 8 votos

El Dr. Oscar Beaujón y el Dr. Felipe Martín Piñate, miembros de la Comisión Electoral, le anuncian a la Presidenta el resultado de la elección de “Individuo de Número para ocupar el Sillón V” resultando electo por mayoría de votos el Dr. José Manuel De Abreu Do Monte (Figura 7).



Figura 7. Dr. José Manuel De Abreu Do Monte.

Segunda convocatoria. Elección del Individuo de Número Sillón VIII vacante por el fallecimiento del Dr. Leopoldo Briceño-Iragorry

El único Candidato es el Dr. Eduardo Morales Briceño, Miembro Correspondiente Nacional Puesto Número 33. Están habilitados 20 Individuos de Número para la votación.

Se indica que pueden ejercer el voto: a) los conectados por Zoom por medio de la planilla de votación electrónica en pantalla de sus monitores y b) los presentes en sala, por medio de las papeletas entregadas por el Dr. Felipe Martín Piñate. Una vez cumplida la votación se procedió al conteo de los votos y el resultado fue el siguiente:

Dr. Eduardo Morales Briceño: 20 Votos, Electo por unanimidad

Los Drs. Oscar Beaujón, y Felipe Martín Piñate, miembros de la Comisión Electoral, le anuncian a la presidencia el resultado de la elección para “Individuo de Número del Sillón VIII”, siendo electo por UNANIMIDAD el Dr. Eduardo Morales Briceño (Figura 8).



Figura 8. Dr. Eduardo Morales Briceño.

Tercera convocatoria. Elección del Individuo de Número que ocupara el Sillón XII, vacante por el fallecimiento del Dr. Alfredo Díaz Bruzual

Los Candidatos son la Dra. Rocca Enriqueta Sileo Giuseffi, Miembro Correspondiente Nacional Puesto Número 38 y el Dr. Oswaldo Guerra Sagarzazu, Miembro Correspondiente Nacional Puesto Número 9.

Se indica que pueden ejercer el voto los conectados por Zoom y los presentes en sala, recibiendo las papeletas del Dr. Felipe Martín Piñate.

Se procedió al conteo de los votos y el resultado fue el siguiente:

Dra. Rocca Enriqueta Sileo Giuseffi, 17 votos.

Dr. Oswaldo Guerra Sagarzazu, 3 votos.

El Dr. Oscar Beaujón, en su condición de Presidente de la Comisión de Electoral anuncia la elección para el Sillón XII como Individuo de Número a la Dra. Rocca Enriqueta Sileo Giuseffi (Figura 9).



Figura 9. Dra. Rocca Enriqueta Sileo Giuseffi.

SESIÓN ORDINARIA DEL JUEVES 26 DE OCTUBRE DE 2023

SIMPOSIO DE LA SOCIEDAD VENEZOLANA DE OFTALMOLOGIA: “NUEVAS TENDENCIAS EN GLAUCOMA, CÓRNEA Y CIRUGÍA DE CATARATAS”

COMISIÓN DE MEDICINA Y ESPECIALIDADES MÉDICAS

COORDINADOR: DR. OSCAR BEAUJON RUBIN, INDIVIDUO DE NÚMERO SILLÓN XIV

Conferencia 1: Glaucoma, presión intraocular, laser, Rho quinasa, campo visual.

Ponente: Dr. Oscar Beaujon-Balbi (Figura 10)

Resumen

El glaucoma sigue siendo una enfermedad ocular importante en 2023, afectando a más de 76 millones de personas en todo el mundo. Es conocido como el “ladrón silencioso de la visión” debido a su naturaleza asintomática en las etapas iniciales. El diagnóstico temprano es crucial para prevenir daños irreversibles. Los tratamientos más novedosos para el glaucoma incluyen la terapia con láser, que mejora el drenaje del líquido intraocular, reduciendo la presión en el ojo. Esta opción no invasiva puede reemplazar la cirugía tradicional. Además, nuevos fármacos como los inhibidores de la Rho quinasa están mostrando eficacia para reducir la presión intraocular al relajar los músculos del ojo y mejorar el flujo de líquido. La terapia génica también está siendo investigada. Se buscan enfoques que introduzcan genes específicos en las células del ojo para proteger el nervio óptico y ralentizar la progresión del glaucoma. Aunque esta terapia está en sus primeras etapas, ofrece un gran potencial para el tratamiento futuro. El glaucoma sigue siendo una preocupación de salud relevante en 2023. La detección temprana y el tratamiento adecuado son fundamentales para evitar la pérdida de visión. Los avances en tecnología y medicamentos han brindado esperanza en la lucha contra esta enfermedad. Los tratamientos con láser y los nuevos fármacos ofrecen opciones efectivas y menos invasivas para los pacientes con glaucoma. La investigación en terapia génica también promete mejorar el manejo de la enfermedad en

el futuro. Es esencial crear conciencia sobre el glaucoma y fomentar la detección precoz para mejorar la calidad de vida de quienes lo padecen.



Figura 10. Dr. Oscar Beaujon-Balbi.

Conferencia 2: Avances en el diagnóstico y tratamiento de la Córnea.

Ponente: Dr. Tomas Ricardo Heredia (Figura 11)

Resumen

En los últimos años, se han producido significativos avances en el diagnóstico y tratamiento de las enfermedades de la córnea, lo cual ha mejorado la calidad de vida de numerosos pacientes alrededor del mundo. En cuanto al diagnóstico, las técnicas tradicionales han sido complementadas por tecnologías de vanguardia que permiten una evaluación más precisa de la córnea. Por ejemplo, la tomografía de coherencia óptica (OCT) ha revolucionado la forma en que se visualiza la estructura corneal, proporcionando imágenes de alta resolución y permitiendo una detección temprana de anomalías. Además, las topografías corneales computarizadas permiten un mapeo tridimensional de la superficie corneal, lo que ayuda a identificar irregularidades y

deformaciones que antes podrían haber pasado desapercibidas. En cuanto al tratamiento, se han desarrollado nuevas opciones terapéuticas que han mejorado los resultados y la recuperación de los pacientes. Una de las innovaciones más destacadas es la cirugía refractiva con láser, como la técnica LASIK, que ha demostrado ser eficaz para corregir defectos de refracción, como la miopía, hipermetropía y astigmatismo. Además, el trasplante de córnea ha experimentado mejoras significativas gracias a técnicas como el trasplante endotelial selectivo, que permite reemplazar solo las capas dañadas de la córnea, acelerando la recuperación y mejorando los resultados visuales. La terapia con células madre también ha abierto nuevas posibilidades en el campo del tratamiento corneal. Las células madre provenientes de diferentes fuentes, como la médula ósea o el limbo corneal, han demostrado su capacidad para regenerar tejido corneal dañado, lo que podría evitar la necesidad de trasplantes y mejorar la visión de los pacientes. En conclusión, los avances en el diagnóstico y tratamiento de la córnea han llevado a una mejor comprensión de las enfermedades corneales y a opciones terapéuticas más efectivas. Estas mejoras han permitido una detección temprana de las enfermedades corneales, así como una recuperación más rápida y resultados visuales mejorados para los pacientes. A medida que la investigación y la tecnología continúen avanzando, es probable que se produzcan aún más avances en este campo, brindando esperanza a aquellos que sufren de enfermedades corneales.



Figura 11. Dr. Tomas Ricardo Heredia.

Conferencia 3: Actualización en lentes intraoculares para cirugía de cataratas

Ponente: Dr. Ángel Pineda (Figura 12)

Resumen

En los últimos años, los avances en tecnología médica han revolucionado la cirugía de cataratas, específicamente en lo que respecta a los lentes intraoculares utilizados en el procedimiento. Estos lentes son implantes colocados en el ojo después de la extracción de la catarata, y su objetivo principal es restaurar la visión del paciente. Una de las principales actualizaciones en los lentes intraoculares es la capacidad de corregir no solo la catarata, sino también otros problemas de visión, como la presbicia o la miopía. Anteriormente, después de la cirugía de cataratas, los pacientes debían depender de anteojos o lentes de contacto para corregir estos problemas adicionales. Sin embargo, los nuevos lentes intraoculares multifocales y acomodativos ofrecen la posibilidad de una visión más completa, reduciendo la dependencia de gafas después de la cirugía. Los lentes intraoculares multifocales son capaces de enfocar tanto a distancia como de cerca, permitiendo a los pacientes realizar actividades diarias sin la necesidad de anteojos. Estos lentes utilizan diferentes zonas ópticas para lograr esta visión multifocal. Por otro lado, los lentes acomodativos imitan el funcionamiento natural del cristalino, permitiendo un enfoque flexible a diferentes distancias.

Además, los avances en los materiales utilizados en los lentes intraoculares han mejorado su calidad y durabilidad. Los lentes modernos están hechos de materiales biocompatibles de alta calidad que reducen el riesgo de complicaciones y mejoran la calidad de la visión del paciente. En resumen, la actualización en los lentes intraoculares ha permitido mejorar significativamente los resultados de la cirugía de cataratas. Los pacientes ahora tienen la opción de corregir no solo la catarata, sino también otros problemas de visión, lo que les brinda una visión más completa y reduce su dependencia de gafas o lentes de contacto. Los avances en los materiales también han contribuido a una mayor calidad y durabilidad de los lentes. Estos avances en la tecnología de lentes intraoculares representan

un gran paso adelante en la mejora de la calidad de vida de las personas que sufren de cataratas y otros problemas de visión relacionados.



Figura 12. Dr. Ángel Pineda.

ELECCIÓN DE CUATRO INDIVIDUOS DE NÚMERO PARA OCUPAR LOS SILLONES XXIV, XXXIII, XXXIV Y XXXV.

JUEVES 09 DE NOVIEMBRE DE 2023

Se convocan a cuatro Sesiones Extraordinarias el 09 de noviembre de 2023 para elegir a los nuevos Individuos de Número que ocuparan los Sillones XXIV, XXXIII, XXXIV y XXXV. La votación se realizó en modalidad mixta presencial y virtual por la plataforma Zoom.

Se procede a nombrar a la Comisión Electoral en la persona de los Académicos Drs. Claudio Aoün y Rafael Apitz, presentes en el Salón de Sesiones. Se habilitan a 23 electores entre la sala electrónica y lo presentes en el Salón.

Primera Convocatoria. Elección de un Individuo de Número para ocupar el Sillón XXIV vacante por el fallecimiento del Académico Dr. Francisco Kerdel Vegas

Los candidatos son el Dr. Andrés Soyano López, Miembro Correspondiente Nacional

Puesto N° 47 y el Dr. José Trinidad Nuñez Tróconis, Miembro Correspondiente Nacional Puesto N° 37.

La Comisión Electoral indica que pueden ejercer el voto por dos opciones, los conectados por la plataforma Zoom por medio de la planilla de votación electrónica en pantalla de sus monitores y los presentes en sala, por medio de las papeletas que el Dr. Rafael Apitz-Castro, entrega y recoge. Se procedió al conteo de los votos, sumando los votos expresados por la boleta electrónica y los votos en físico y el resultado fue el siguiente:

Dr. Andrés Soyano López: 19 votos

Dr. José Trinidad Nuñez Tróconis: 3 votos

Nulos: 1 voto

Los Drs. Claudio Aoün y Rafael Apitz, miembros de la Comisión Electoral, le anuncian a la presidencia el resultado de la elección para “Individuo de Número del Sillón XXIV”, informando que resultó electo el Dr. Andrés Soyano López (Figura 13).



Figura 13. Dr. Andrés Soyano López.

Segunda Convocatoria. Elección del Individuo de Número para ocupar el Sillón XXXIII, vacante por el fallecimiento del Dr. Nicolás Bianco Colmenares

Los candidatos son los Drs. Mirian del Valle Marcano Torres, Miembro Correspondiente Nacional Puesto N° 15 y el Dr. Nelson Urdaneta Lafeé, Miembro Correspondiente Nacional Puesto N° 31.

La Comisión Electoral indica que pueden ejercer el voto por dos opciones, los conectados por la plataforma Zoom por medio de la planilla de votación electrónica en pantalla de sus monitores y los presentes en sala, por medio de las papeletas que el Dr. Rafael Apitz-Castro, entrega y recoge. Se procedió al conteo de los votos, sumando los votos expresados por la boleta electrónica y los votos en físico y el resultado fue el siguiente:

Dra. Mirian Del Valle Marcano Torres: 17 votos

Dr. Nelson Urdaneta: 5 votos

Nulos: 1 voto

Los Drs. Claudio Aoün y Rafael Apitz, miembros de la Comisión Electoral, le anuncian a la presidencia el resultado de la elección para “Individuo de Número del Sillón XXXIII”, informando que resultó electa la Dra. Mirian del Valle Marcano Torres (Figura 14).



Figura 14. Dra. Mirian del Valle Marcano Torres.

Tercera Convocatoria. Elección del Individuo de Número para ocupar el Sillón XXXIV, por fallecimiento del Dr. Otto Lima Gómez

Los Candidatos son el Dr. Sergio Aquiles Osorio Morales, Miembro Correspondiente Nacional Puesto N° 13 y el Dr. José Efraín Rodríguez Casas, Miembro Correspondiente Nacional Puesto N° 29.

La Comisión Electoral indica que pueden ejercer el voto por dos opciones, los conectados por la plataforma Zoom por medio de la planilla de votación electrónica en pantalla de sus monitores y los presentes en sala, por medio de las papeletas que el Dr. Rafael Apitz-Castro, entrega y recoge. Se procedió al conteo de los votos, sumando los votos expresados por la boleta electrónica y los votos en físico y el resultado fue el siguiente:

Dr. Sergio Aquiles Osorio Morales: 12 votos

Dr. José Efraín Rodríguez Casas: 10 votos

Nulo: 1 voto

Los Drs. Claudio Aoün y Rafael Apitz, miembros de la Comisión Electoral, le anuncian a la presidencia el resultado de la elección para “Individuo de Número del Sillón XXXIV”, informando que resultó electo el Dr. Sergio Aquiles Osorio Morales (Figura 15)..



Figura 15. Dr. Sergio Aquiles Osorio Morales.

Cuarta Convocatoria. Elección de un Individuo de Número que ocupará el Sillón XXXV, vacante por el fallecimiento del Dr. Italo Marsiglia.

Los Candidatos son el Dr. Franco José Calderaro Di Ruggiero, Miembro Correspondiente Nacional Puesto N° 41 y el Dr. Israel Nicasio Montes de Oca Daggert, Miembro Correspondiente Nacional, Puesto N° 5.

La Comisión Electoral indica que pueden ejercer el voto por dos opciones, los conectados por la plataforma Zoom por medio de la planilla de votación electrónica en pantalla de sus monitores y los presentes en sala, por medio de las papeletas que el Dr. Rafael Apitz-Castro, entrega y recoge. Se procedió al conteo de los votos, sumando los votos expresados por la boleta electrónica y los votos en físico y el resultado fue el siguiente:

Dr. Israel Montes de Oca: 11 votos

Dr. Franco José Calderaro Di Ruggiero: 10 votos

Nulos: 2 votos

Los Drs. Claudio Aoün y Rafael Apitz, miembros de la Comisión Electoral, le anuncian a la presidencia el resultado de la elección para “Individuo de Número del Sillón XXXV, informando que resultó electo el Académico Dr. Israel Montes de Oca Daggert (Figura 16).



Figura 16. Dr. Israel Montes de Oca Daggert.

**SESIÓN ORDINARIA DEL JUEVES 9 DE
NOVIEMBRE DE 2023**

**COMISIÓN DE MEDICINA Y ESPECIALIDADES
MÉDICAS**

SIMPOSIO SOBRE DEMENCIA PARTE I

**RESÚMENES DE LOS TRABAJOS
PRESENTADOS**

Conferencia 1: Demencias. Epidemiología y factores de riesgo

Ponente: Dr. Aquiles Rafael Salas Jiménez (Figura 17)

Resumen

Las demencias representan las enfermedades neurodegenerativas de mayor relevancia, aunque existen diversas causas asociadas a su origen, es la enfermedad de Alzheimer (EA) la de mayor prevalencia representando el 65 % a 70 % de los casos. El peso de la enfermedad de Alzheimer en los individuos y en la sociedad unido al incremento en la longevidad de los seres humanos, han resultado en el incremento del interés por el diagnóstico y el tratamiento de estas enfermedades neurodegenerativas. Con el desarrollo durante las últimas 3 décadas de biomarcadores específicos que identifica la patología molecular de la EA, está claro que la demencia Alzheimer es una patología crónica que se desarrolla en forma silenciosa por al menos 10 años previos a la aparición de los síntomas. Una consecuencia importante del desarrollo de estos biomarcadores es que la EA, habiendo sido reconocida por más de un siglo por sus manifestaciones clínicas, ahora es codificada por biomarcadores anormales del proceso patológico de EA. Se ofrecen herramientas para el diagnóstico en estadios más tempranos de la enfermedad y más precisión para diferenciar de otras demencias.

En el año 2020 habían más de 55 millones de personas viviendo con demencia en el mundo, para el año 2030 se estiman 78 millones y 139 millones en el año 2050. El 60 % de estas personas viven en países de bajos y medianos ingresos y para el año 2050 se elevará al 71 %. Estudios de población realizados en 8 países, Brasil, Chile,

Cuba, Perú y Venezuela, muestran prevalencia de 7,1 % que se duplica cada 5 años en mayores de 65 años. La incidencia de demencia fue 13,8 por mil personas - año, la enfermedad de Alzheimer fue 7,7. En revisión sistemática de 17 países en Latino América, la prevalencia de todas las causas de demencia fue 16,66 % y se observó mayor prevalencia en mujeres 8,97 % y en residentes rurales 8,68 %. Las personas sin educación formal tuvieron el doble de frecuencia 21,3 % comparados con aquellos con al menos 1 año de educación. La mortalidad por demencia se incrementó 148 % entre 1990 y 2016. En 2016 las demencias fueron la quinta causa de muerte en todo el mundo, responsable de 2,6 millones de muertes. Cada año se identifican 10 millones de nuevos casos, 3,2 segundos un caso nuevo. La incidencia anual de demencia en USA genera una cifra de incremento significativo después de la séptima década de 0,4 % entre 65 a 74 años cambia a 7,6 % en mayores de 75 años; con el incremento de la población mayor de 65 años, se estima que el número total se duplica en 30 años. Sin embargo, tanto en EE.UU como en países desarrollados de Europa Occidental se han reportado evidencias de la disminución de la frecuencia de incidencia y prevalencia en las últimas dos décadas, relacionado a una disminución de riesgos asociados a salud como enfermedades cardiovasculares y cerebrovasculares y el incremento en logros educacionales. En cuanto a factores de riesgo no modificables, la edad es el más fuerte riesgo para EA; otro factor es genético, el 80 % de las variantes de casos están atribuidos a factor genético siendo el alelo E4 de APOE el más fuerte. Un alelo E4 genera 2 a 3 veces mayor riesgo que los no portadores y homocigotos E4 representa un riesgo 10 veces mayor que homocigotos E3/E3. Las mujeres tienen el doble de riesgo de padecer EA, no se ha aclarado la razón más allá que tienen una mayor expectativa de vida comparado a hombres. En cuanto a los factores de riesgo modificables, en un metaanálisis realizado en 2020 de 400 estudios publicados a nivel mundial, las evidencias de factores protectores fueron la longitud mayor de la educación en la infancia, el mayor Índice de Masa Corporal (IMC) en adultos mayores, y mayor participación activa en actividades cognitivas. Los factores negativos identificados fueron diabetes, hipotensión ortostática, hipertensión en edad mediana, trauma craneano, estrés, depresión,

obesidad en edad mediana y cirugía coronaria, adicionalmente, la carencia del ejercicio en la edad mediana y en mayores se han identificado. La hiperhomocisteinemia puede incrementar el riesgo de demencia y el tratamiento con vitamina B6, B12 y ácido fólico lo disminuye. En las últimas dos décadas han propuesto etiología infecciosa para la demencia. Se han publicado en Asia y Europa estudios de población que sugieren que infecciones con herpes tipo 1 y 2 o varicela zoster aumentan el riesgo de demencia en edad avanzada.



Figura 17. Dr. Aquiles Rafael Salas Jiménez.

Conferencia 2: Enfermedad de Alzheimer. Luego de más de 100 años ¿Qué marcadores diagnósticos y perspectivas terapéuticas tenemos?

Ponente: Dr. Ciro Gaona Yáñez (Figura 18)

Resumen

Existe urgente necesidad para el diagnóstico precoz y tratamiento de la Enfermedad de Alzheimer. Al clásico criterio diagnóstico definitivo en autopsia por la cuantificación histológica de 2 lesiones históricas, las placas de



Figura 18. Dr. Ciro Gaona Yáñez.

Beta-Amiloide (β -A) y los ovillos neurofibrilares intracelulares con presencia de la proteína tau (t), se le suma la evaluación de biomarcadores desde el trastorno cognitivo leve (TCL) hasta el estudio de personas con factores de riesgo en fase pre-clínica/pre-sintomática. Biomarcadores: a) En fluidos biológicos: Ha sido exitoso en líquido cefalorraquídeo debido a su contacto directo con el espacio extracelular cerebral. Destacando la presencia de isoformas del β -A (β -A 1-42, β -A 1-40 y su relación), la tau total (T-tau) y la cadena ligera de neurofilamentos (NfL) reflejando degeneración neuronal, y de tau hiperfosforilada y sus variantes (P-tau) en relación con la formación de ovillos neurofibrilares. Otros marcadores se asocian con la neuroinflamación, estrés oxidativo, apoptosis, neuroprotección, etc. Se ha logrado, de manera mínimamente invasiva, la medición de estos biomarcadores en plasma; b) Neuroimagen: La Tomografía de Emisión de Positrones (PET) detecta la carga de β -A y la visualización de tau neurofibrilar mostrando extraordinaria correlación entre las imágenes pre-mortem y el estudio histológico en autopsias. Los inhibidores de colinesterasa (Iche) intentan mejorar el déficit colinérgico y la Memantina, disminuye la excitotoxicidad del glutamato. Estos fármacos no alteran la fisiopatología ni curso de la enfermedad, podrían enlentecer el déficit cognitivo, mejorar síntomas cognitivos y no

cognitivos, aunque este resultado no es universal. La fecunda investigación actual muestra que más del 80 % de los agentes están destinados a modificar el proceso de la enfermedad (entre ellos, los anticuerpos monoclonales anti-amiloide), casi un 10 % intentarían estimular la cognición y el resto van dirigidos a síntomas neuropsiquiátricos.

El hallazgo de biomarcadores confiables permite un diagnóstico temprano y una intervención terapéutica oportuna.

**SESIÓN ORDINARIA DEL JUEVES 16 DE
NOVIEMBRE DE 2023**

**COMISIÓN DE MEDICINA Y ESPECIALIDADES
MÉDICAS**

SIMPOSIO SOBRE DEMENCIA PARTE II

**RESÚMENES DE LOS TRABAJOS
PRESENTADOS**

Conferencia: Demencias. Momentos clínicos y registros vivenciales

Ponente: Dr. Carlos Rojas Malpica (Figura 19)

Resumen

El abordaje médico del problema de las demencias exige una alta capacidad de comprensión del enfermo y sus circunstancias. Una lista de chequeos puede ayudar a sistematizar el diagnóstico y decidir el tratamiento, pero no puede sustituir la entrevista a profundidad de la mejor práctica clínica. El encuentro que propone la fenomenología y la analítica existencial exige penetración empática, estudio del mundo vivencial y el curso biográfico del paciente, para lograr aprehender la continuidad de sentido de cada momento clínico. Es decir, se trata de un encuentro existencial entre el médico y su paciente, de profundidad y significación antropológica. Cada momento de la evolución clínica presenta peculiaridades

ontológicas de alta importancia. Comenzando con la entrevista inicial, donde se revela el diagnóstico, dependiendo del estado evolutivo de la enfermedad, ya se presentan vivencias y tensiones de alta relevancia, como la aceptación y/o rechazo al diagnóstico, el riesgo suicida y los límites de discapacidad que el enfermo está dispuesto a sobrellevar. A medida que la enfermedad avanza y se empobrece la actividad cognitiva y el control psicomotor, o se presentan crisis conductuales, se va haciendo más difícil y agotador para la familia el manejo del paciente. La decisión de internar o seguir con el cuidado en el hogar no está exenta de tensiones y conflictos. Se llega gradualmente a los momentos finales donde se debe decidir la suspensión del tratamiento, que ya resulta ineficaz, y conformarse con cuidados paliativos, mantenerlo tranquilo y que logre dormir. Por último, se plantea el dilema de la eutanasia/distanasia que debe ser considerado por los familiares y el médico tratante, en un consenso nada fácil de lograr. Es imposible hacer buena atención a la salud ignorando el mundo vivencial del paciente y su familia. La fenomenología y la analítica existencial ofrecen una posibilidad para aproximarse al problema antropológico de las demencias que va más allá el mero registro sintomatológico.



Figura 19. Dr. Carlos Rojas Malpica.

Dr. Rogelio Pérez D'Gregorio

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