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por el

DR. LUIS RAZETTI

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y del Congreso Venezolano de Ciencias Médicas

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de Caracas

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y del Congreso Venezolano de Ciencias Médicas

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Ferry Efendi

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Dr. Luis Razetti

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Guest Editor
Ferry Efendi

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Calderaro Di Ruggiero Franco	francocalderarod@hotmail.com
Cardozo Alba	aeco6000@hotmail.com
De Abreu José Manuel	josemanueldeabreu@gmail.com
Díaz Bolaños Jaime	jaime.diazbolaos@gmail.com
Guarecuco Jesús Romero	jesus.jg5.jrg@gmail.com
Krivoy Saúl	alfabeta38@gmail.com
López-Loyo Enrique Santiago	lopezloyoe@gmail.com
Martín Piñate Felipe	felipemartinp@yahoo.es
Miranda Sigfrido	sigfrido.miranda@gmail.com
Mora Eddy Verónica	eddyveronica@gmail.com
O'Daly Carbonel José Antonio	jaocjesus@hotmail.com
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Francisco José Manuel	chenofra@gmail.com
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Mondolfi María Eugenia	memondolfi@gmail.com
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González Reyes Marino	marinogonzalez@gmail.com
Lobo David	davidloboker@gmail.com
Morales Briceño Eduardo	eduardomoralesb@gmail.com
Oletta José Félix	jofeole@hotmail.com
Peña Arciniegas Saul	saulpena09@gmail.com
Reyes Omar	oreyesmorales@gmail.com
Sánchez Daniel	danielsanchez24@yahoo.com
Stegemann Herbert	hstegema@gmail.com
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Goihman Yahr Mauricio	mgoihmanyahr@yahoo.com
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Palacios Igor	ipalacios@mgh.harvard.edu
Perdomo de Ponce Doris	dorisdeponce21@gmail.com
Rodríguez Ramírez Jesús	drjmrodriguezr@yahoo.es
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Rojas Loyola Germán	grojasloyola@gmail.com
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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 impor-tantes? (datos concretos y en lo posible su signifi-cancia 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

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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.,

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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

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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).

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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.

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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.

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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 ingles (máximo 100 palabras) en formato libre.

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Esta sección estará dedicada a contribuciones tendientes a informar al médico acerca de las disposi-ciones 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).

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http:/www.ateproca.com • E-mail: ateproca@gmail.com

EDITORIAL

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Transforming Health in Indonesia: A Pathway to Sustainable Development

Ferry Efendi

Good health is a crucial aspect of human well-being and an important indicator of a nation's progress. To achieve sustainable development in the healthcare industry of Indonesia, it is essential to address the social determinants of health. Factors such as poverty, education, housing, and clean water availability play a significant role in determining the overall health of individuals and communities. By implementing policies that address these determinants, Indonesia can create an environment that promotes healthy living and improves health outcomes. In addition, encouraging community engagement and participation in healthcare decision-making processes can empower individuals and create a sense of ownership in their health, ultimately contributing to the success of Indonesia's health transformation. Recently, Indonesia has taken steps to improve its healthcare system and overcome challenges. This special issue explores Indonesia's ongoing health transformation and the critical measures being taken to achieve sustainable development in the healthcare sector. The papers discuss many issues related to the health of the population as well as factors affecting their health status.

ORCID: 0000-0001-7988-9196

Indonesia's health transformation was driven by a commitment to improve access, promote preventive healthcare, invest in infrastructure, develop human resources, and foster public-private partnerships. Since 2021, the Ministry of Health of Indonesia has launched a health transformation. The six pillars comprise primary service transformation, referral services, health resilience systems, healthcare financing systems, healthcare human resources, and healthcare technology (1). The implementation of the National Health Insurance Program (JKN) has extended coverage and financial protection to millions of Indonesians, but efforts are still needed to ensure equitable access to healthcare across regions and address disparities. Focus on preventive measures is being emphasized to reduce the burden of non-communicable diseases through health education, awareness programs, and regular screenings. Infrastructure development is a priority, with investments aimed at expanding and upgrading healthcare facilities, particularly in rural areas, and strengthening the supply chain for medicines and medical equipment. Additionally, investments in human resources for health, such as education, training, and professional development, are crucial to building a skilled healthcare workforce. Collaboration between the public and private sectors through partnerships is seen as a key driver to mobilizing resources, facilitating knowledge exchange, and developing innovative healthcare solutions (2,3).

Indonesia's efforts to transform its healthcare system reflect its dedication to achieving sustainable development. They have improved access to healthcare, prioritized preventative measures, invested in infrastructure and human resources, and fostered collaborations. These actions lead the way to a healthier and more prosperous future. However, sustaining these efforts requires ongoing commitment, resource allocation, and effective policy implementation. It's essential to prioritize the health and well-being of all Indonesians, ensuring that no one is left behind on the path to a healthier nation.

REFERENCES

1. Ministry of Health. Minister of Health: Health System Transformation Readiness Needs Support from All Parties. 2021. Available from: https://sehatnegeriku.kemkes.go.id/baca/ umum/20211122/1138879/menkes-kesipan-transformation-sistem-kesehatan-butuh-supportan-seat-stakes/
2. Ministry of Health. Rows of Health Transformation by the Minister of Health Budi. Ministry of Health of the Republic of Indonesia. 2022.
3. Ministry of Health. Blueprint for Digital Health Transformation Strategy 2024. Jakarta, Indonesia; 2021.

Transformando la salud en Indonesia: un camino hacia el desarrollo sustentable

Ferry Efendi

La buena salud es un aspecto crucial del bienestar humano y un indicador importante del progreso de una nación. Para lograr un desarrollo sustentable en la industria de la salud en Indonesia, es esencial abordar los determinantes sociales de la salud. Factores como la pobreza, la educación, la vivienda y la disponibilidad de agua limpia juegan un papel importante en la determinación de la salud general de las personas y las comunidades. Al implementar políticas que aborden estos determinantes, Indonesia puede crear un entorno que promueva una vida saludable y mejore los resultados de salud. Además, alentar el compromiso y la participación de la comunidad en los procesos de toma de decisiones sobre atención médica puede empoderar a las personas y crear un sentido de propiedad sobre su salud, lo que en última instancia contribuirá al éxito de la transformación de la salud en Indonesia. Recientemente, Indonesia ha tomado medidas para mejorar su sistema de salud y superar los desafíos. Este número especial explora la transformación de la salud en curso en Indonesia y las medidas críticas que se están tomando para lograr un desarrollo sustentable en el sector de la salud. Los documentos discuten muchos temas relacionados con la salud de la población, así como los factores que afectan su estado de salud.

ORCID: 0000-0001-7988-9196

La transformación de la salud de Indonesia fue impulsada por el compromiso de mejorar el acceso, promover la atención médica preventiva, invertir en infraestructura, desarrollar recursos humanos y fomentar asociaciones público-privadas. Desde 2021, el Ministerio de Salud de Indonesia ha lanzado la transformación de la salud. Los seis pilares comprenden la transformación del servicio primario, los servicios de referencia, los sistemas de resiliencia de la salud, los sistemas de financiación de la atención médica, los recursos humanos de la atención médica y la tecnología de la atención médica (1). La implementación del Programa Nacional de Seguro de Salud (JKN) ha extendido la cobertura y la protección financiera a millones de indonesios, pero aún se necesitan esfuerzos para garantizar el acceso equitativo a la atención médica en todas las regiones y abordar las disparidades. Se está enfatizando el enfoque en medidas preventivas para reducir la carga de enfermedades no transmisibles a través de educación para la salud, programas de concientización y exámenes de detección regulares. El desarrollo de la infraestructura es una prioridad, con inversiones destinadas a expandir y mejorar las instalaciones de atención médica, particularmente en áreas rurales, y fortalecer la cadena de suministro de medicamentos y equipos médicos. Además, las inversiones en recursos humanos para la salud, como la educación, la capacitación y el desarrollo profesional, son cruciales para crear una fuerza laboral de atención médica calificada.

La colaboración entre los sectores público y privado a través de asociaciones se considera un factor clave para movilizar recursos, facilitar el intercambio de conocimientos y desarrollar soluciones sanitarias innovadoras (2,3).

Los esfuerzos de Indonesia por transformar su sistema de salud reflejan su dedicación para lograr un desarrollo sustentable. Han mejorado el acceso a la atención médica, priorizado las medidas preventivas, invertido en infraestructura y recursos humanos y fomentado las colaboraciones. Estas acciones marcan el camino hacia un futuro más saludable y próspero. Sin embargo, sostener estos esfuerzos requiere un compromiso continuo, la asignación de recursos y la implementación efectiva de políticas. Es esencial priorizar la salud y el bienestar de todos los indonesios, asegurando que nadie se quede atrás en el camino hacia una nación más saludable.

REFERENCIAS

1. Ministry of Health. Minister of Health: Health System Transformation Readiness Needs Support from All Parties. 2021. Available from: https://sehatnegeriku.kemkes.go.id/baca/ umum/20211122/1138879/menkes-kesipan-transformation-sistem-kesehatan-butuh-supportan-seat-stakes/
2. Ministry of Health. Rows of Health Transformation by the Minister of Health Budi. Ministry of Health of the Republic of Indonesia. 2022.
3. Ministry of Health. Blueprint for Digital Health Transformation Strategy 2024. Jakarta, Indonesia; 2021.

ARTÍCULO ORIGINAL

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Forming Factors of Family Immunity in Healthy Status and Confirmed COVID-19 Families

Factores Formadores de la Inmunidad Familiar en Familias Saludable y con COVID-19 Confirmado

Nur Mukarromah[1a*], Achmad Zakaria[2b]

SUMMARY

Background: *Family COVID-19 immunity is an approach to responding to stressors and crises caused by COVID-19. This study aimed to analyze the factors that formed family immunity in healthy families with confirmed COVID-19.*
Methods*: A case-control research design of two groups was carried out in August 2021 – March 2022 to analyze the factors forming family immunity in preventing COVID-19 infection, in Surabaya, Indonesia. One hundred four respondents were selected through convenience sampling. Data was collected using a family immunity questionnaire based on sub-variables 1) family belief system; 2) organizational patterns; 3) communication processes; and 4) controlling the spread of infectious disease. Data were analyzed using Chi-Square, and all statistical correlations were considered significant with p-value < 0.05.*
Results: *Several variables were significantly related to COVID-19 status, including family beliefs, an optimistic outlook, organizational adaptability, clear communication, and practical strategies to prevent the virus's transmission. These data highlight the significance of these factors in strengthening family immunity and preventing COVID-19.*
Conclusion: *Family immunity is formed from 10 indicators, namely making meaning of adversity, positive outlook, transcendence and spirituality, social and economic resources, clarity, open emotional expression, building ethical principles, preventing transmission, and limiting contact.*

Keyword*: Immunity, family, healthy, COVID-19.*

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ORCID: 0000-0001-9506-3773[1]
ORCID: 0000-0002-9469-8141[2]

[a]Department of Fundamental and Nursing Management, Faculty of Health Science, Universitas Muhammadiyah Surabaya, Surabaya, Indonesia.
[b]Department of Fundamental and Nursing Management, Faculty of Health Science, Darul Ulum Islamic Boarding School, Jombang, Indonesia.

*Corresponding Authors: Nur Mukarromah
E-mail: nurmukarromah@fik.um-dsurabaya.ac.id

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RESUMEN

Antecedentes: *La inmunidad familiar contra la COVID-19 es un enfoque familiar para responder a los factores estresantes y las crisis causadas por la COVID-19. El propósito de este estudio fue analizar los factores que forman la inmunidad familiar en familias saludables y con COVID-19 confirmado.*
Métodos: *Se llevó a cabo un diseño de investigación de casos y controles de dos grupos, en agosto de 2021 - marzo de 2022, para analizar los factores que forman la inmunidad familiar en la prevención de la infección por COVID-19, en Surabaya, Indonesia. 104 encuestados fueron incluidos a través de un muestreo por conveniencia. Los datos se recopilaron mediante*

un cuestionario de inmunidad familiar evaluado en función de las subvariables 1) sistema de creencias familiares; 2) patrones organizacionales; 3) procesos de comunicación; y 4) control de la propagación de enfermedades infecciosas. Los datos se analizaron mediante Chi-Cuadrado y todas las correlaciones estadísticas se presentaron con un valor de $p < 0.05$.
Resultados: *Se demostró que varias variables están significativamente relacionadas con el estado de COVID-19, incluidas las creencias familiares, una perspectiva optimista, la adaptabilidad organizacional, una comunicación clara y estrategias efectivas para prevenir la transmisión del virus. Estos datos resaltan la importancia de estos factores para fortalecer la inmunidad familiar y prevenir la COVID-19.*
Conclusión: *La inmunidad familiar se forma a partir de 10 indicadores, a saber, dar sentido a la adversidad, actitud positiva, trascendencia y espiritualidad, recursos sociales y económicos, claridad, expresión emocional abierta, construcción de principios éticos, prevención de la transmisión y limitación del contacto.*

Palabra clave: *Inmunidad, familia, saludable, COVID-19.*

INTRODUCTION

Corona Virus Disease 2019 (COVID-19) is an emerging pandemic with many impacts, especially in the health sector, creating an international health crisis (1,2). The transmission of COVID-19, which occurs very quickly through droplet transmission, increases the number of cases, and the virus undergoes continuous mutations, giving rise to new variants (3-5). The emergence of a new variant of COVID-19 will prolong the existence of the virus. As a result, humans must coexist with the virus and naturally experience herd immunity (6-9).

Herd immunity, or community immunity, is a term when a large part of the population of an area is immune to a specific disease such as the COVID-19 virus. If enough people are resistant to the cause of a disease, such as a virus or bacteria, it has nowhere to go. While not every single individual may be immune, the group as a whole has protection. Society will be immune through vaccination and natural immunity from virus infection. The immunity developed in individuals will increase resilience in a very long pandemic (5). However, individual immunity is not enough to break the pandemic chain; collaboration from all sectors and levels of society is needed to prevent and deal with COVID-19 (7). Prevention carried out by the community involves the whole community and the smallest unit, namely the family, through family empowerment (10-12). Family empowerment is expected to make the family the spearhead in resolving COVID-19 cases, starting from the minor scale, namely the household unit (13,14).

Both, healthy families and those confirmed with COVID-19 may have immunity in preventing infection transmission (15). The family will provide confidence, organize, communicate, and try to break the chain of transmission for the health of their family members. Through family integration, the handling of COVID-19 can reach the smallest unit (16). The evidence indicates that the status of confirmation of COVID-19 depends on the independence and ability of the family to carry out the health protocol, a family that is healthy and has never been confirmed with COVID-19 is a family that always follows a healthy lifestyle, adheres to the protocol and does not ignore existing policies (17). However, families confirmed with COVID-19 do not mean they are unhealthy, but family immunity that is more careful about COVID-19 is better (18,19).

Family immunity has several sub-indicators that explain the family's importance in preventing COVID-19; the intended sub-indicators are 1) family belief system; 2) organizational patterns; 3) communication processes; and 4) controlling the spread of infectious disease (12,20-22). Family immunity against COVID-19 can be described as a form of approach that is oriented towards family strength in involving the family system through active processes in the form of coping, adaptation, and positive behaviour patterns so that they have resilience in responding to stressors and crises caused by COVID-19. Because of this, it is necessary to identify the characteristics of family immunity from the community in dealing with the pandemic situation in Indonesia (1,23,24). This study aimed to analyze the factors that formed family immunity in healthy and confirmed COVID-19 families.

METHOD

Research design

A case-control research design of two groups was carried out in August 2021 – March 2022 to analyze the factors forming family immunity in preventing COVID-19 infection, in Surabaya, Indonesia. There were assessed indicators of the Family Immunity sub-variable in preventing the spread of COVID-19 in healthy and affected COVID-19 families so that they will know which indicators are valid for forming family immunity.

Study Participants

The respondents were 104 people in Surabaya who were recruited using convenience sampling. Respondents were divided into healthy families and families with confirmed COVID-19. Healthy Families were defined as participants who did not have any confirmed cases of COVID-19 in their family. In comparison, the families with confirmed COVID-19 group were defined by participants with a family history of COVID-19. Both groups were chosen based on eligibility criteria such as age range 18-54 years, residency in Surabaya, absence of mental problems, and ability to read and write.

Instrument and Data Collection

Data was collected using a family immunity questionnaire assessed based on sub-variables 1) family belief system; 2) organizational patterns; 3) communication processes; and 4) controlling the spread of infectious disease. Data collection was carried out by first carrying out the licensing process. Data was collected using a questionnaire through closed questions. Before the instrument was given to the respondents, it was tested with validity and reliability first in the 30 patients with the same characteristics as the study respondents. The average validity value was 0.486 – 0.647 (r table = 0.321), and the validity value was 0.885. The instrument uses a Likert scale with five levels, namely strongly disagree (score 1), disagree (score 2), disagree (score 3), agree (score 4), and strongly agree (score 5). The indicator family belief system with sub-indicators making meaning of adversity, positive outlook, transcendence, and spirituality consists of 10 questions with the highest score being 50, score interpretation being good 26-50, and less than 1-25. Organizational patterns with sub-indicators of Flexibility, Connectedness, and Social and Economic Resources consist of 10 questions with good (score 26-50) and poor (1-25) categories. Communication Processes consisting of Clarity, Open emotional expression, and Collaborative problem-solving sub-indicators comprised of 9 questions with the highest score being 45, a good category in the range of 24-45 and less with a score of 1-23. While the indicator controlling the spread of infectious disease with the sub-indicator builds ethical principles, preventing transmission and limiting contact with 11 questions, for the good category, the score is 29-55, and for the poor category is 1-28.

Data Analysis

Data collected were tabulated and given the coding for analysis in SPSS version 21. Data were analyzed using descriptive and inferential statistics presented in the descriptive statistic table and inferential statistics using Chi-Square; all statistical correlations were presented with p-value < 0.05.

Ethical Consideration

Ethical approval of this study was certified by the Ethical Committee of the Muhammadiyah University of Surabaya, with the number of certificates being 12/EC/KEPK/2020. The respondents first signed the informed consent; they signed voluntarily after they got some explanation about the study from the researcher.

RESULTS

Research conducted on 104 healthy family respondents and families with confirmed COVID-19 status in Surabaya showed that most were aged >40 years, 81 respondents (77.9 %). The most dominant respondents were women (91.3 %), and the education level of senior high school graduates was the most (51.9 %) (Table 1).

Table 1. Characteristics of research respondents

Category	N	%
Age		
< 30 years	8	7.7
30 – 40 years	15	14.4
> 40 years	81	77.9
Gender		
Male	9	8.7
Female	95	91.3
Educational background		
Junior High School	10	9.6
Senior High School	54	51.9
University	40	38.5

According to the findings in Table 2, from the family belief system indicator, healthy families had a greater perspective of diversity, a positive outlook, transcendence, and spirituality than families with confirmed COVID-19. All these variables were strongly associated with the families' COVID-19 status (p-value <0.0001). In COVID-19 prevention, the structure of a family organization, flexibility, and social and economic resources was significantly related to COVID-19 status (p-value < 0.0001). Healthy families had more flexibility and socioeconomic resources, whereas confirmed COVID-19 families had higher connectivity values. Healthy families exhibited higher clarity and openness in their communication procedures, but collaborative problem-solving produced unsatisfactory results. Clarity and openness were significantly related to COVID-19 status (p-value < 0.0001). The ability of healthy families to control the spread of infectious disease demonstrated better ethical standards, which was highly associated with COVID-19 status (p-value < 0.0001). The family's ability to prevent transmission and limit contacts was likewise linked to COVID-19 status (p-value < 0.0001 and 0.0002).

The Bartlett of Sphericity Test results determine whether there was a correlation between variables; the more significant the sample, the more sensitive the Bartlett test was to detect correlations between indicators. The test showed that the value of Kaiser Meyer Olkin (KMO) ed 0.898 so that factor analysis can be carried out. Likewise, with the Bartlett test value with Chi-Squares = 511.309 and significant at 0.0001, it can be concluded that the factor analysis test can be continued (Table 3).

The results of the eigenvalue > one only on indicator 1 (eigenvalue = 5.224) and indicator 2 (eigenvalue = 1.015). Therefore, the two indicators explain the variation of 62.389 %, which was divided into family belief systems (52.236 %) and organizational patterns (10.154 %) (Table 4).

The sub-indicators of family immunity are grouped into 1 component, proving that the sub-indicators meet the requirements and showed valid results. The highest value of the sub-indicators was shown in a positive outlook (0.862) and building ethical principles (0.797). Thus, the construction of family immunity according to the loading factor based on the highest value to the lowest includes a positive outlook, building ethical principles, clarity of communication, flexibility, transcendence, spiritualism, preventing contagion, collaboration, understanding differences, social and economic resources, and limiting contact. So, to assess the Family Immunity variable can be seen from the ten indicators (Table 5).

Table 2. Indicators of Family Immunity in healthy and Confirmed COVID-19 families

Indicator	Sub Indicator	COVID-19 Status				P Value; X^2
		Healthy Family		Positive COVID-19		
		n	%	n	%	
Family belief system	Understanding the Difference					
	Less	14	13.5	37	35.6	0.0001*
	Good	45	43.3	8	7.7	34.951
	Positive outlook					
	Less	10	9.6	38	36.5	0.0001*
	Good	49	47.1	7	6.7	46.797
	Transcendence and spirituality					
	Less	19	18.3	38	36.5	0.001*
	Good	40	38.5	7	6.7	28.129
Organizational pattern	Flexibility					
	Less	13	12.5	40	38.5	0.0001*
	Good	46	44.2	5	4.8	45.658
	Connectedness					
	Less	33	31.7	28	26.9	0.519
	Good	26	25.0	17	16.3	0.416
	Social and economic resources					
	Less	17	16.3	35	33.7	0.000*
	Good	42	40.4	10	9.6	24.482
Communication Process	Clarity					
	Less	20	19.2	30	28.8	0.001*
	Good	39	37.5	15	14.4	10.981
	Openness					
	Less	16	15.4	42	40.4	0.0001*
	Good	43	41.5	3	2.9	45.375
	Collaborative					
	Less	36	34.6	28	26.9	0.900
	Good	23	22.1	17	16.3	0.016
Controlling the spread of infectious disease	Establish ethical principles					
	Less	11	10.6	37	35.6	0.0001*
	Good	48	46.2	8	7.7	41.523
	Prevent transmission					
	Less	19	18.3	38	36.5	0.0001*
	Good	40	38.5	7	6.7	28.129
	Limit contacts					
	Less	25	24.0	33	31.7	0.002*
	Good	34	32.7	12	11.5	9.920

*p-value < 0.05

Table 3. Results of Factor Analysis of the Bartlett of Sphericity Test

Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		0.898
Bartlett's Test of Sphericity	Approx. Chi-Square	511.309
	df	45
	Sig.	0.0001

Table 4. Results of Principal Component Analysis for Family Immunity Sub-Indicators

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	5.224	52.236	52.236	5.224	52.236	52.236
2	1.015	10.154	62.389	1.015	10.154	62.389
3	.867	8.669	71.059			
4	.753	7.534	78.593			
5	.527	5.266	83.859			
6	.420	4.201	88.060			
7	.367	3.669	91.729			
8	.332	3.324	95.053			
9	.271	2.712	97.766			
10	.223	2.234	100.000			

Extraction Method: Principal Component Analysis.

Table 5. Results of Component Matrix Analysis of Family Immunity Sub-Indicators

Indicator	Component	
	1	2
Understanding the Difference	0.667	0.386
Positive outlook	0.862	0.211
Transcendence and spirituality	0.746	0.379
Flexibility	0.762	-0.193
Social and economic resources	0.600	-0.034
Clarity	0.768	-0.242
Openness	0.688	-0.123
Establish ethical principles	0.797	-0.311
Prevent transmission	0.726	-0.448
Limit contacts	0.558	0.518

Extraction Method: Principal Component Analysis.
a. two components extracted.

DISCUSSION

Analysis of the factors that make up family immunity consists of indicators of family belief systems, organizational patterns, communication processes, and controlling the spread of infectious disease (25). Each of these indicators consists of 3 sub-indicators family belief system with sub-indicators making meaning of adversity, positive outlook, transcendence and spirituality, Organizational patterns with sub-indicators Flexibility, Connectedness, Social and Economic Resources, Communication Processes consisting of sub-indicators Clarity, Open emotional expression and Collaborative problem solving and controlling the spread of infectious disease with sub-indicators Build ethical principles, Preventing transmission and Limiting contact. In the research results from 12 sub-indicators, only ten indicators are significant, so only ten indicators can form family immunity, namely making meaning of adversity, positive outlook, transcendence and spirituality, social and

economic resources, clarity, open emotional expression, building ethical principles, preventing transmission and Limiting contact (2,10,12,26).

The family belief system is essential and can influence a family's intention to do something; through self-belief, attitudes and actions will also be implemented (27). In preventing COVID-19, families with higher confidence are described as healthy families than families with confirmed COVID-19; healthy families are appropriate because, through this belief, families can take precautions against COVID-19 (20). Beliefs are formed from making meaning of adversity, positive outlook, transcendence, and spirituality. Families will form beliefs if they can give meaning to what they encounter, always think positively, and have reasonable spiritual beliefs (28). In line with research showing that trust in the family is formed due to the strengthening of each other from family members, family beliefs will be stronger if family relationships are closer; the positive impact is that families can become independent and understand more about the health status of their family members (20,21,29,30).

Family organizational patterns show how families can organize their members to be better. Through good administrative management, families can control their activities, health conditions, harmonization, and all things so that families become more comfortable and close to each other (31). A good family can perform family functions by coordinating and managing the family to create harmony. Families with good organization can be more flexible and organize social and economic resources within the family (32).

The ability of the family to communicate is an essential element in fostering good relationships in the family. Within the family, the communication that is established is communication that can provide something that can be given to every other family member so that with this communication, problems that occur between family members can be discussed by taking the best solution (33). Communication is a source of the emergence of a problem if it is not done correctly and causes a lot of miscommunications; communication needs to be done carefully and adjusted to the communication partner of an individual. The ability to communicate in the family will reflect family conditions (34). Families with good communication provide support, give advice, and tell if other family members are not right. Communication can also make the family calmer, and another will tell each other stories to express the emotions other family members are feeling (35-37).

The family's ability to control the spread of infectious disease is built on the ethical principle of Build, preventing transmission, and Limiting contact. The principles of the family to control the spread of the COVID-19 virus infection must be instilled in family members from an early age. Families with healthy conditions are always healthy because they comply with health protocols so that before they fall sick, the family can prevent it with the knowledge that the family already has (25). Prevention capabilities will build awareness from the family to form commitment and resilience in dealing with a pandemic (7).

The limitations of research conducted during a pandemic are that researchers cannot optimally interact directly with respondents, so all coordination and data collection is done online. The selection of respondents is still not evenly distributed in all Surabaya locations, so it is necessary to identify them from the entire Surabaya community.

CONCLUSION

Family immunity in the family is formed by the family belief system, organizational patterns, communication processes, and controlling the spread of infectious diseases. There are ten significant sub-indicators to explain family immunity: making meaning of adversity, positive outlook, transcendence and spirituality, social and economic resources, clarity, open emotional expression, building ethical principles, preventing transmission, and limiting contact.

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Conflict of Interest

The researcher declares that there is no conflict of interest in this study so that the research is guaranteed to have no problems between members and the article's authorship.

REFERENCES

1. Adhikari SP, Meng S, Wu Y-J, Mao Y-P, Ye R-X, Wang Q-Z, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: A scoping review. Infect Dis poverty. 2020;9(1):1-12.
2. Nursalam N, Sukartini T, Priyantini D, Mafula D, Efendi F. Risk factors for psychological impact and social stigma among people facing COVID-19: A systematic review. Systematic Reviews in Pharmacy. Medknow Publications. 2020;11:1022-1028.
3. Leo BF, Lin CY, Markandan K, Saw LH, Mohd Nadzir MS, Govindaraju K, et al. An overview of SARS-CoV-2 transmission and engineering strategies to mitigate risk. J Build Eng. 2023;73.
4. Lauer SA, Grantz KH. Qifang Bi, Forrest K J, Qulu Zheng, Hannah R M, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann Intern Med. 2020;172(9):577-582.
5. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020;109:102433.
6. Duff E. Global health emergency declared by WHO. Midwifery. 2020;102668.
7. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-1242.
8. Zu ZY, Jiang M Di, Xu PP, Chen W, Ni QQ, Lu GM, et al. Coronavirus disease 2019 (COVID-19): A perspective from China. Radiology. 2020;296(2):E15-25.
9. Wei J, Xu H, Xiong J, Shen Q, Fan B, Ye C, et al. 2019 Novel coronavirus (COVID-19) pneumonia: Serial computed tomography findings. Korean J Radiol. 2020;21(4):501.
10. Park YJ, Choe YJ, Park O, Park SY, Kim YM, Kim J, et al. COVID-19 national emergency response center, epidemiology and case management team. Contact tracing during coronavirus disease outbreak, South Korea, 2020. Emerg Infect Dis. 2020;26(10):2465-2468.
11. Li S, Wang Y, Xue J, Zhao N, Zhu T. El impacto de la declaración de la epidemia de COVID-19 en las consecuencias psicológicas: un estudio sobre usuarios activos de Weibo. Rev Int Investig Ambient Salud Públ. 2020;17.
12. Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. Management of COVID-19: the Zhejiang experience. J Zhejiang Univ Med Sci. 2020;49(2):147-157.
13. Schwaiger K, Zehrer A, Braun B. Organizational resilience in hospitality family businesses during the COVID-19 pandemic: A qualitative approach. Tour Rev. 2022;77(1):163-176.
14. Prime H, Wade M, Browne DT. Risk and resilience in family well-being during the COVID-19 pandemic. Am Psychol. 2020;75(5):631.
15. Sya'diyah H, Widayanti DM, Myra M, Mahmudah, Efendi F. Resilience Influenced with Anxiety Level among Family with Elderly in Facing the COVID-19 Pandemic: A Correlational Study. Malaysian J Nurs. 2022;14(2):138-142.
16. Qur'Aniati N, Krisnana I, Putri DAE, Handasari M. The family dynamics of COVID-19 survivors: The perspectives of parents and their children. J Pak Med Assoc. 2023;73(2):S80-83.
17. Arief YS, Kurnia ID, Nurkholida S. Parents, behaviour in individual-level prevention in children during the COVID-19 pandemic in Surabaya. J Pak Med Assoc. 2023;73(2):S96-99.
18. Kalaman CR, Ibrahim N, Shaker V, Cham CQ, Ho MC, Visvalingam U, et al. Parental Factors Associated with Child or Adolescent Medication Adherence: A Systematic Review. Healthc. 2023;11(4).
19. Isasi F, Naylor MD, Skorton D, Grabowski DC, Hernández S, Rice VM. Patients, Families, and Communities COVID-19 Impact Assessment: Lessons Learned and Compelling Needs. NAM Perspect. 2021;2021.
20. Fadmawaty A, Wasludin W. The Effect of The Belief System, Family Organizations and Family Communication on COVID-19 Prevention Behavior: The Perspective of Family Resilience. Int J Disaster Manag. 2021;4(2):9-22.

21. Hart JL, Turnbull AE, Oppenheim IM, Courtright KR. Family-centered care during the COVID-19 era. J Pain Symptom Manage. 2020;60(2):e93-97.
22. Moher D, Tetzlaff J, Tricco AC, Sampson M, Altman DG. Epidemiology and reporting characteristics of systematic reviews. PLoS Med. 2007;4(3):e78.
23. Jernigan DB. 19 Response Team (2020) Update public health response to the coronavirus disease 2019 outbreak US Feb 24, 2020. Morb Mortal Wkly Rep. 2020;69(8):216-219.
24. Rao ASRS, Vazquez JA. Identification of COVID-19 can be quicker through artificial intelligence framework using a mobile phone–based survey when cities and towns are under quarantine. Infect Control Hosp Epidemiol. 2020;41(7):826-830.
25. Betsch C, Wieler L, Bosnjak M, Ramharter M, Stollorz V, Omer S, et al. Germany COVID-19 Snapshot MOnitoring (COSMO Germany): Monitoring knowledge, risk perceptions, preventive behaviours, and public trust in the current coronavirus outbreak in Germany. 2020.
26. Jones AP, Remmington T, Williamson PR, Ashby D, Smyth RL. High prevalence but low impact of data extraction and reporting errors were found in Cochrane systematic reviews. J Clin Epidemiol. 2005;58(7):741-742.
27. Mahmud I, Kabir R, Rahman MA, Alradie-Mohamed A, Vinnakota D, Al-Mohaimeed A. The health belief model predicts intention to receive the COVID-19 vaccine in saudi arabia: Results from a cross-sectional survey. Vaccines. 2021;9(8).
28. Rachmawati DS, Priyantini D, Aini Q. Family Factors and Their Relation to the Treatment Adherence of Pulmonary TB Patients in Surabaya. J Ners. 2020;15(2 Special Issue):45-49.
29. Mansoor T, Mansoor S, Bin Zubair U. Surviving COVID-19: Illness narratives of patients and family members in Pakistan. Ann King Edward Med Univ. 2020;26(Special Issue):157-164.
30. Iswatun, Yusuf A, Efendi F, Susanto J, Dewi WK, Hidaayah N. Relationship between anxiety and spiritual well-being of the elderly with hyper tension during the COVID-19 pandemic. J Pak Med Assoc. 2023;73(2):S46-49.
31. Wahidah, Widyawati IY, Dewi LC, Liem K. Factors related to adherence with the implementation of COVID-19 health protocols in a traditional market trader, community in East Java, Indonesia. J Pak Med Assoc. 2023;73(2):S76-79.
32. Li Y, Shin J, Sun Ji, Kim HM, Qu Y, Yang A. Organizational sensemaking in tough times: The ecology of NGOs' COVID-19 issue discourse communities on social media. Comput Human Behav. 2021;122:106838.
33. Utami S, Susilaningrum R, Nursalam. The effect of health promotion based on the health promotion model with a peer group approach regarding the utilization of maternal and child health handbook. Indian J Public Heal Res Dev. 2019;10(10):1987-1992.
34. Kusumawardani W, Yusuf A, Ni'mah L. Family burden and coping in family caregivers of patient with schizophrenia. Indian J Public Heal Res Dev. 2019;10(9):1506-1510.
35. Gandaputra SA, Waluyo I, Efendi F, Wang J-Y. Insomnia status of middle school students in Indonesia and its association with playing games before sleep: Gender difference. Int J Environ Res Public Health. 2021;18(2):1-10.
36. Rindayati, Yusuf A, Efendi F, Illahiati NK, Nasir A. Experience of caregiver coping mechanisms when taking care of a schizophrenic patient. Int J Psychosoc Rehabil. 2020;24(7):7964-7975.
37. Sustrami D, Yusuf A, Fitryasari R, Efendi F, Aysha RF. Relationship between social support and family caregiver burden in schizophrenia patients. J Pak Med Assoc. 2023;73(2):S42-45.

ARTÍCULO ORIGINAL

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Early Warning for Humans Regarding Contamination with Salmonella bacteria Originating from Duck

Alerta temprana para humanos por la contaminación con la bacteria Salmonella originada en el pato

Reina Puspita Rahmaniar[1a], Freshinta Jellia Wibisono[2a]*, Khoirul Muhroni Aziz[3a], Lusitania Darmayanti Ikeng[4a], Dandi Ernando Syaputra[5a], Zuriya Zuriya[6a]

SUMMARY

Introduction: *Pathogenic bacteria of the genus Salmonella are one of the leading causes of foodborne disease. Salmonella sp. are pathogenic bacteria excreted through feces from the digestive tract of animals and humans. These bacteria can contaminate food of animal origin, both from animals to humans and humans to animals. This study aimed to determine the presence of Salmonella in Surabaya duck farms.*
Methods: *The research samples were taken from 24 duck eggs and 24 cloacal swabs. The criteria for the egg samples taken were newly hatched eggs. The sample were placed in a sterile plastic bag and labeled to prevent bacterial contamination from other eggs. Cloacal swab samples were taken from newly laid ducks using a sterile cotton swab and put into Tetrathionate broth as an enrichment medium. Samples were isolated on Salmonella Shigella Agar (SSA) medium and incubated at 37°C for 24 hours and identified by microscopic examination with gram staining and biochemical tests on Triple Sugar Iron Agar (TSIA), Sulphide Indole Motility (SIM), Simon's Citrate Agar (SCA), urease.*
Results: *The results showed three positive samples of Salmonella enterica in cloacal swabs, and no Salmonella was detected in the egg white samples.*
Conclusion: *The detection of Salmonella enterica from cloacal swabs of ducks is undoubtedly an early warning so that the community is more aware of the dangers of Salmonella disease.*

Keywords: *Salmonella, albumin, cloacal swab.*

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ORCID: 0000-0003-2665-6043[1]
ORCID: 0000-0001-9716-2230[1]
ORCID: 0000-0001-9716-2230[3]
ORCID: 0000-0003-3665-3727[4]
ORCID: 0000-0001-9829-995X[5]
ORCID: 0000-0002-3902-7353[6]

[a]Faculty of Veterinary Medicine, University of Wijaya Kusuma Surabaya, Surabaya, Indonesia

*Corresponding Author: Freshinta Jellia Wibisono
E-mail: freshinta.uwks@gmail.com

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RESUMEN

Introducción: *Las bacterias patógenas del género Salmonella son una de las principales causas de enfermedades transmitidas por alimentos. Salmonella sp. son bacterias patógenas excretadas con heces del tracto digestivo de animales y humanos. Estas bacterias pueden contaminar alimentos de origen animal, tanto de animales a humanos como de humanos a animales. Este estudio tiene como objetivo determinar la presencia de Salmonella en las granjas de patos de Surabaya.*
Métodos: *Las muestras de investigación se tomaron de 24 huevos de pato y 24 hisopos cloacales. Los*

criterios para las muestras de huevos tomadas fueron huevos recién puestos. La muestra se colocó en una bolsa de plástico estéril y se etiquetó para evitar la contaminación bacteriana de otros huevos. Se tomaron muestras de hisopos cloacales de patos recién puestos utilizando un hisopo de algodón estéril y se sembraron en cultivo de tetrationato como medio de enriquecimiento. Las muestras se aislaron en medio Agar de Salmonella Shigella (SSA) y se incubaron a 37°C durante 24 horas y se identificaron mediante examen microscópico con tinción de Gram y pruebas bioquímicas en Triple Sugar Iron Agar (TSIA), Sulphide Indole Motility (SIM), Simon's Citrate Agar (SCA), ureasa.

Resultados: *Los resultados mostraron que hubo tres muestras positivas de Salmonella entérica en hisopos cloacales y no se detectó Salmonella en las muestras de clara de huevo.*

Conclusión: *La detección de Salmonella entérica a partir de hisopos cloacales de patos es sin duda una alerta temprana para que la comunidad sea más consciente de los peligros de la enfermedad de Salmonella.*

Palabras clave: *Salmonella, albúmina, hisopado cloacal*

INTRODUCTION

Salmonella has been considered an important pathogen that threatens global public health (1,2). These bacteria are the source of foodborne diseases that cause infection and food poisoning in humans (3). In China, 70 %-80 % of foodborne pathogens are caused by Salmonella (2). Ducks proved to be an essential reservoir for Salmonella species. Salmonellosis in ducks can cause acute, subclinical forms, while chronic non-lethal or carrier status usually develops in adult ducks (4,5). Poultry products contaminated with Salmonella can seriously impact life, health, and food safety. The spread of salmonellosis from ducks to humans may be higher than from chickens, and the main factor is the presence of infection without recognizable clinical signs and poor hygiene conditions (6). Salmonella bacterial contamination in ducks in Yangzhou, Jiangsu province, and Gaomi, Shandong province, China, shows a severe condition with a Salmonella isolation rate of 35.7 % observed at the hatching stage, indicating a potential threat to the downstream duck production chain (7).

Although ducks are resistant to systemic infections caused by Salmonella, ducks are a potential reservoir of these microorganisms and can release them in feces and contaminate the environment (8). Outbreaks of human salmonellosis caused by contact with ducks have been reported in several countries, such as Australia, the United States, America, and Denmark. In addition, consuming contaminated duck eggs has been reported as a cause of salmonellosis outbreaks in Italy, Thailand, and the United States (9,10). Eggs are one of the essential products that can transmit Salmonella infection to humans (11). Eggs and egg products have been identified as the most common food vehicle for salmonellosis in humans in Europe, mainly caused by *Salmonella enterica* serovar Enteritidis (12).

There are very few studies on the incidence of Salmonella in ducks in Indonesia. However, there is a need for continuous monitoring of the presence of *Salmonella spp*. in ducks, especially in Surabaya, Indonesia, to help authorities protect the public and minimize the risk of foodborne outbreaks. This study aimed to determine the presence of Salmonella in Surabaya duck farms.

METHODS

Design Study

This research was conducted at a duck farm in Surabaya City. The design of the study was an observational laboratory.

Population and Sample

A total of 48 samples were taken from duck farms from breeders in the city of Surabaya, consisting of 24 egg samples and 24 cloacal swab samples.

Data Collection

Sampling used sterile equipment, including a cotton swab and a tube containing enrichment tetrathionate broth media. Isolation of bacteria using Salmonella Shigella Agar (SSA) OXOID

media. Microscopic examination using Gram staining with materials such as Crystal Violet, Lugol, Alcohol acetone, and Safranin. The biochemical tests used include Triple Sugar Iron Agar (TSIA), Simons Citrate Agar (SCA), Sulphide Indole Motility (SIM), and Urease.

Sampling was carried out in duck breeders in Surabaya. Before sampling, the cage was observed with the criteria that the cage had a temperature between 27°C to 30°C. Egg sampling was carried out by meeting the criteria for newly hatched with the characteristics of still sticking feces from the eggshell and then putting it in a plastic bag. It was labelled to prevent bacterial contamination from other eggs. After that, the fecal samples from the cloacal swab were taken from the mother ducks that had just laid eggs. Then samples were taken using a sterile cotton swab and put in the Tetrathionate broth solution. Eggs taken from the farm were immediately taken to the Microbiology Laboratory of the Faculty of Veterinary Medicine, Wijaya Kusuma University, Surabaya. The egg whites were then taken using a 1 mL syringe and placed in a solution of Tetrathionate broth. The two samples were dissolved in Tetrathionate broth and incubated for 24 h at 37°C. Bacteria were isolated by streaking on SSA media. The enrichment process was carried out, and the colony morphology was observed after incubation at 37°C for 24 h. Only colonies with rounded, transparent edges with black spots in the middle were purified. A microscopic examination was carried out to examine the morphology of Salmonella bacteria cells and the bacteria's purity. Bacterial colonies whose purity was confirmed were subjected to biochemical tests to determine the species of Salmonella.

Data Analysis

The data collected in this study were analyzed using descriptive statistics. The descriptive analysis involves summarizing and describing the collected data, such as calculating measures of central tendency (mean, median) and measures of dispersion (standard deviation, range).

RESULTS

The study's results on detecting Salmonella in duck egg whites at three farms in Surabaya showed 0 %. There was no Salmonella. In contrast, the results of the study on cloacal swab samples contained three of the 24 samples identified as Salmonella. The data is presented in Table 1.

Table 1. Results of detection of Salmonella enterica on egg whites and cloacal swabs.

Duck Farmer	Number of samples	Egg whites		Cloacal Swab	
		Positive (+)	Negative (-)	Positive (+)	Negative (-)
Duck Farmer 1	6	0 % (0/6)	100 % (6/6)	0 % (0/6)	100 % (6/6)
Duck Farmer 2	6	0 % (0/6)	100 % (6/6)	16 % (1/6)	84 % (5/6)
Duck Farmer 3	12	0 % (0/12)	100 % (12/12)	16 % (2/12)	84 % (10/12)
	24	0 % (0/24)	12.5 % (3/24)		

Figure 1 showcases the colony morphology of Salmonella on Salmonella-Shigella Agar (SSA). The image displays multiple colonies of Salmonella, which appear as small, opaque, and colorless colonies with a dark center. The colonies have a smooth and slightly raised appearance, indicating the presence of Salmonella on the agar plate. Figure 2 illustrates the biochemical reactions of *Salmonella enterica* using various test media. The leftmost panel represents Triple Sugar Iron Agar (TSIA) test, where Salmonella shows an alkaline/alkaline reaction. The middle panel represents Sulphide Indole Motility Agar (SIM) test, indicating the production of hydrogen

sulphide (H_2S) gas and motility. The rightmost panel represents the Urease test, with Salmonella demonstrating a positive reaction by turning the medium pink. Lastly, the bottom panel represents Selenite-Cystine Agar (SCA) test, showing the growth of Salmonella colonies on the medium.

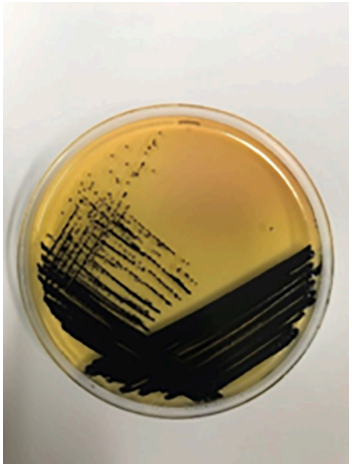

Figure 1. Salmonella colony morphology on SSA.

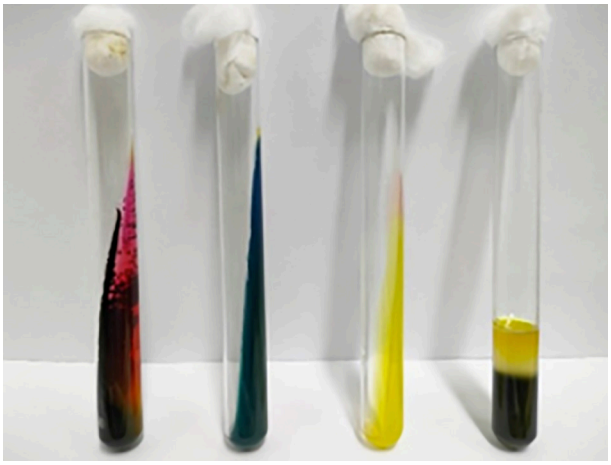

Figure 2. Biochemical reactions of *Salmonella enterica* from left to right: TSIA, SCA, Urease, SIM.

DISCUSSION

Biochemical assays are necessary for identifying *Salmonella enterica* species and serovars (13). While serotyping is required for precise serovar identification, many biochemical features are shared by Salmonella strains (14). These include alkaline slant and acid butt reactions in the Triple Sugar Iron Agar (TSIA) test, hydrogen sulphide (H2S), and gas generation. The Sulphide Indole Motility (SIM) test usually yields positive findings, indicating motility and H_2S generation. Furthermore, *Salmonella enterica* strains typically show positive results in the Selenite-Cystine Agar (SCA) and urease tests (15). However, specifically Salmonella enterica serovars may have distinct biochemical profiles. In the TSIA test, for example, Salmonella typhi exhibits alkaline slant and acid butt reactions, H_2S generation, a negative SCA test, motility, a positive urease test, and indole negativity. *Salmonella paratyphi* A, on the other hand, exhibits alkaline slant and acid butt reactions with gas production in the TSIA test but lacks H_2S production, it is motile but does not make H_2S in the SIM test, and is motile but does not produce H_2S in the SCA and urease tests (16,17).

The present data show that 12.5 % of Salmonella bacteria were found in duck cloacal swabs (3 of 24 samples). While, Adzitey et al., 2012 (18) showed that 28 of 100 (28.0 %) intestinal contents and 15 of 75 (20.0 %) cloacal swabs obtained from ducks in wet markets and farms were positive for Salmonella. The prevalence of Salmonella in duck intestine and a cloacal swab was not significantly different. However, the dominant Serovar was *S. typhimurium*, followed by *S. hadar* and *S. enteritidis*, *S. braenderup* and *S. Albany* (15,19). Another bacteriological examination also resulted in 94 positive samples from 630 isolates, of which 28 were from 33 sick ducks and 66 isolates from 72 recently died ducks. Three Salmonella serogroups were obtained by serological identification, *Salmonella typhimurium*, *Salmonella enteritidis*, and Salmonella blegdam (20).

Characterization of Salmonella isolated from duck farms and slaughterhouses in Shandong

province, from a total of 49 strains of Salmonella isolated from 2 342 samples from four duck farms and one duck slaughterhouse in Jinan and Tai'an, Shandong province, China, showed the presence of *S. enteritidis* 20/49 samples (40.8 %) and S. anatum 10/49 (20.4 %), which were the most common (2). Another study that took samples from the cecum, liver, spleen, and gall bladder identified Salmonella by 7 % in 50 samples. Salmonella from waste samples around the farm was also found to be 6 % (3).

Samples taken from the processing environment can also be positive for Salmonella. Salmonella species can survive well in feces, soil, pond water, drinking water, feed, transport crates, eggshells, floor treatment, cutting tables and washing water. This shows that Salmonella is proven to be able to contaminate the environment around farms. Pathogens can survive in duck farms and slaughter areas and infect other animals (18). In effect, in a study was shown that Salmonella was found in feces (92 %), followed by eggshells (34 %) and cloacal swabs (4 %), and there was no Salmonella sp. present in egg contents (21), which is line with our present results. Overall, a total of 180 Salmonella isolates (25.7 %) were obtained from the duck production chain, 82 (35.7 %) isolates were from hatchery samples, followed by 64 (29.2 %) from market samples, 17 (23.6 %) from livestock samples, and 17 (9.4 %) from abattoirs. All isolates were divided into nine serotypes, of which *S. typhimurium, S. anatum*, and *S. enteritidis* were the dominant serotypes (7).

In contrast to other studies, the main Salmonella serotypes detected from 155 isolates were S. pullorum (82.6 %) and S. enteritidis (17.4 %). Salmonella species are considered intracellular pathogens and carry several virulence factors for entry and survival in the intracellular environment (15,22). Salmonella can spread not only horizontally but also vertically through embryonic chicken eggs. Salmonella can settle in poultry's reproductive tract, contaminate fresh eggs, and infect chicken embryos. Chicken embryos that do not die will still carry Salmonella after hatching, which will cause healthy chicks to become infected with salmonella disease, such as *Salmonella pullorum* (23). Zhao et al., 2016 (24), on native chickens in China, showed that 38 out of 300 samples (12.7 %) were identified as positive for Salmonella, and the most common serotype found was *S. enteritidis*. Pullorum disease caused by *S. pullorum* is strongly associated with direct vertical transmission from egg contamination in the genital tract or indirectly from chicken contact in hatcheries. In this study, no *Salmonella pullorum* or *Salmonella gallinarum* were found. *S. pullorum* is not excreted extensively in feces, unlike many other Salmonella serotypes, which are more commonly associated with human food poisoning (25). Salmonella infection in humans usually occurs when contaminated food products are ingested, resulting in gastroenteritis. Contaminated food such as milk, ice cream, cheese, butter, eggs, pork, beef, poultry, fruits, and vegetables have been implicated as sources of human infection (26).

CONCLUSIONS

Salmonella is a significant cause of foodborne disease in humans. Salmonella infection in poultry is humans' most important source of salmonella-related food poisoning. Although ducks are highly resistant to systemic infections caused by Salmonella, ducks are highly penetrating and become potential reservoirs of Salmonella and can release microorganisms in feces, thereby contributing to environmental contamination.

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REFERENCES

1. Sandrasaigaran P, Kuan CH, Radu S, Abidin UFUZ, Rukayadi Y, New CY, et al. Multiple antibiotic-resistant *Salmonella enterica* serovars Enteritidis and Typhimurium in ready-to-eat battered street foods,

and their survival under simulated gastric fluid and microwave heating. Food Control. 2023;146.

2. Yang J, Ju Z, Yang Y, Zhao X, Jiang Z, Sun S. Serotype, antimicrobial susceptibility and genotype profiles of Salmonella isolated from duck farms and a slaughterhouse in Shandong province, China. BMC Microbiol. 2019;19(1):1-12.
3. Abou Zeid MAM, Nasef SA, Ali GIE, Hegazy AM. A Field Study on Biochemical Changes Associated with Salmonella Infection in Ducklings. J World's Poult Res. 2020;10:250-262.
4. Buchholz PS, Fairbrother A. Pathogenicity of *Salmonella pullorum* in northern bobwhite quail and mallard ducks. Avian Dis. 1992;36(2):304-312.
5. Ljubojević Pelić D, Vidaković Knežević S, Pelić M, Živkov Baloš M, Milanov D. The epidemiological significance of duck meat as a source of *Salmonella spp*. A review. Worlds Poult Sci J. 2021;77(1):105-114.
6. Wong JX, Kuan CH, Saw SH, Chen SN, Tan CW, Yeo SK, et al. Quantitative *Salmonella enterica* serovar enteritidis risk assessment from consumption of hard-boiled eggs, half-boiled eggs and raw eggs among Malaysians. Food Res. 2021;5(3):385-392.
7. Kang X, Wang M, Meng C, Li A, Jiao X, Pan Z. Prevalence and whole-genome sequencing analysis of Salmonella reveal its spread along the duck production chain. Poult Sci. 2022;101(9):101993.
8. Lestari SD, Nikmah L, Kurniawati ND. Family Counselling Enhances Environmental Control of Allergic Patients. J Ners. 2019;14(3 Special Issue):351-356.
9. Ribeiro SAM, Galleti MCM, Orsi MA, Ferrati AR, Mendonça AO, Doretto L, et al. Incidence of Salmonella in imported day-old ducklings. Brazil, 1998-2003. Rev Bras Cienc Avic. 2006;8(1):39-43.
10. Merritt TD, Herlihy C. Salmonella outbreak associated with chicks and ducklings at childcare centers. Med J Aust. 2003;179(1):63–4.
11. Chousalkar K, Gast R, Martelli F, Pande V. Review of egg-related salmonellosis and reduction strategies in United States, Australia, United Kingdom and New Zealand. Crit Rev Microbiol. 2018;44(3):290-303.
12. Gast RK, Jones DR, Guraya R, Anderson KE, Karcher DM. Research Note: Contamination of eggs by *Salmonella enteritidis* and *Salmonella typhimurium* in experimentally infected laying hens in indoor cage-free housing. Poult Sci. 2021;100(11):101438.
13. Praja RN, Yudhana A, Haditanojo W, Oktaviana V. Short communication: Antimicrobial properties in cloacal fluid of olive ridley sea turtle (lepidochelys olivacea). Biodiversitas. 2021;22(9):3671-3676.
14. Asih DW, Widodo ADW, Setiabudi RJ, Sulistiawati, Tyasningsih W, Wahyunitisari MR. Biofilm formation by the interaction of fungi (*Candida tropicalis*) with various bacteria. J Adv Biotechnol Exp Ther. 2023;6(1):84-93.
15. Wibisono FM, Wibisono FJ, Effendi MH, Plumeriastuti H, Hidayatullah AR, Hartadi EB, et al. A review of salmonellosis on poultry farms: Public health importance. Syst Rev Pharm. 2020;11(9):481-486.
16. Witaningrum AM, Wibisono FJ, Permatasari DA, Effendi MH. Detection of Class 1 Integron Encoding Gene in Multidrug Resistance (MDR) Citrobacter freundii Isolated from Healthy Broiler Chicken. Trop Anim Sci J. 2021;44(3):363-368.
17. Mikoleit M. Biochemical Identification of Salmonella and Shigella Using an Abbreviated Panel of Tests. WHO Glob Foodborne Infect Netw. 2015;5(33):1-43.
18. Adzitey F, Rusul G, Huda N. Prevalence and antibiotic resistance of Salmonella serovars in ducks, duck rearing and processing environments in Penang, Malaysia. Food Res Int. 2012;45(2):947-952.
19. Handijatno D, Ahmad N-A, Yusoff SM, Salleh A, Zamri-Saad M. Efficacy of a recombinant vaccine against pasteurellosis in chickens and ducks. Adv Anim Vet Sci. 2019;7(12):1134-1139.
20. Abdelaziz I, Abd El-Tawab A, Maarouf A, Elhofy F. Bacteriological and molecular studies on Salmonella isolated from duckling farmsat Kaliobia, Egypt. Benha Vet Med J. 2020;39(1):169-174.
21. García C, Soriano JM, Benítez V, Catalá-Gregori P. Assessment of salmonella spp. in feces, cloacal swabs, and eggs (eggshell and content separately) from a laying hen farm. Poult Sci. 2011;90(7):1581-1585.
22. Riwu KHP, Effendi MH, Rantam FA, Khairullah AR, Widodo A. A review: Virulence factors of Klebsiella pneumonia as emerging infection on the food chain. Vet World. 2022;15(9):2172-2179.
23. Cui L, Liu Q, Jiang Z, Song Y, Yi S, Qiu J, et al. Characteristics of Salmonella From Chinese Native Chicken Breeds Fed on Conventional or Antibiotic-Free Diets. Front Vet Sci. 2021;8(March):1-10.
24. Zhao X, Gao Y, Ye C, Yang L, Wang T, Chang W. Prevalence and Characteristics of Salmonella Isolated from Free-Range Chickens in Shandong Province, China. Biomed Res Int. 2016;2016.
25. Hu Y, Wang Z, Qiang B, Xu Y, Chen X, Li Q, et al. Loss and Gain in the Evolution of the *Salmonella enterica* Serovar Gallinarum Biovar Pullorum Genome. mSphere. 2019;4(2):1-20.
26. Pal M, Merera O, Rahman MT. Salmonellosis: A major foodborne disease of Global significance Biological Control View project Water Quality View project. Beverage Food World. 2015;42(12).

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Male Family Caregivers of Schizophrenic Patients have a Higher Risk of Hypertension and Lower Quality of Life : A Cross-Sectional Study

Cuidadores familiares masculinos de pacientes esquizofrénicos tiene un mayor riesgo de hipertensión y baja calidad de vida: un estudio transversal

Chlara Yunita Prabawati[1a]*, Reliani Reliani[2a], Erfan Rofiqi[3b], Septian Galuh Winata[4b], Diah Priyantini[5b]

SUMMARY

Background: *A limited study has identified the essential information on the physical health of family caregivers with patients with schizophrenia in Indonesia. This study aimed to assess the correlations between blood pressure and quality of life in family caregivers of patients with schizophrenia.*
Methods*: A retrospective and cross-sectional study design used convenience sampling conducted in several mental hospitals in Indonesia. Measurement of a calibrating sphygmomanometer and WHO Quality of Life-BRIEF were used to collect the data from the family caregiver. Participants received questionnaires and signed informed consent.*
Results: *There was a significantly positive association between the domain of family caregiver's Physical Health, Blood pressure, and Quality of Life (Beta =1.27, p <0.01). The prevalence of high blood pressure was significantly higher among male caregivers than female caregivers (65.3 %). The negative predictor of Quality of Life was the relationship between patients (Beta = – 3.11, p <0.01) and diastolic hypertension level (Beta = – 3.08, p <0.01). The positive predictor was elevated blood pressure (Beta = 2.08, p <0.01).*
Conclusion: *Male Indonesian family caregivers tended to respond to their physical health with more inappropriate strategies. Future research about physical health and education programs is needed to enhance male family caregivers to monitor their blood pressure while they are taking care of schizophrenic patients, which might lead to a better of their quality of life.*

Keywords*: Blood pressure, quality of life, family caregivers, schizophrenia.*

RESUMEN

Antecedentes: *Un estudio limitado ha identificado la información esencial sobre la salud física de los cuidadores familiares de pacientes con esquizofrenia*

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ORCID: 0000-0003-3661-7769[1]
ORCID: 0000-0003-4904-5720[2]
ORCID: 0000-0003-4254-2740[3]
ORCID: 0000-0002-2202-0892[4]
ORCID: 0000-0002-9535-8456[5]

[a]Department of Psychiatric Nursing, School of Nursing, Universitas Muhammadiyah Surabaya, Surabaya, Indonesia.

[b]Department of Surgical Nursing, School of Nursing, Universitas Muhammadiyah Surabaya, Surabaya, Indonesia.

*Corresponding author: Chlara Yunita Prabawati
E-mail: chlarayunitaprabawati@um-surabaya.ac.id

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en Indonesia. Este estudio tuvo como objetivo evaluar las correlaciones entre la presión arterial y la calidad de vida en cuidadores familiares de pacientes con esquizofrenia.

Métodos: *Un diseño de estudio retrospectivo y transversal que utilizó un muestreo de conveniencia realizado en varios hospitales psiquiátricos en Indonesia. Se utilizó la medición mediante un esfigmomanómetro de calibración y la calidad de vida de la OMS-BRIEF para recopilar los datos del cuidador familiar. Los participantes recibieron cuestionarios y firmaron el consentimiento informado.*

Resultados: *Hubo asociación significativamente positiva entre el dominio Salud Física, Presión Arterial y Calidad de Vida del cuidador familiar (Beta =1,27, p <0,01). La prevalencia de hipertensión arterial fue significativamente mayor entre los hombres cuidadores que entre las mujeres cuidadoras (65,3 %). El predictor negativo de la Calidad de Vida fue la relación entre los pacientes (Beta = – 3,11, p < 0,01) y el nivel de hipertensión diastólica (Beta = – 3,08, p < 0,01). El predictor positivo fue la presión arterial elevada (Beta = 2,08, p <0,01).*

Conclusión: *Los cuidadores familiares varones indonesios tendían a responder a su salud física con estrategias más inapropiadas. Se deben realizar investigaciones futuras sobre programas de educación y salud física para mejorar a los cuidadores familiares masculinos para controlar su presión arterial mientras cuidan a pacientes esquizofrénicos, lo que podría conducir a una mejor calidad de vida.*

Palabras clave: *Presión arterial, calidad de vida, cuidadores familiares, esquizofrenia.*

INTRODUCTION

In Indonesia, approximately 87 % of family caregivers living with schizophrenia patients are identified. At the same time, the incidence of cases has increased by 1.1 million from 241 million individuals, the majority of whom accompany their family caregivers (1). An estimated 2.6 million people with schizophrenia and 87 % live with their family caregivers (1,2). A study of 368 schizophrenia patients and their caregivers indicates that 81.5 % of caregivers were parents, with an average age of 58.1 years. The study also shows that 85.3 % had some level of objective workload, with the total objective score of the Family Burden Interview Schedule (FBIS) being 22.69 (3). Moreover, while caring for and staying in the home, the patients and family caregiver remarkably show their attitude and interaction toward each other, but the patients still show their symptoms (4,5). Thus, situations might lead to showing their attitudes and behaviors of several specific emotions expressed (6-8).

The family caregivers eventually show their attitude in caring for and completing their role as the person in charge of schizophrenic patients in their families (9). This situation influences their health outcomes, especially in their physical health; taking care system might be considerate even though the prognosis of schizophrenia cases might lead toward chronic illness that occurs for a long time, estimated to be more than ten years (10-13). Vice versa, the patient will stimulate the interaction process involving the onset of psychotic symptoms, which are positive and negative (14,15). Thus, it might influence health outcome factors such as elevating the situation (15), including the symptom of high-risk hypertension and uncertainty of the quality of life (10).

A limited study has identified the essential information on the physical health of family caregivers with patients with schizophrenia in Indonesia. This study aimed to evaluate the correlates of family caregivers' physical health and blood pressure and examine the role of the quality of life in family caregivers of patients with schizophrenia.

METHODS

Research Design and Study Participants

This study conducted a quantitative study with a cross-sectional design. The family caregivers who participated in the study were chosen using convenience sampling conducted in various mental hospitals in Indonesia. Participants were recruited from Central Java, Yogyakarta, and East Java Province in Indonesia. The inclusion criteria were Family caregivers with patients that were diagnosed with schizophrenia based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) at a local mental health center. Family caregivers have lived with patients for at least three months, being mother or father, wife or husband, and son or daughter, directly interacting with patients and understanding the Indonesian language. The exclusion criteria are family caregiver (FCG) with

patients with a head injury, having certain types of chronic physical illness, uncorrected sight, or hearing impairment, and having a mental illness.

The sample size was estimated by G-Power Software Version 3.1.9.2, used F-test and multiple linear regression, α error probability = 0.05, effect size = 0.15, power level = 0.80, and ten predictors with a total of 150 Primary family caregivers of schizophrenic patients.

Instrument and Data Collection

Measurement of a calibrating sphygmomanometer and WHO Quality of Life-BRIEF (WHO QoL-BRIEF) (16) were used to collect the data from the patient and family caregiver, respectively. In the current study, the WHO QoL-BRIEF was translated into Indonesian and tested valid with a Cronbach alpha of 0.86.

The researcher would track the schizophrenic patients accompanied by their families, visit the outpatient department of the mental hospital in their waiting consult with the doctors, and briefly introduce the study to the FCG. If the family is interested in participating in the study, the researcher will explain the purpose, procedure, data confidentiality, security, participant rights, and concerns. After whom is responsible for taking care of the patient's health to fill in the questionnaire, the researcher assesses the blood pressure measurement. All participants signed the informed consent document. All the questionnaires and assessments were administered at a single time point. The Mental Hospital Committee on Human Research Protection and Ethics Committee approved the study.

Data Analysis

SPSS for Windows version 17.00 was used for data analysis. To summarize the data, descriptive statistics were utilized, and simple linear regression and multiple linear regression models were used for statistical analysis. The statistical significance of the findings was determined using a significance level of 0.05 (p-value 0.05).

Ethical Consideration

The studies involving human participants were reviewed. And they were approved by the Standardized Ethics Committee Board of Mental Hospital No.070/4026/09/2018. The patients/participants provided written informed consent to participate in this study.

RESULTS

Demographic data is shown in Table 1. The average age of family caregivers is 46.5 ± 13.1 years, the duration of care is 6.1 ± 6.6 years, and the duration of taking care of patients in their onset is 36.2 ± 60.5 (Hours). Regarding gender, 52.7 % of FCGs were male, while 47.3 % were female. Regarding educational level, 62.0 % had primary education, while 38.0 % had advanced education. Most FCGs (58.7 %) were parents of schizophrenic patients, and 41.3 % were siblings. The marital status indicated that 36.7 % of FCGs were in a romantic relationship, while 63.3 % were single or divorced. Nearly all FCGs (99.3 %) were employed, except for one participant. The table also includes information about the systolic/diastolic blood pressure of the FCGs. Approximately 41.3 % had normal blood pressure, 13.3 % had elevated blood pressure, 30.7 % had hypertension level 1, and 14.7 % had hypertension level 2.

Participants' Description of high blood pressure prevalence was significantly higher among male caregivers than among female caregivers (male: 65.3 % vs. female 34.7 %) shown in Figure 1.

Table 2 shows the demographic characteristics of family caregivers associated with quality of life (QoL) using simple linear regression. Marital status and educational level were significantly associated with QoL, with higher scores observed in caregivers in a romantic relationship with advanced education. The number of hours spent taking care of patients during their onset of symptoms was negatively associated with QoL, indicating that longer hours of care were associated with lower QoL. The duration of

Table 1. Demographic Information of Family Caregivers

		Family Caregivers (n = 150)	
		Mean ± SD	Range
Age (Years)		46.5 ± 13.1	(18-73)
Duration of care (Years)		6.1 ± 6.6	(1-35)
FCG taking care of patients in their Onset (Hours)		36.2 ± 60.5	(2-336)
		n	%
Gender	Male	79	52.7
	Female	71	47.3
Educational level	Basic	93	62.0
	Advanced	57	38.0
Relationship FCG of Schizophrenic Patients	Parents	88	58.7
	Sibling	62	41.3
	Romantic Relationship	55	36.7
Marital status	Single/divorced	95	63.3
	No	1	0.7
	Yes	149	99.3
Employment	Normal	62	41.3
	Elevated	20	13.3
Systolic/ Diastole Blood Pressure	Hypertension Level 1	46	30.7
	Hypertension Level 2	22	14.7
Actual Values of Diastolic and Systolic Blood Pressured Measured in the FCG.	Normal Systolic (Less than 120 mmHg)	62	41.3
	Normal Diastolic (Less than 80 mmHg)	62	41.3
	Systolic Elevated (120-129 mmHg)	20	13.3
	Diastolic Elevated (less than 80 mmHg)	20	13.3
	Systolic Hypertension Level 1 (130-139 mmHg)	46	30.7
	Diastolic Hypertension Level 1 (80-89 mmHg)	46	30.7
	Systolic Hypertension Level 2 (140 -180 mmHg)	22	14.7
	Diastolic Hypertension level 2 (90-120 mmHg)	22	14.7

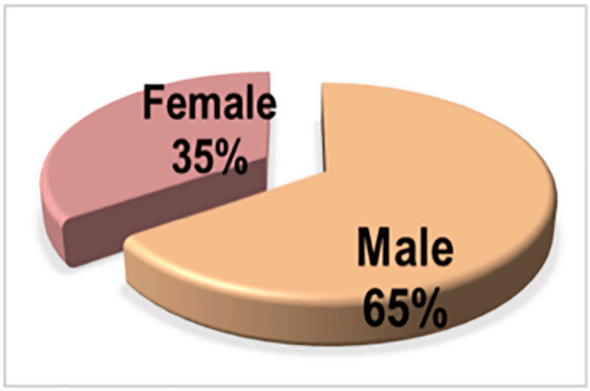

Figure 1. Prevalence of High Blood Pressure among Male and Female Caregivers.

care and the caregiver's relationship with the schizophrenic patients also showed significant associations with QoL.

Table 3 presents the relationship between systolic blood pressure (SBP), diastolic blood pressure (DBP), and QoL as measured by the QoL BRIEF scale. Among the different blood pressure categories, elevated blood pressure (EBP) and hypertension level 1 were significantly associated with lower QoL scores than the normal blood pressure category. Overall, there was a trend towards higher blood pressure being associated with lower QoL, although the results were not statistically significant.

Table. 2 FGC Demographic characteristics associated with QoL (n= 150)

Characteristic	*B*	*t*	*p*
Family Caregiver's factor			
Marital status (single or divorced/romantic relationship)	6.56	2.07	0.04
Educational level (advanced/basic)	0.48	2.07	0.04
FCG taking care of patients in their onset (hours)	–0.06	–2.41	0.02
Duration of Care (years)	0.46	2.00	0.05
Relationship FCG with Schizophrenic Patients (Parents/Siblings)	–4.69	–3.51	0.01

FCG: Family Caregivers; EBP: Elevated Blood Pressure; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; QoL BRIEF: Quality of Life

Table. 3 The Relationship between the SBP, DPB, and QoL BRIEF (n= 150)

Characteristic	Systole Blood Pressure			Diastolic Blood Pressure		
	B	*t*	*p*	*B*	*t*	*p*
1. Normal	0.76	1.52	0.12	0.70	1.39	0.10
2. EBP	1.47	1.78	<0.01	1.46	1.74	<0.01
3. Hypertension Level 1	–1.27	–2.67	<0.01	–1.22	–2.56	<0.01
4. Hypertension Level 2	–0.07	–0.13	0.89	–0.05	–0.10	0.89
Total	0.30	1.69	0.09	0.28	1.65	0.09

FCG: Family Caregivers; EBP: Elevated Blood Pressure; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; QoL BRIEF: Quality of Life

Table 4 presents multiple linear regression analysis results to predict the QoL of family caregivers caring for schizophrenic patients. The finding suggests that the negative predictor of quality of life was the relationship with patients (Beta = – 3.11, p <0.01) and Diastolic Hypertension Level (Beta = – 3.08, p <0.01), the positive predictor was the Elevated Blood Pressure (Beta = 2.08, p <0.01). Our study, it might fit one of the demographic characteristics of the FCG. Increasing the diastolic hypertension level might reduce the signs of the FCG Quality of Life; instead, systolic hypertension and other categories were not significantly predicted.

Table. 4 Multiple Linear Regression analysis for variable predicting QoL of Family Caregivers taking care of patients with schizophrenia (n =150)

	Model 1			Model 2			Model 3		
	B	*t*	*p*	*B*	*t*	*p*	*B*	*t*	*p*
(constant)	47.12	7.91	0.00	57.05	7.87	0.00	44.17	4.69	0.0001
Educational level (advanced/basic	0.42	1.80	0.07	0.34	0.90	0.37	0.41	1.09	0.280
FCG taking care of patients in their onset (hours)	–0.04	–1.66	0.10	–0.03	–1.33	0.18	–0.03	–1.03	0.310
Marital status (single or divorced/romantic relationship)	6.01	1.90	0.06	5.62	1.79	0.08	7.05	2.82	0.200
Fcg's duration of care				0.16	0.43	0.67	0.03	0.09	0.930
Relationship FCG with Schizophrenic Patients				–4.11	–2.35	.035	–3.11	–2.32	0.023*
EBP							2.08	2.11	0.029*
SHL1							–0.79	–0.92	0.360
DHL1							–3.08	3.11	0.043*
SHL2							0.64	–0.89	0.380
DHL2							0.40	0.80	0.430
R^2	0.08			0.11			0.19		
Adjusted R^2	0.06			0.08			0.13		

FCG: Family Caregivers; EBP: Elevated Blood Pressure; SHL: Systolic Hypertension Level; DHL: Diastolic Hypertension Level

DISCUSSION

The average age of family caregivers was 46.5 years, and those involved in this study were male. This could be explained by the fact that the father or brother, as the male family caregivers, will provide a good family environment in Indonesian culture. FCG provides financial support and safety guard for patients and other family members. In addition, female family caregivers did all personal care toward patients (17-20). For the FCG marital status, we found that 63.3 % were single/divorced. The standardized average married in the healthy Indonesian population was 25 years old (21). Those reflected the reality of 2/3 schizophrenic patients in the current study who did not get married, whether they persistent being single or divorced is higher.

In Indonesian culture, people believe marriage is the principal for completing their life (22). The high single or divorced rates in patients with schizophrenia revealed that they need to face social pressure from gossip and verbal bullied by the family or social ties (5,23-26), or the pattern reflected that patients still face uttered humiliation in society in Indonesian culture (27). People believed this phenomenon revealed it might cause the patient to feel less optimistic about recovery and relatively felt pessimistic (11,25,28-30), or the pattern reflected that the patient got less to respond and faced underprivileged outcomes.

In line with prior research findings, primary family caregivers who were parents (31), had a low education level (31-33) and had a decreased monthly household income, or there is no employment (31,34) experienced lower QoL. It might influence by the effect of the parent's tendency to be taking care of all the schizophrenic needs and demands in our study is performed by parents. Indonesian parents tend to show more control, and at the same time, they face stigmatization.

Our study found that family caregiver characteristics involved marital status, educational background, hours of caretaking, and their relationship with people with schizophrenia were strongly correlated with the FCG QoL. This phenomenon means their characteristics tend more toward what they feel might stimulate their well-being. FCG with schizophrenic patients is more prominent while caretaking (35-37). Thus, it might be influenced by the social and cultural background of all family members showing acceptance and feeling for what their relatives suffered.

Our study finding suggests a relationship between SBP, DPB, and QoL BRIEF. Thus, the study result shows that the classification of hypertension, especially the elevated blood pressure and hypertension level 1 on their SBP and DPB categories, are correlated to the Quality of Life. A previous study on caretaking depression and mental illnesses in the elderly shows it is more likely to be associated with anxiety (38,39). Hypertension and elevated blood pressure were also associated with anxiety through disruption of the autonomic nervous system, leading to higher variations in blood pressure and cardiovascular events (38,40,41). The most interesting phenomenon occurs in males; instead, other studies suggest the contrary findings on women that might correlate to the women's anxious and depressed feelings (42). In our opinion, the characteristic of Javanese family caregivers who are taking care of a person with schizophrenia shows controlling all aspects of caring trajectories. Thus, the feeling of fear, anxiety, uncertainty, and the unknown might stimulate the increase in blood pressure. The phenomenon reflects that the current negativity of emotional statuses might affect Javanese FCG blood levels while taking care of their family member with schizophrenia (7,43,44).

Our final finding suggests that the negative predictor of Quality of Life was the relationship between patients and Diastolic Hypertension levels. The positive predictor was Elevated Blood Pressure. In our study, it might fit one of the demographic characteristics of the FCG, and Increasing the Diastolic Hypertension level might reduce the significance of the FCG Quality of Life (45). Instead, systolic hypertension and other categories were not significant predictors. Previous studies explained that the etiology of the EBP and DHL is a heterogeneous condition involving biological factors, genetics, depressive episodes, anxiety level, psychosocial aspect, cerebrovascular pathology, disorders of the endocrine system, presence of inflammatory processes, and nutritional status (46,47). Aligned with some previous studies (7,8,23,25,26,39,43,48), it is suggested the existence of a close relationship between hypertension disorders and mental health. The study shows that patients with cerebrovascular disease, especially in the anterior hemisphere, show mood lability. It seriously impacts the prognosis of hypertension in FCG and the overall effectiveness of the health system. Thus, the elevated blood pressure of FCG is related to their concern for their relatives and life, considering the stimulation stressor they face might influence their lower coping, self-efficacy, and self-concept. Other studies conducted by Maeng et al. (5) and Webb et al. (49) found it might relate to the longer-term motivation of caretaking all trajectories. However, this condition might stimulate the prediction of decreasing the FCG QoL.

CONCLUSION

This finding is the first Indonesian study assessing the family caregiver's physical health of schizophrenic patients. Results suggest that male caregivers are at a higher risk of chronic illness conditions than female caregivers of patients with schizophrenia. Male Indonesian family caregivers tended to respond to their physical health with more inappropriate strategies. Future research about physical health and education programs is needed to enhance male family caregivers to monitor their blood pressure while they're taking care of schizophrenic patients, which might lead to improving their quality of life.

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Authors' contributions

Chlara Yunita Prabawati, Diah Priyantini, Reliani, and Erfan Rofiqi analyzed and interpreted the data and drafted the manuscript. Chlara Yunita Prabawati contacted participants and collected data. Septian Galuh and Diah Priyantini designed the study and revised the manuscript. All authors have read, reviewed, and approved the final manuscript.

Availability of data and materials

The authors will make the raw data supporting this article's conclusions available.

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Conflict of Interest

The authors declare that the research was conducted without relation that could be made as a potential conflict of interest.

REFERENCES

1. Ministry of Health of the Republic of Indonesia. Basic Health Research Results 2018. Health Research and Development Agency. 2019. Available from: http://labdata.litbang.kemkes.go.id/images/download/report/RKD/2018/Laporan_Nasional_RKD2018_FINAL.pdf
2. Idaiani S, Yunita I, Tjandrarini DH, Indrawati L, Darmayanti I, Kusumawardani N, et al. Prevalence of Psychosis in Indonesia based on the 2018 Basic Health Research. J Health Service Researcher and Developer. 2019;3(1):9–16.
3. Lasebikan VO, Ayinde OO. Family Burden in Caregivers of Schizophrenia Patients: Prevalence and Socio-demographic Correlates. Indian J Psychol Med. 2013;35(1):60-66.
4. Ang CW, Tan MM, Bärnighausen T, Reininghaus U, Reidpath D, Su TT. Mental distress along the cascade of care in managing hypertension. Sci Rep. 2022;12(1):15910.
5. Maeng S-R, Kim W-H, Kim J-H, Bae J-N, Lee J-S, Kim C-E. Factors Affecting Quality of Life and Family Burden among the Families of Patients with Schizophrenia. Korean J Schizophr Res. 2016;19(2):78.
6. Su Z, Zou Z, Hay SI, Liu Y, Li S, Chen H, et al. Global, regional, and national time trends in mortality for congenital heart disease, 1990-2019: An age-period-cohort analysis for the Global Burden of Disease 2019 study. E Clin Med. 2022;43:101249.
7. Warner AR, Lavagnino L, Glazier S, Hamilton JE, Lane SD. Inpatient Early Intervention for Serious Mental Illnesses Is Associated with Fewer Rehospitalizations Compared with Treatment as Usual in a High-volume Public Psychiatric Hospital Setting. J Psychiatr Pract. 2022;28(1):2435.
8. Marutani T, Chhim S, Taing S, Nishio A. Causal beliefs regarding schizophrenia and help-seeking behaviors among patients with schizophrenia and family caregivers attending psychiatric clinics in Cambodia. Transcult Psychiatry. 2022;13634615221107208.
9. Nenobais A, Jatimi A, Jufriyanto M. Family Burden for the Caregivers of People with Mental Disorders: A Systematic Review. J Ners. 2019;14(3 Special Issue):26-34.
10. Dong L, Xie Y, Zou X. Association between sleep duration and depression in US adults: A cross-sectional study. J Affect Disord. 2022;296:183-188.
11. Stanley S, Balakrishnan S, Ilangovan S. Psychological distress, perceived burden and quality of life in caregivers of persons with schizophrenia. J Ment Health. 2017;26(2):134-141.
12. Wei Y, Peng Y, Li Y, Song L, Ju K, Xi J. Caregivers' burden and schizophrenia patients' quality of life: Sequential mediating effects of expressed emotion and perceived expressed emotion. Frontiers in Psychiatry. 2022;13.
13. ZamZam R, Midin M, Hooi LS, Yi EJ, Ahmad SN, Azman SF, et al. Schizophrenia in Malaysian families: A study on factors associated with quality of life of primary family caregivers. Int J Ment Health Syst. 2011;5(1):16.
14. Solomon-Moore E, Lambert J, Grey E, Gillison F, Townsend N, Busam B, et al. Life in lockdown: aAlongitudinal study investigating the impact of the UK COVID-19 lockdown measures on lifestyle behaviours and mental health. BMC Public Health. 2022;22(1):1495.

15. Armando M, Hutsebaut J, Debbané M. A Mentalization-Informed Staging Approach to Clinical High Risk for Psychosis. Front Psychiatry. 2019;10:385.
16. Vahedi S. World Health Organization Quality-of-Life Scale (WHOQOL-BREF): Analyses of Their Item Response Theory Properties Based on the Graded Responses Model. Iran J Psychiatry. 2010;5(4):140-153.
17. Caqueo-Urízar A, Gutiérrez-Maldonado J, Miranda-Castillo C. Quality of life in caregivers of patients with schizophrenia: A literature review. Health Qual Life Outcomes. 2009;7:84.
18. Łopuszańska UJ, Skorzyńska-Dziduszko K, Lupa-Zatwarnicka K, Makara-Studzińska M. Mental illness and metabolic syndrome--a literature review. Ann Agric Environ Med. 2014;21(4):815-821.
19. Turana Y, Tengkawan J, Chia YC, Nathaniel M, Wang J-G, Sukonthasarn A, et al. Hypertension and stroke in Asia: A comprehensive review from HOPE Asia. J Clin Hypertens (Greenwich). 2021;23(3):513-521.
20. Baller JB, McGinty EE, Azrin ST, Juliano-Bult D, Daumit GL. Screening for cardiovascular risk factors in adults with serious mental illness: A review of the evidence. BMC Psychiatry. 2015;15(1):55.
21. Ekoriano M, Muthmainnah M, Titisari A, Devi YP, Widodo T, Purwoko E. The average age of first marriage for Indonesian women in their reproductive period who give birth to an average of two children: National survey (2017 – 2019) [version 1; peer review: awaiting peer review]. F1000Research. 2023;12.
22. Prabawati CY. The challenges of the family caregivers in caring of late-onset schizophrenia and very late-onset schizophrenia-like psychosis: Caregiver risk of burden and neurodegenerative disease. Alzheimer's Dement. 2021;17(S10):e050251.
23. Natour S, Damri O, Agam G. The Effect of Global Warming on Complex Disorders (Mental Disorders, Primary Hypertension, and Type 2 Diabetes). Int J Environ Res Public Health. 2022;19(15).
24. Tolin DF, Gilliam CM, Davis E, Springer K, Levy HC, Frost RO, et al. Psychometric Properties of the Hoarding Rating Scale-Interview. J Obsessive Compulsive Relat Disord. 2018;16:76-80.
25. Prabawati CY. The challenges of the family caregivers in caring of late-onset schizophrenia and very late-onset schizophrenia-like psychosis: Caregiver risk of burden and neurodegenerative disease. Alzheimer's Dement. 2021;17(S10):e050251.
26. Baller JB, McGinty EE, Azrin ST, Juliano-Bult D, Daumit GL. Screening for cardiovascular risk factors in adults with serious mental illness: A review of the evidence. BMC Psychiatry. 2015;15(1):55.
27. Wei J, Yin X, Liu Q, Tan L, Jia C. Association between hypertension and cognitive function: A cross-sectional study in people over 45 years old in China. J Clin Hypertens (Greenwich). 2018;20(11):1575-1583.
28. Pradevi AF, Fitriani N, Prabawati CY. Effect of the nurse-client therapeutic alliance toward positive symptoms of patient with schizophrenia. Alauddin Sci J Nurs. 2022;3(1 SE-):43-47.
29. Shahimi NH, Lim R, Mat S, Goh C-H, Tan MP, Lim E. Association between mental illness and blood pressure variability: a systematic review. Biomed Eng Online. 2022;21(1):19.
30. Wei Y, Peng Y, Li Y, Song L, Ju K, Xi J. Caregivers' burden and schizophrenia patients' quality of life: Sequential mediating effects of expressed emotion and perceived expressed emotion. Frontiers in Psychiatry. 2022;13.
31. Lua PL, Bakar ZA. Health-related quality of life profiles among family caregivers of patients with schizophrenia. Fam Community Health. 2011;34(4):331-339.
32. Zeng Y, Hu X, Li Y, Zhen X, Gu Y, Sun X, et al. The Quality of Caregivers for the Elderly in Long-Term Care Institutions in Zhejiang Province, China. Int J Environ Res Public Health. 2019;16(12).
33. Wong C, Merrilees J, Ketelle R, Barton C, Wallhagen M, Miller B. The experience of caregiving: differences between behavioral variant of frontotemporal dementia and Alzheimer disease. Am J Geriatr Psychiatry J Am Assoc Geriatr Psychiatry. 2012;20(8):724–8.
34. Brodaty H, Donkin M. Family caregivers of people with dementia. Dialogues Clin Neurosci. 2009;11(2):217-228.
35. Kusumawardani W, Yusuf A, Fitryasari R, Ni'mah L, Tristiana RD. Family burden effect on the ability in taking care of schizophrenia patient. Indian J Public Heal Res Dev. 2019;10(8):2654-2659.
36. Rindayati, Yusuf A, Efendi F, Illahiati NK, Nasir A. Experience of caregiver coping mechanisms when taking care of a schizophrenic patient. Int J Psychosoc Rehabil. 2020;24(7):7964-7975.
37. Sustrami D, Yusuf A, Fitryasari R, Efendi F, Aysha RF. Relationship between social support and family caregiver burden in schizophrenia patients. J Pak Med Assoc. 2023;73(2):S42-45.
38. Khatimah CH, Adami A, Abdullah A, Marthoenis. Quality of life, mental health, and family functioning of schizophrenia caregivers: A community-based cross-sectional study. Asia-Pacific psychiatry Off J Pacific Rim Coll Psychiatr. 2022;14(1):e12467.
39. Frajerman A, Morin V, Chaumette B, Kebir O, Krebs M-O. Management of cardiovascular co-morbidities in young patients with early onset psychosis: State of the art and therapeutic perspectives. Encephale. 2020;46(5):390-398.

40. Iswatun, Yusuf A, Efendi F, Susanto J, Dewi WK, Hidaayah N. Relationship between anxiety and spiritual well-being of the elderly with hypertension during the COVID-19 pandemic. J Pak Med Assoc. 2023;73(2):S46-49.
41. Kurniawati ND, Ariyanti YP, Nikmah L, Wahyuni ED. Relationship between disease duration and preventive motivation with quality of life of patients with coronary heart disease at productive age in cardiology. Int J Pharm Res. 2020;12(4):1754-1760.
42. Alzheimer's Association Report. 2023 Alzheimer's disease facts and figures. Alzheimer's Dement. 2023;19(4):1598-1695.
43. Souza ALR, Guimarães RA, de Araújo Vilela D, de Assis RM, de Almeida Cavalcante Oliveira LM, Souza MR, et al. Factors associated with the burden of family caregivers of patients with mental disorders: A cross-sectional study. BMC Psychiatry. 2017;17(1):353.
44. Sambasivam R, Liu J, Vaingankar JA, Ong HL, Tan M-E, Fauziana R, et al. The hidden patient: Chronic physical morbidity, psychological distress, and quality of life in caregivers of older adults. Psychogeriatrics. 2019;19(1):65-72.
45. Lestari R, Yusuf A, Hargono R, Ahsan A. A community-resilience model: A new way in optimizing medication adherence among schizophrenic patients. Res J Pharm Technol. 2020;13(11):5083-5087.
46. Lai JS, Aung YN, Khalid Y, Cheah S-C. Impact of different dietary sodium reduction strategies on blood pressure: A systematic review. Hypertens Res. 2022;45(11):1701-1712.
47. Bosch J, Lonn EM, Jung H, Zhu J, Liu L, Lopez-Jaramillo P, et al. Lowering cholesterol, blood pressure, or both to prevent cardiovascular events: Results of 8.7 years of follow-up of Heart Outcomes Evaluation Prevention (HOPE)-3 study participants. Eur Heart J. 2021;42(31):2995-3007.
48. Hou M-R, Wang J, Xue J-H, Pei J-Q, Shi Y, Li X-W. Gender differences among long-stay inpatients with schizophrenia in China: A cross-sectional study. Heliyon. 2023;9(5):e15719.
49. Webb C, Pfeiffer M, Mueser KT, Gladis M, Mensch E, DeGirolamo J, et al. Burden and well-being of caregivers for the severely mentally ill: The role of coping style and social support. Schizophr Res. 1998;34(3):169-180.

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Relationship between Early Initiation Breastfeeding, Exclusive Breastfeeding, Complementary Feeding, and Nutritional Education with Nutritional Status of Children under Three years

Relación entre el inicio precoz de la lactancia materna, la lactancia materna exclusiva, la alimentación complementaria y la educación nutricional con el estado nutricional de los niños menores de tres años

Sa'diah Multi Karina[1a], Meilinasari Meilinasari[2a], Rosmida Magdalena Marbun[3a], Fairuz Dhia Rabbani[4a], Gurid Pramintarto Eko Mulyo[5b*], Tarjuman Tarjuman[6b], Sugeng Wiyono[7a]

SUMMARY

Introduction: *Nutritional status according to the height-to-age index was influenced by many factors, such as maternal or child factors. Now, the government's nutrition program focuses on the problem of malnutrition in toddlers, especially stunting. The study aimed to determine the relationship between a history of early initiation breastfeeding, exclusive breastfeeding, complementary feeding, and nutrition education with the nutritional status of toddlers according to height-to-age index.*

Methods: *The study had a cross-sectional design, and 356 samples were selected systematically and randomly from children under three years old. Data on the history of early initiation breastfeeding, exclusive breastfeeding, complementary feeding, and nutrition education were collected by interviewing toddlers' mothers using a questionnaire, and anthropometric measurements collected data on toddlers' nutritional status. The Chi-Square test was conducted to evaluate the relationships among variables, with a significance value <0.05.*

Results: *There was a significant relationship between the history of exclusive breastfeeding and the nutritional status of toddlers according to the height-to-age index ($p = 0.032$). There was no significant relationship between early initiation breastfeeding, the time of giving the first complementary feeding, the origin and type of complementary feeding, and nutrition education about breast milk and complementary feeding with the nutritional status of toddlers ($p > 0.05$).*

Conclusion: *Nutrition education initiatives should be strengthened to improve moms' knowledge and activate community health cadres in accompanying toddler families related to child nutrition and health problems. Healthy nursing practices and clear guidance on exclusive breastfeeding can enhance child nutrition.*

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ORCID: 0000-0002-2289-2586[1]
ORCID: 0000-0001-8663-0684[2]
ORCID: 0000-0002-9057-6905[3]
ORCID: 0000-0000-7561-5788[4]
ORCID: 0000-0003-4701-9588[5]
ORCID: 0009-0009-1225-1716[6]
ORCID: 0000-0002-8513-7246[7]

[a]Jurusan Gizi, Politeknik Kesehatan Kemenkes Jakarta II, Jakarta, Indonesia.
[b] Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia.

*Corresponding Author: Gurid Pramintarto Eko Mulyo
E-mail: gurid@staff.poltekkesbandung.ac.id

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Keywords: *Child health, nutritional status, health care, malnutrition, breastfeeding.*

RESUMEN

Introducción: *El estado nutricional según el índice de talla para la edad estuvo influenciado por muchos factores, como factores maternos o infantiles. Ahora, el programa de nutrición del gobierno se enfoca en el problema de la desnutrición en los niños pequeños, especialmente en el retraso del crecimiento. El objetivo del estudio fue determinar la relación entre el antecedente de inicio temprano de la lactancia materna, lactancia materna exclusiva, alimentación complementaria y educación nutricional con el estado nutricional de los lactantes según índice talla-edad.*
Métodos: *El estudio tuvo un diseño transversal y se seleccionaron 356 muestras sistemáticamente al azar de niños menores de tres años. Los datos sobre la historia del inicio temprano de la lactancia materna, la lactancia materna exclusiva, la alimentación complementaria y la educación nutricional se recopilaron mediante entrevistas a las madres de los niños pequeños mediante un cuestionario. Los datos sobre el estado nutricional de los niños pequeños se recopilaron mediante mediciones antropométricas. Se realizó la prueba de Chi-Cuadrado para evaluar la relación entre variables, con valor de significación <0.05.*
Resultados: *Hubo una relación significativa entre el antecedente de lactancia materna exclusiva y el estado nutricional de los lactantes según el índice talla-edad (p = 0.032). No hubo relación significativa entre el inicio temprano de lactancia materna, el momento de dar la primera alimentación complementaria, el origen y tipo de alimentación complementaria, así como la educación nutricional sobre leche materna y alimentación complementaria con el estado nutricional de los lactantes (p > 0.05).*
Conclusión: *Las iniciativas de educación nutricional deben fortalecerse para mejorar el conocimiento de las madres, activar cuadros de salud comunitarios en el acompañamiento de las familias de niños pequeños relacionados con la nutrición infantil y los problemas de salud. Las prácticas saludables de enfermería y una orientación clara sobre la lactancia materna exclusiva pueden mejorar la nutrición infantil.*

Palabras clave: *Salud infantil, estado nutricional, atención a la salud, desnutrición, lactancia materna.*

INTRODUCTION

Stunting is a chronic malnutrition disorder in which children are shorter in stature than others their age (1-2). It can cause developmental abnormalities and have long-term consequences in adulthood (3-4). Early childhood stunting has been demonstrated in studies to impact cognitive development and cause developmental delays negatively. It also impacts motor abilities and social connections (5,6). Stunting is caused by various factors, including family circumstances, poor nutrition, breastfeeding patterns, and infectious diseases (7). In Indonesia, maternal height, preterm birth, and low family income contribute to toddler stunting. Stunting must be addressed to promote healthy growth and development in children (8–10).

Stunting affects an estimated 162 million children under five worldwide, posing a substantial public health concern (11). In Indonesia, the prevalence of stunting among children under five is 29.9 %, indicating a severe problem (12). Within Central Java, regions such as Banyumas have recorded a prevalence of 13.87 % for children with short nutritional status and 15.53 % for children with deficient nutritional status (13). This suggests that many youngsters are not reaching optimal growth and development. According to the 2021 Indonesian Nutrition Status Study (SSGI), the nationwide prevalence of stunting in children under five is 24.4 %, with Central Java Province accounting for 20.9 % and Banyumas Regency accounting for 21.6 % (14). These figures underscore the ongoing problem of stunting, which has surpassed the World Health Organization's (WHO) 20 % threshold. As a result, the Ministry of Health has prioritized stunting, with strategic plans to lower stunting cases to 14.0 % and wasting cases to 7.0 % by 2024. These aims highlight the necessity of addressing Indonesia's high prevalence of stunting, which now ranks second among the Association of Southeast Asian Nations (ASEAN) countries in stunting cases (15).

Breastfeeding characteristics contributing to stunting include delayed initiation and non-exclusive breastfeeding before six months. Inadequate complementary feeding practices originate from low food quality, incorrect feeding procedures, and insufficient food and water hygiene. Central Java Province has an early initiation breastfeeding rate of 85.0 %, with Banyumas Regency at 65.6 %. Research in Banten found a link between early initiation

breastfeeding and stunting in children aged 0-24 months, with those who did not receive early initiation breastfeeding having an 11-fold higher risk of stunting (16). The prevalence of exclusive breastfeeding in Central Java infants aged 0-6 months is expected to be 72.5 %, reaching 65.2 % in the Banyumas District (17). Toddlers with a history of non-exclusive nursing are 8.2 times more likely to be stunted (18). Supplemental feeding practices also influence stunting instances, as improper timing, texture, and nutrient content of complementary foods harm children's nutritional status and development (19). Nutrition education for mothers or caregivers, focusing on food diversity, complementary feeding, and food and beverage hygiene, has been shown to drastically reduce the rate of malnutrition in preschool children (20).

Even though early feeding practices significantly impact toddler nutritional status, there has been a lack of comprehensive studies examining the relationship between a history of early initiation breastfeeding, exclusive breastfeeding, complementary feeding, and nutritional education with toddler nutritional status. Existing research has generally focused on individual elements or specific feeding techniques rather than the combined influence of these factors on the nutritional condition of toddlers. This study aimed to determine the relationship between a history of early initiation breastfeeding, exclusive breastfeeding, and complementary feeding, as well as nutritional education about breastfeeding and complementary feeding, with the nutritional status of toddlers.

METHODS

This quantitative study used a descriptive observational design with a cross-sectional approach. The research was conducted in the Sumbang District area, Indonesia, on April 23-28, 2018. The sample for this study was children under three years old (toddlers) in the Sumbang District area, as many as 356 people. The sample was obtained using a systematic random sampling method.

The independent variables in this study were the history of early initiation breastfeeding, exclusive breastfeeding, complementary feeding, and nutrition education. Early initiation breastfeeding is a method of initiation of breastfeeding within 1 hour after the baby is born. Exclusive breastfeeding is breastfeeding without consuming food or other drinks, except medicine, for six months from the baby's birth. Complementary feeding is given during the transition period between exclusive breastfeeding and family food, which is given when breast milk is no longer able to meet the energy and nutritional needs of the baby. The nutrition education referred to in this study was education regarding breastfeeding and complementary feeding. The dependent variable in this study was the nutritional status of toddlers, which was assessed using the height-for-age index.

Data were collected through interviews with respondents, namely the mothers of the sample, using a questionnaire. Early initiation breastfeeding data were grouped into groups. Yes, for those who received, and No, for those who did not. The data on exclusive breastfeeding was categorized into two groups: the exclusive breastfeeding group and the non-exclusive breastfeeding group. The complementary feeding data included when the child started consuming solid foods, categorized as before six months or at six months or older. It also included whether the complementary feeding was purchased or homemade and whether it was instant (commercial) or local (using local food ingredients). Toddlers' nutritional status data was obtained by measuring their height and comparing it to their age in months. It was categorized as usual (Z-score > -2 S.D.), short (Z-score between -2 SD and -3 S.D.), and very short (Z-score < -3 S.D.).

The research data were analyzed statistically using univariate and bivariate analysis. The univariate analysis produces the percentage of each group on each variable. Bivariate analysis was carried out using the Chi-Square test, which aimed to assess whether there was a significant relationship between the independent and dependent variables, with a p-value <0.05.

RESULTS

The characteristics of the respondents in the study are presented in Table 1. Regarding

the father's age, it was found that the majority (80.9 %) fell within the range of 20 to 40 years, with the highest proportion (52.8 %) having completed only elementary school. On the mothers' age, it was observed that the majority (76.7 %) were between 20 and 35 years old, with the highest percentage (53.4 %) of mothers who had completed only elementary school. Of the total sample, 236 toddlers (66.4 %) had a normal height-for-age, indicating they were within the expected range for their age.

The average born length and current age of toddlers are shown in Table 2. The average born length of toddlers in the Sumbang area reached 48.32 cm. It is still within the normal range of born length which is 49 – 50 cm. The average current age of toddlers in the Sumbang Area during the measurement was 14.98 months or almost 1 year and 3 months old.

The results of the analysis of the relationship between the independent and dependent variables in this study are shown in Table 3. The analysis using the Chi-Square test shows a significant relationship between exclusive breastfeeding and the nutritional status of toddlers (p=0.032).

Table 1. Demographic Characteristics of Study Participants

Characteristics	n	%
Father's age		
20-40 years	288	80.9
<20 or >40 years	68	19.1
Father's education level		
Elementary school	188	52.8
Junior high school	105	29.5
Senior high school	48	13.5
University	14	3.9
No education	1	0.3
Mother's age		
20-35 years	273	76.7
<20 or >35 years	83	23.3
Mother's education level		
Elementary school	190	53.4
Junior high school	107	30.1
Senior high school	44	12.4
University	12	3.4
No education	3	0.8
Nutritional status of toddlers		
Normal	236	66.4
Short	89	25.0
Very short	31	8.7

Table 2. Average Born Length and Age of Toddlers in the Sumbang Area

Length & Age	Mean ± Standard Deviation
Born length (cm)	48.32 ± 2.70
Toddler's age (months)	14.98 ± 5.96

DISCUSSION

In this study, exclusive breastfeeding up to 6 months of age was shown to have a significant relationship with the nutritional status of toddlers according to height to age index. Several studies have indicated a relationship between exclusive breastfeeding and the occurrence of stunting in toddlers (21,22). A similar result with a study in Makassar, Indonesia, showed a significant relationship between six-month exclusive breastfeeding and stunting in toddlers aged 6-24 months (23). However, the results differed in the West Java, Indonesia research that no significant relationship existed between exclusive breastfeeding for six months and cases of stunting (24). This difference could be due to differences in the exclusion criteria used in determining the sample: babies who consumed the first complementary feeding before reaching 6 months of age, babies with serious illnesses, and babies with a history of premature birth. Although several studies have shown that infant formula consumption can increase weight and height faster when compared to consumption of breast milk, this weight gain can cause excess weight in infants, which can be a driving factor for obesity and obesity-related degenerative diseases such as hypertension, diabetes mellitus, to cardiovascular disease in adulthood (25,26).

Exclusive breastfeeding for the first six months of age is the most effective way to reduce the incidence of morbidity and mortality in children and the incidence of asthma, cancer, obesity, diabetes mellitus, and cardiovascular disease (27). Consumption of exclusive breastfeeding also increases cognitive abilities and the chances of living a healthy life as an adult compared to babies who do not consume exclusive breastfeeding (28). Giving formula to infants

Table 3. Bivariate Analysis on Independent Variables with Nutritional Status of Toddlers

Variable	N	%	p-value
Early initiation breastfeeding			
Yes	189	53.1	0.375
No	167	46.9	
Exclusive breastfeeding			
Yes	245	68.8	0.032*
No	111	31.2	
First complementary food consumption			
≥ 6 months	323	90.7	0.801
< 6 months	33	9.3	
Complementary food type			
Purchased	180	50.6	0.745
Homemade	176	49.4	
Type of complementary feeding			
Instant (commercial products)	140	39.3	0.645
Local food	216	60.7	
Nutrition education on breastfeeding			
Yes	218	61.2	0.926
No	138	38.8	
Nutrition education on complementary feeding			
Yes	192	57.6	0.399
No	164	42.4	

under six months, especially in families with lower middle income, tends to be discouraged, considering the risk of water contamination used for brewing formulas and inadequate sanitary conditions (26,29).

The results of our study showed that the early initiation breastfeeding variable did not have a significant relationship with the nutritional status of toddlers from height to age index. Similar results were shown in Fitriyani and Sunarto's study of children aged 6-23 months in Central Java Province, namely that there was no significant relationship between early initiation of breastfeeding and the incidence of stunting in under-five (30). However, different results were shown in the study results of Sunartiningsih et al., in children aged 12 - 24 months at the Gunungsari Health Center, Bojonegoro, namely, there is a significant relationship between early initiation of breastfeeding and cases of stunting in children aged 12 - 24 months (31). This difference could be due to differences in the sample collection method used by simple random sampling in Bojonegoro and systematic random sampling for research in Sumbang District. In addition, there are different data sources, namely secondary data for research in Bojonegoro and primary data for research on toddlers in Sumbang District.

According to our study findings, no significant association exists between the origin and kind of complementary feeding eaten and toddler nutritional status. Other research has found similar results, indicating that the time of introducing complementary feeding and the origin/type of complementary feeding may not significantly impact toddlers' nutritional status (23,32–35). However, numerous research has yielded different results, and this study's small sample size and uneven data distribution may have influenced the results. The availability of caretakers, mothers' work commitments, and the hygienic preparation of supplemental foods all play critical roles in assuring toddler nutrition (36). Further research is needed to explore the relationship between the type and origin of complementary feeding and nutritional status more comprehensively.

The present study found no link between the history of nutrition education on breastfeeding and complementary feeding and the nutritional status of children in the Sumbang District.

Nutrition education, on the other hand, is critical for boosting mothers' knowledge and awareness of feeding methods (36-37). Inconsistent results could be attributed to a lack of data on nutrition education quality and delivery. Overall, treating malnutrition necessitates a multifaceted strategy, including nutrition education (39), given that the incidence of stunting among toddlers in the Sumbang District is 26.5 %, which is comparable to the prevalence in Situbondo Regency (26 %) (40). Further initiatives may be required to address the high prevalence of stunting among toddlers in the Sumbang District and adjacent places.

CONCLUSION

This study concluded that exclusive breastfeeding significantly affects children's nutritional status. In contrast, other variables such as early initiation of breastfeeding, the type and origin of complementary foods consumed, and nutrition education about breastfeeding and complementary feeding have no significant impact on toddlers' nutritional status. However, more research is needed to investigate additional factors that may alter the nutritional health of children under five. Nutrition education programs are suggested to improve quality and effectiveness to boost mothers' knowledge and habits. Healthcare practitioners should promote healthy nursing practices and provide clear guidance for exclusive breastfeeding to improve toddlers' nutritional status.

REFERENCES

1. Kementerian Kesehatan Republik Indonesia. Regulation of the Minister of Health of the Republic of Indonesia Number 2 of 2020 concerning Child Anthropometry Standards. Kementerian Kesehatan Republik Indonesia. Indonesia; 2020M;2:1-12.
2. Safaah N, Yunitasari E, Efendi F, Sunanita S, Suhartono S. Relationship between exclusive breastfeeding and stunting among children aged 2-5 years in Indonesia. Gac Med Caracas. 2022;130:S1019-1024.
3. Mustakim MRD, Irwanto, Irawan R, Irmawati M, Setyoboedi B. Impact of Stunting on Development of Children between 1-3 Years of Age. Ethiop J Heal Sci. 2022;32(3):569-578.
4. Taqwin T, Ramadhan K, Hadriani H, Nasrul N, Hafid F, Efendi F. Prevalence of stunting among 10-year-old children in Indonesia. J Glob Pharma Technol. 2020;12(2):768-775.
5. Alam MA, Richard SA, Fahim SM, Mahfuz M, Nahar B, Das S, et al. Impact of early-onset persistent stunting on cognitive development at 5 years of age: Results from a multi-country cohort study. PLoS One. 2020;
6. Supriatin E, Sudrajat DA, R. AF, Lindayani L. The Effect of Stunting on Cognitive and Motor Development in Toddler Children: Literature Review. J Ilmu Keperawatan Anak. 2020;3(2).
7. Sekartaji R, Suza DE, Fauziningtyas R, Almutairi WM, Susanti IA, Astutik E, et al. Dietary diversity and associated factors among children aged 6-23 months in Indonesia. J Pediatr Nurs. 2021;56:30-34.
8. Mastuti NLPH, Indahwati L. The Effect of Stunting on the Development of Fine Motoric, Gross Motoric, Language and Personal Social in Toddlers Aged 2-5 Years in Madiredo Village, Pujon District, Malang Regency. J Issues Midwifery. 2021;5(3):111-120.
9. Beal T, Tumilowicz A, Sutrisna A, Izwardy D, Neufeld LM. A review of child stunting determinants in Indonesia. Matern Child Nutr. 2018;14(4):e12617.
10. Ezeh OK, Abir T, Zainol NR, Mamun AA, Milton AH, Haque MR, et al. Trends of stunting prevalence and its associated factors among Nigerian children aged 0–59 months residing in the northern Nigeria, 2008–2018. Nutrients. 2021;13(12).
11. World Health Organization (WHO). Stunting policy brief. Glob Nutr Targets. 2014.
12. Kementerian Kesehatan RI. Basic health research report 2018. Lap Nas Riskesdas 2018. 2018;
13. Badan Litbang Kesehatan Jawa Tengah. Laporan Provinsi Jawa Tengah Riskesdas 2018 [central java province report 2018 basic Health research]. Kementerian Kesehatan RI. 2018.
14. Kementerian Kesehatan Republik Indonesia. Pocket Book of Indonesian Nutrition Status Study Results (SSGI) for Districts/Cities in 2021. Kementerian Kesehatan Republik Indonesia. 2021.
15. Kementerian Kesehatan RI. Peraturan Menteri Kesehatan Republik Indonesia Nomor 13 Tahun 2022 tentang Perubahan Atas Peraturan Menteri Kesehatan Nomor 21 Tahun 2020 tentang Rencana Strategis Kementerian Kesehatan Tahun 2020-2024 [Regulation of the Minister of Health of the Republic. 2022.
16. Lintang SS, Azkiya F. Relationship between Early Breastfeeding Initiation and Stunting Incidence in Infants Aged 0-24 Months at the Kramatwatu Health Cen. J Midwifery. 2022;10(2):155-160.

17. Tengah DKPJ. Profil Kesehatan Jawa Tengah Tahun 2021. 2021.
18. Sutarto S, Yadika ADN, Indriyani R. Analysis of the History of Exclusive Breastfeeding with Stunting in Toddlers Aged 24-59 Months in the Work. J Kesehat Masy Indones. 2021;16(3):148.
19. Resti E, Wandini R, Rilyani R. Providing Complementary Food for Breastfeeding is Associated with Incidence of Stunting in Toddlers. J Kebidanan Malahayati. 2021;7(2):274-278.
20. Bidira K, Tamiru D, Belachew T. Effect of nutritional education on anthropometric deficits among preschool aged children in south West Ethiopia: a quasi-experimental study. Ital J Pediatr. 2022;
21. Ibad M, Lutfiya I, Herdiani N, Sari MP, Fuadah AZ, Nadila A, et al. Determinants of stunting events in Indonesia using path analysis. In: Young Scholar Symposium on Science Education and Environment 2022. Faculty of Health, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia: American Institute of Physics Inc.; 2023.p.090019.
22. 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.
23. Novianti H. Relationship Of Early Complementary Food And Diarrhea In Infants Aged 0-6 Months In Posyandu Sedap Night Tengger East Kandangan Surabaya. Str J Ilm Kesehat. 2021;10(1):232-237.
24. Wangiyana NKA, Karuniawaty T, John R, Qurani R, Tengkawan J, Septisari A, et al. The Complementary Feeding Practice And Risk Of Stunting Among Children Aged 6-12 Months In Central Lombok. J Nutr Food Res. 2021 Jul;43(2 SE-Articles).
25. Shofiya D, Sumarmi S, Sulistyono A, Suyanto B. Determinants of successful exclusive breastfeeding in primiparas mothers. J Public Health Africa. 2023;14(S2).
26. Salsabila HY, Putera AM, Baskoro A. Correlation between nutritional status and children's activity with food allergy: A cross-sectional study. Ann Med Surg. 2021;68.
27. Manurung TN, Wungu CDK, Utomo MT. The Role of Breast Milk on Reducing the Risk of Neonatal Sepsis in Preterm and Low Birth Weight Infants: A Systematic Review and Meta-Analysis. Pharmacogn J. 2022;14(6):1067-1074.
28. Hadi H, Fatimatasari F, Irwanti W, Kusuma C, Alfiana RD, Ischaq Nabil Asshiddiqi M, et al. Exclusive breastfeeding protects young children from stunting in a low-income population: A study from eastern Indonesia. Nutrients. 2021;13(12).
29. Nasrul N, Hafid F, Ramadhan K, Suza DE, Efendi F. Factors associated with bottle feeding in children aged 0–23 months in Indonesia. Child Youth Serv Rev. 2020;116.
30. Fitriyani AR, Sunarto S. Adequacy of Energy and Early Breastfeeding Initiation (IMD) for Stunting in Toddlers Age 6-23 Months. LINK. 2021;17(1):67-72.
31. Rusmil VK, Prahastuti TO, Erlangga Luftimas D, Hafsah T. Exclusive and Non-Exclusive Breastfeeding among Stunted and Normal 6-9 Month-Old-Children in Jatinangor Subdistrict, Indonesia. Althea Med J. 2019;6(1):35-41.
32. Putri PAC, Widarti IGA, Dewantari NM. Patterns of Providing MP-ASI and Nutritional Status of Infants Aged 6-12 Months in the UPT Public Health Work Area, Tampaksiring I. J Ilmu Gizi. 2018;7(4):138-144.
33. WHO. WHO Appropriate complementary feeding. e-Library of Evidence for Nutrition Actions (eLENA). 2019.
34. Anggraeni EM, Herawati DMD, Rusmil VK, Hafsah T. Differences in the nutritional status of infants aged 6-9 months who were given factory-made and home-made MPASI. J Gizi Klin Indones. 2020;16(3):106.
35. Reverri EJ, Arensberg MB, Murray RD, Kerr KW, Wulf KL. Young Child Nutrition: Knowledge and Surveillance Gaps across the Spectrum of Feeding. Nutrients. 2022;14(15).
36. Sumiaty, Abdullah T, Bahar B, Jafar N, Hadju V, Muis M, et al. Factors associated with the appropriate time of complementary feeding among infants in Jeneponto Districts, South Sulawesi. Indian J Public Heal Res Dev. 2019;10(10):1498-1502.
37. Jeinie MHB, Guad RM, Hetherington MM, Gan SH, Aung YN, Seng WY, et al. Comparison of nutritional knowledge, attitudes and practices between urban and rural secondary school students: A cross-sectional study in Sabah, East Malaysia. Foods. 2021;10(9).
38. Amaliyah E, Mulyati M. Effectiveness of Health Education and Nutrition Rehabilitation Toward Community Empowerment for Children Aged Less Than 5 Years with Stunting: A Quasi-Experimental Design. J Ners. 2020;15(2):173-177.
39. Green L. Health Education: A Diagnosis Approach. The John Hopkins University. 1980.
40. Umiyah A, Hamidiyah A. Exclusive Breastfeeding With Stunting. Str J Ilm Kesehat. 2020;9(2):471-477.

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Factors Related to Maternal Readiness at Telehealth in Prenatal Care in Rural Areas of Indonesia

Factores Relacionados con la Preparación Materna en la Telesalud en Atención Prenatal en Áreas Rurales de Indonesia

Sri Mulyati[1a*], Dewi Purwaningsih[2a], Rika Resmana[3a], Saur Sariaty[4a]

SUMMARY

Introduction: *Pregnancy is a physiological process, but if not managed properly it could become pathological. Telehealth is the use of information and telecommunications technology to support prenatal care. This study aimed to determine the factors related to maternal readiness at Telehealth Prenatal care in rural areas of Indonesia.*
Methods: *This research method was a crossectional study. The respondents were 65 pregnant women in rural areas in Indonesia. Sampling was done with quota sampling. The variables of this study were the Readiness Factor and Readiness for Prenatal Telehealth. The data were analyzed using univariate data using frequency distribution and bivariate using the Chi-Square test.*
Results: *The results showed that maternal Telehealth readiness was high (61.5 %). The results showed that there was a relationship between education and income on maternal readiness for Telehealth prenatal care (p<0.05), and there was no relationship between age, education, or occupation in Telehealth prenatal care (p>0.05).*
Conclusion: *Telehealth applications can be developed for prenatal care in rural Rural Areas of Indonesia because the community has proven to be ready to carry out Telehealth.*

Keywords: *Readiness, telehealth, prenatal care, maternal child health care.*

RESUMEN

Introducción: *El embarazo es un proceso fisiológico, pero si no se maneja adecuadamente se puede convertir en patológico. La telesalud es el uso de la tecnología de la información y las telecomunicaciones para apoyar la atención prenatal. El propósito de este estudio fue determinar los factores relacionados con la preparación materna en la atención prenatal de telesalud en áreas rurales de Indonesia.*
Métodos: *Esta investigación fue un estudio transversal. Las encuestadas fueron 65 mujeres embarazadas en áreas rurales de Indonesia. La muestra fue con muestreo por cuotas. Las variables de este estudio son el Factor de Preparación y Preparación de Telesalud Prenatal. El análisis de datos fue univariado mediante distribución de frecuencias y bivariados mediante prueba Chi-Cuadrado.*
Resultados: *Los resultados mostraron que la preparación materna para la telesalud fue categorizada como alta (61,5 %). Los resultados mostraron que hubo una relación entre la educación y los ingresos*

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ORCID: 0009-0005-6406-2264[1]
ORCID: 0009-0007-6600-0774[2]
ORCID: 0009-0004-5103-6465[3]
ORCID: 0009-0009-7834-9900[4]

[a]Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia

*Corresponding Author: Sri Mulyati
E-mail: srimulyati@staff.poltekkesbandung.ac.id

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en la preparación materna en la atención prenatal de telesalud (P<0,05) y no hubo relación entre la edad, la educación y la ocupación en la atención prenatal de telesalud (P>0,05).
Conclusión: *Las aplicaciones de telesalud se pueden desarrollar en la atención prenatal en las áreas rurales de Indonesia porque la comunidad ha demostrado estar lista para llevar a cabo la telesalud.*

Palabras clave: *preparación, telesalud, atención prenatal, atención de salud materno infantil*

INTRODUCTION

The World Health Organization (WHO) has determined that every pregnant woman and newborn should receive quality care during pregnancy, childbirth, and postnatal. However, Maternal mortality is unacceptably high. About 287 000 women died during and following pregnancy and childbirth in 2020. Almost 95 % of all maternal deaths occurred in low and lower-middle-income countries in 2020, and most could have been prevented (1). Therefore, quality prenatal care is essential to reduce maternal mortality, such as identification, prevention, and management of pregnancy-related or concomitant diseases, health education, and health promotion (2-5). Apart from pregnancy complications, there is also a COVID-19 pandemic which can cause morbidity and mortality for pregnant women (3). Pregnant women infected with COVID-19 are expected to experience severe symptoms due to physiological changes in pregnancy, potentially experiencing an increased risk of complications from respiratory diseases. These include decreased lung function, increased oxygen consumption, and immune changes (6).

Telehealth, or information and telecommunications technology for remote healthcare, offers accessible and adaptable virtual care via voice and video calls (7,8). During the COVID-19 pandemic, it improved care and lowered exposure risks. Telehealth has shown potential in removing barriers to medical care delivery, particularly in rural areas (9). It can be used across medical disciplines to keep patients safe and prevent the spread of COVID-19 (10). In addition, telehealth aid provides rapid and easy answers to treatment-related questions (11). Telehealth development improvements for prenatal care in remote areas demand consideration. Future research into telehealth services in rural areas is needed to improve prenatal care delivery (12).

A prior study evaluated high-risk scores and pregnancy outcomes between standard care and telemedicine groups. The telehealth group had significantly more prenatal visits and a higher proportion of high-risk women. Maternal mortality was decreased in the telehealth group. Combining telemedicine with routine treatment can enhance outcomes in high-risk pregnancies (13). Early detection and intervention improve maternal health and reduce maternal and perinatal mortality. Recent research has investigated the feasibility and efficacy of telemedicine techniques for managing high-risk pregnancies. Telehealth exchanges information through computerized systems, video conferencing, and mobile devices. It is a very young study area, and their findings differ (9).

Many factors can affect the readiness of mothers in Telehealth, which are formed from the readiness of attitudes, needs, information, access to the internet and information technology tools, and the ability to use Prenatal care (PNC) information technology. Such factors are characteristic of the patient. Factors that can influence include age, education, occupation, and maternal income (14). However, there is a lack in the literature concerning the parameters related to maternal readiness for Telehealth Prenatal Care in developing-country rural locations. As a result, this study aimed to analyze the factors related to maternal readiness for Telehealth Prenatal Care in rural areas of developing Countries. Understanding these factors allows for developing appropriate treatments and strategies to improve the preparedness and utilization of telehealth services among mothers.

METHODS

The design was a cross-sectional study. The sample of this study was all pregnant women in Bandung Regency, Indonesia, who met the inclusion and exclusion criteria. The inclusion criteria were pregnant women domiciled in rural areas. A participant who was not willing

to participate in this research was excluded. Sampling was performed through quota sampling. The sample size formula for analyzing the relationship between the independent and dependent variables for the proportion of a single population in one sample. This study determined a type I error of 5 %, a one-way hypothesis so that $Z_{\alpha=}$ 1.96. Type II error is 20 %, hence $Z_{\beta} = 0.84$. The proportion of dependent and independent variables in the previous study was 73 %, and the proportion of dependent and independent variables expected was at least 83 %. So, the number of samples consists of 65 people.

The variables of this study were the readiness factor of prenatal care telehealth and readiness of prenatal care telehealth. Data analysis was performed with univariate text using frequency distribution and bivariate using the Chi-Square test. The instruments in this study were modified questionnaires from the telehealth readiness questionnaire from the Maryland assessment tool (14) and the National Center for Farmworker Health questionnaire (15). In this study, the data analysis design was carried out using quantitative analysis using the Chi-Square test with a significance value < 0.05.

RESULTS

As shown in Table 1, readiness obtained on Telehealth in the district Bandung was relatively high at 61.5 % and the unprepared at 38.5 %. In addition to the above categorization, the study results show attitudes, needs, information, access to the Internet, and technological tools navigation capabilities using information technology that can form readiness for Telehealth. Based on the results of the study, it was found that mothers' attitudes towards Telehealth Prenatal care were categorized as good (58.5 %), the need for Telehealth was high (95.4 %), namely wanting to go through WhatsApp (86.2 %), E-mail (1.5 %), web internet (55.4 %), special applications (44.6 %). Mothers have received information about Prenatal care telehealth before (93.8 %), namely from friends (15.4 %), TV (27.7 %), Internet (24.6 %), health workers (6.2 %), and social media (44.6 %). Access to the Internet is categorized as good (83.1 %). All mothers had cellphone (HP) (100 %) that were used personally (81.5 %) and with family (18.5 %). 100 % of mothers have internet access, with 98.5 % using mobile data and 92.3 % using stable internet networks. 95.4 % of mothers have internet access skills, Able to use WhatsApp 80 %, Instagram 38.5 %, telegram 30.8 %, Facebook 60 %, and health applications 29.2 %. Mothers can access Wi-Fi as much as 89.2 %. The ability to navigate information technology through HP was categorized as high (70.8 %).

Table 2 depicts the association between factors and readiness in Telehealth Prenatal Care. The study found no link between age and readiness ($p = 0.278$). However, there was a substantial relationship between education and readiness, with higher education levels indicating greater readiness ($p = 0.028$). Income was also strongly linked with readiness, with higher-income people being more prepared for Telehealth prenatal care ($p = 0.002$). While work status did not demonstrate a significant association ($p = 0.079$), further analysis may be required. These findings highlight the need to consider education and poverty levels when adopting telehealth services for prenatal care.

DISCUSSION

Our present results indicate that Telehealth readiness was relatively high up to 61.5 % readiness, while a 38.5 % was low. This indicates that Telehealth applications can be developed in rural areas in Indonesia. Telehealth can be a solution for patients who cannot reach health services directly or can be reached by patients whose residences are far from health services (16). In the current public health emergency, Telehealth can maintain patient access and continuity of care while minimizing the risk of COVID-19 transmission (9). Telehealth is an alternative mode of service delivery that allows people living in rural and remote areas to access health care within their local communities. Telehealth is the distribution of health-related services and information via electronic information and telecommunication technologies that utilize information and communication technologies such as telephone, videoconferencing, electronic messaging, or digital monitoring to improve health services (7). It allows long-distance patient

Table 1. Overview of Readiness on Prenatal Care Telehealth

Variable	Category	F	%
Readiness on Prenatal Care Telehealth	Less	25	38.5
	High	40	61.5
Sub Variable			
Attitude	Less	26	40
	High	38	58.5
Necessity	No need	3	4.6
	Need	62	95.4
	Desired means:	56	86.2
	- Whatsapp	1	1.5
	- E-mail	36	55.4
	- Web Internet	29	44.6
	- Health Apps		
Information	Never get information	4	6.2
	Get information	61	93,8
	Resources		
	-Friend	10	15.4
	-Television	18	27.7
	-Internet	16	24.6
	- Health Workers	4	6.2
	- Social Media	29	44.6
Access to Information Technology and the	Less	11	16.9
Internet:	Good	54	83.1
HP Ownership	Doesn't have	0	0
	Have:		
	1. With Family	12	18.5
	2. Personal	53	81.5
Internet network	No.	0	0
	Yes	100	100
	Wifi	12	18.5
	Data cellphone	64	98.5
Internet network stability	No stable	5	7.7
	Stable	60	92.3
Ability to access platforms on the Internet with a mobile phone	Can't afford it	3	4.6
	Can, through:	62	95.4
Wi-Fi access capability	- WhatsApp	52	80.0
Navigation Capabilities with HP	- Instagram	25	38.5
	- Telegram	20	30.8
	- Facebook	39	60.0
	- Health apps	19	29.2
	Can't afford it	7	10.8
	Can	58	89.2
	Low	19	29.2
	High	46	70.8

Table 2. Relationship between Determinants and Readiness in Telehealth Prenatal Care

Variable	f	%	P-value*
Age			
Median	28	-	0.278
Range	16-42		
Education			
Primary School	6	9.20	
Junior High School	25	38.5	0.028
High School or above	34	52.3	
Income			
Low	42	64.6	0.002
High	23	35.4	
Work			
Work	53	81.5	0.079
Does not work	12	18.5	

*Chi-Square test

and clinician contact, care, advice, reminders, education, intervention, monitoring, and remote admissions. With the Internet and infrastructure improvement, video conferencing, in particular, improved the excellence of Telehealth delivery in health services (17).

Telehealth programs overcome physical barriers to provide patients and caregivers access to convenient medical care, however, in the process of implementing Telehealth, there are still obstacles experienced by health workers regarding the ability to implement Telehealth to support the continuity of outpatient care during the pandemic (18,19), by minimizing in-person visits and reducing face-to-face contact between physicians and patients, the use of virtual care solutions can decrease the transmission of the virus and also protect medical practitioners from infection. The difficulties in implementing telehealth solutions are also influenced by financial and medical-legal considerations. In addition, some of the physicians themselves are troubled with technical difficulties, and many issues concerning the decision-making capability in this constellation, and the appropriate standards of quality, safety, and privacy, that should be maintained in such services. Telehealth has also proven beneficial for inpatient care, specifically to help balance clinical service provision with surging demand across physical or geographic boundaries, conserving personal protective equipment, and providing remote patients connections to family and friends (20,21). Telehealth has several key strengths that can improve emergency response services when the environment is in a biological hazard and during infectious disease outbreaks (22).

This research showed that there was no relationship between age and occupation factors on PNC telehealth readiness; meanwhile, there was a significant relationship between education and income with readiness in PNC telehealth. Several determinants such as characteristics influence patient readiness for Telehealth. Characteristics of the patient population, such as age, education, occupation, and income, can affect telehealth admissions (14).

CONCLUSION

Maternal readiness for Telehealth was categorized as high. The results showed a relationship between education and income on maternal readiness on telehealth PNC and no relationship between age, education, and occupation on Telehealth PNC. It is hoped that telehealth applications will be developed for PNC practice because the community has proven to be ready to carry out Telehealth.

REFERENCES

1. Ryan LM, Mahmood DMA, Laurence PCO. Incidence of concomitant illnesses in pregnancy in Indonesia: Estimates from 1990–2019, with projections to 2030. Lancet Reg Heal - West Pacific. 2021;10.
2. Fouly H, Debee J, Elnaeem MMA. Nurses' perspectives of families' needs of the maternal critically ill cases in woman health hospital: An educational program. J Ners. 2022;17(2):121-130.
3. Sudaryanti L, Mardhika A, Qona'Ah A, Tyas APM, Chan CM. Prenatal care of pregnant women during pandemic: A phenomenology study. J Pak Med Assoc. 2023;73(2):S71-75.
4. Tjahjadi B, Soewarno N, Gunawan GM. Effect of Information Capital Readiness on Business Performance in Indonesian MSMEs: Does Online Market Orientation Matter?. J Asian Financ Econ Bus. 2020;7(12):267-274.

5. Kurniati A, Chen C-M, Efendi F, Berliana SMM. Factors influencing Indonesian women's use of maternal health care services. Health Care Women Int. 2018;39(1):3-18.
6. UNFPA. COVID-19 Technical Brief Package for Maternity Services Technical Brief Package for Maternity Services UNFPA. 2020.
7. Lin SC, Rajagopal H, Ling TC. Smart Telehealth Appointment System – WI Care. In: Y. J, T. I, J.-J. L, editors. 28th International Conference on Artificial Life and Robotics, ICAROB 2023. Institute of Computer Science and Digital Innovation, UCSI University, Kuala Lumpur, 56000, Malaysia: A Life Robotics Corporation Ltd; 2023.p.653-659.
8. Long AF. Book Review: Manual of Epidemiology for District Health Management. Health Services Management Research. 1991;4:76-76.
9. Li L, Lake R, Raban MZ, Byrne M, Robinson M, Westbrook J, et al. Medication-related calls received by a national telenursing triage and advice service in Australia: A retrospective cohort study. BMC Health Serv Res. 2017;17(1):1-11.
10. Wosik J, Fudim M, Cameron B, Gellad ZF, Cho A, Phinney D, et al. Telehealth transformation: COVID-19 and the rise of virtual care. J Am Med Informatics Assoc. 2020;27(6):957-962.
11. Hussein WF, Bennett PN, Pace S, Chen S, Legg V, Atwal J, et al. The mobile health readiness of people receiving in-center hemodialysis and home dialysis. Clin J Am Soc Nephrol. 2021;16(1):98-106.
12. Butzner M, Cuffee Y. Telehealth Interventions and Outcomes Across Rural Communities in the United States: Narrative Review. J Med Internet Res. 2021;23(8).
13. Zhu XH, Tao J, Jiang LY, Zhang ZF. Role of Usual Healthcare Combined with Telemedicine in the Management of High-Risk Pregnancy in Hangzhou, China. J Healthc Eng. 2019;2019.
14. Maryland Health Care Commission. Telehealth Readiness Assessment Tool. 2019;73.
15. Health NC for F. Patient telehealth readiness assessment tool. 2020:1-4.
16. Algifnita AO, Prasetyo B, Wittiarika ID. Perceptions, attitudes, and practices of midwives towards the use of telehealth. Indones J Heal Adm. 2022;10(2):155-164.
17. Mataxen PA, Webb LD. Telehealth nursing: More than just a phone call. Nursing (Lond). 2019;49(4).
18. Aditya DMN, Kalanjati VP, Pamungkas DBB, Syamhadi MR, Wibowo JAS, Soetanto KM. The use of telemedicine in COVID-19 pandemic era: a systematic review. Bali Med J. 2022;11(3):1987-1995.
19. Yunara Y, Efendi F, Makhfudli. Technology- and non-technology-based primary healthcare innovations for the elderly: A systematic review. Enferm Clin. 2023;33:S60-65.
20. Anis W, Devy SR, Prasetyo B, Indriani D, Amalia RB, Dewi ER. Implementation and recommendation of postpartum visit methods during COVID-19 pandemic: A qualitative study from Indonesia. J Public Health Africa. 2023;14(S2).
21. Astutik, Cahyani P, Putri AF, Fikri MH. Authority of Health Workers in Telemedicine Medical Services: Indonesian Perspective. Malaysian J Med Heal Sci. 2023;19:99-105.
22. Wang H, Jia S, Li Z, Duan Y, Tao G, Zhao Z. A Comprehensive Review of Artificial Intelligence in Prevention and Treatment of COVID-19 Pandemic. Front Genet. 2022;13(April):1-15.

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Oral Combination of Vitamin B1, B6, and B12 Supplementation on CD4+ T Cell and IFN-γ in Pulmonary Tuberculosis Patients with First-Line Opioid agonist therapy

Combinación oral de la suplementación con vitamina B1, B6 y B12 en el recuento de células T CD4+ y IFN-γ en pacientes con tuberculosis pulmonar con terapia de agonistas de opioides de primera línea

Yogi Khoirul Abror[1a*], Wiwin Wiryanti[2a], Sulaeman Sulaeman[3a]

SUMMARY

Introduction: *Tuberculosis (TB) is a wasting or consumption disease which causes metabolic changes in tuberculosis patients. The metabolic changes that can occur are decreased appetite, micronutrient malabsorption, and malnutrition. The purpose of this research was to determine the differences in the result of an oral combination of vitamins B1, B6, and B12 supplementations on Interferon Gamma (IFN-γ) levels and CD4+ T-cell counts in pulmonary tuberculosis patients receiving first-line Opioid Agonist Therapy (OAT) compared to only OAT therapy.*
Methods: *The type of research used was experimental research with a randomized pre-test and post-test control group design. The samples were obtained by purposive sampling. The sampling location was at Health Public Center in East Java from Juli – December 2019. The samples were divided into two groups, the group of TB patients who received first-line OAT supplementation with a combination of vitamins B1, B6 and B12 as the test group and the group of TB patients who only received OAT as the control group. In each group, the CD4+ T cell count and IFN-γ levels were quantified twice as pre and post-test using flow cytometry and ELISA. The data were analyzed with Mann-Whitney and Wilcoxon test using a p-value of 0.05.*
Results: *The results showed a significant decrease in IFN-γ levels and an increase in the number of CD4+ T cells in the test group compared to the control group.*
Conclusion: *Vitamins B1, B6 and B12 are recommended to be given as a complementary treatment to OAT at the public health center to increase the immunity of TB patients. Health staff can play a role in enhancing the compliance of TB patients toward medication.*

Keywords: *Supplementation vitamins B1, B6, B12, tuberculosis, OAT, CD4+ T cells and IFN γ*

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ORCID: 0009-0002-9835-7595[1]
ORCID: 0009-0005-1803-2136[2]
ORCID: 0009-0009-3298-0297[3]

[a]Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia

*Corresponding Author: Yogi Khoirul Abror
E-mail: yogiabror@staff.poltekkesbandung.ac.id

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RESUMEN

Introducción: *La tuberculosis (TB) es una enfermedad de desgaste o consumo que provoca cambios metabólicos en los enfermos de tuberculosis. Los cambios metabólicos que pueden ocurrir son disminución del apetito, malabsorción de micronutrientes y desnutrición. El propósito de esta investigación fue determinar las diferencias en el resultado de la combinación oral de suplementos de vitaminas B1, B6 y B12 sobre los niveles de interferón gamma (IFN-γ) y los recuentos de células T CD4+ en pacientes con tuberculosis pulmonar que reciben terapia con agonista opioides (TAO) de primera línea en comparación con los que reciben solo terapia TAO.*
Métodos: *El tipo de investigación utilizado es la investigación experimental con un diseño de grupo de control aleatorio antes y después de la prueba. Las muestras se obtuvieron por muestreo intencional. El lugar de muestreo en el Centro Público de Salud en Java Oriental durante julio - diciembre de 2019. Las muestras se dividieron en dos grupos, el grupo de pacientes con TB que recibieron TAO de primera línea con una combinación de suplementos de vitaminas B1, B6 y B12 como el grupo de experimental y el grupo de pacientes con TB que solo recibieron TAO como grupo de control. En cada grupo, el recuento de las células T CD4+ y los niveles de IFN-γ se cuantificaron dos veces, antes y después de la prueba mediante citometría de flujo y ELISA. Los datos fueron analizados con la prueba de Mann-Whitney usando alfa 0.05.*
Resultados: *Los resultados mostraron una disminución significativa en los niveles de interferón gamma (IFN-γ) y un aumento en la cantidad de células T CD4+ en el grupo experimental en comparación con el grupo de control.*
Conclusión: *Se recomienda administrar las vitaminas B1, B6 y B12 como tratamiento suplementario del TAO en el centro de salud pública para aumentar la inmunidad de los pacientes con TB. El personal de salud puede desempeñar un papel en la mejora del cumplimiento de la medicación por parte de los pacientes con TB.*

Palabras clave*: Suplementación de vitaminas B1, B6, B12, tuberculosis, TAO, células T CD4+, IFN γ*

INTRODUCTION

Tuberculosis (TB) is still a health problem in the world even though control efforts with the DOTS (Directly Observed Treatment Short Course Chemotherapy) strategy have been implemented in many countries (1,2). Tuberculosis is the third cause of death worldwide after HIV/AIDS and Malaria (3). Globally in 2016, there were 10.4 million incident cases of tuberculosis (CI 8.8 million – 12 million), equivalent to 120 cases per 100 000 population. The five countries with the highest incidence of cases are India, Indonesia, China, the Philippines, and Pakistan (4). TB is a wasting or consumption disease that causes metabolic changes in tuberculosis patients. The metabolic changes that occur are anabolic blocks. An anabolic block is a condition in which amino acids cannot be built into more complex proteins. Metabolic changes that can occur are decreased appetite, malabsorption of nutrients, and malabsorption of micronutrients (5,6).

There are two relationships between malnutrition and tuberculosis, namely, the effect of tuberculosis on nutritional status and the effect of malnutrition on the clinical manifestations of tuberculosis due to a weak immune system. Malnutrition is also a significant risk factor for the onset of active tuberculosis, and malnutrition can worsen the prognosis of TB disease. Malnutrition affects cell-mediated immunity (CMI). CMI is the body's primary defense against TB (7). The association between TB and undernutrition has long been known. TB worsens undernutrition and weakens immunity, thereby increasing the likelihood of latent TB developing into active disease. Based on World Health Organization (WHO) data, 9.7 million individuals with active TB in 2016 were in a catabolic state and experienced weight loss, and some showed signs of vitamin and mineral deficiencies at diagnosis (8).

Based on these conditions, comprehensive and thorough treatment of tuberculosis patients must be carried out to increase the percentage of successful treatment of tuberculosis patients (9-11). The provision of nutritional intake is also essential to note. Micronutrients are needed for the body's immune system to function normally. A deficiency of micronutrients can suppress immunity by affecting the innate immune response, T cells and adaptive immune response resulting in an imbalance (12). One of the micronutrients that can be used to improve the work and response of the body's immunity is the provision of vitamin intake (13). Inadequate vitamin intake can lead to suppression of the immune system and can increase the risk of

infection. Administering vitamins B1, B6, and B12 can increase the number of T lymphocytes and the activity of Natural Killer cells (NK cells), both of which can trigger the release of interferon-gamma (INF-γ). Giving vitamins can reduce the risk of recurrence of tuberculosis by 45 % and reduce the incidence of extrapulmonary tuberculosis (14).

Recent research in 2019 suggested that the combination of Opioid Agonist Therapy (OAT) and vitamin D supplementation may improve the success of TB treatment (15). Similarly, a study in 2017 showed that administering Vitamin B1, B6, and B12 along with probiotics could induce an immune response involving interleukin-10 (IL-10) and interferon-gamma (IFN-γ), which are important in the immune defense against infections (16). Building on these findings, novel research in 2023 would be focused on pulmonary TB patients and investigated the effects of providing vitamin B1, B6, and B12 supplements, with and without OAT, on the levels of IFN-γ and CD4+ T-cell counts. Based on this, this study aimed to analyze the effects of oral supplementation of vitamins B1, B6, and B12 with OAT and OAT alone on Interferon Gamma (IFN-γ) levels and CD4**+** T-cell counts in pulmonary tuberculosis patients.

METHODS

This was an experimental research with quasi-experimental research with pre-and post-test control group design. The population was tuberculosis patients enrolled at Public Health Center in East Java, with 34 samples taken by purposive sampling. The inclusion criteria were new TB patients for whom OAT was never applied. The exclusion criteria are TB patients with autoimmunity and comorbidities. The samples were divided into two groups, TB patients who received first-line OAT drugs with a combination of vitamins B1, B6 and B12 as supplements as the test group, and the TB patient group who only received OAT drugs without supplementation of vitamins B1, B6 and B12, as the control group. Vitamins B1, B6 and B12 used in this study were in tablet form containing 100 mg B1, 100 mg B6 and 5000 mcg B12. Tablets for vitamin B1, B6 and B12 preparations were produced by PT PnG Health, giving the treatment group 1 tablet once a day for two months. The sample collection was performed from July – December 2019.

The samples were assessed for CD4+ T-cell counts and IFN-γ levels twice as a pre-test before the patient's administration of OAT and Post-Test after patients were treated with OAT and Vitamins B1, B6 and B12 for two months. Quantification of IFN-γ levels was carried out by using ELISA assay at the Institute for Tropical Diseases (ITD) Campus C, Airlangga University, and evaluation of the number of CD4+ T cells was carried out by using Flow Cytometry at the Pramita Laboratory Surabaya. The CD4+ T-cell counts, and IFN-γ levels test were carried out immediately after patients finished their OAT and Vitamins B1, B6 and B12 therapy for two months. The procedure is shown in Figure 1.

This research has been declared ethically feasible by the Health Research Ethical Clearance Commission, Faculty of Dental Medicine, Universitas Airlangga Number: 239/HRECC. FODM/V/202. Before enrolling in the study, patients were provided with detailed information about the experiment and procedures, and they were required to present signed informed consent indicating their voluntary participation and

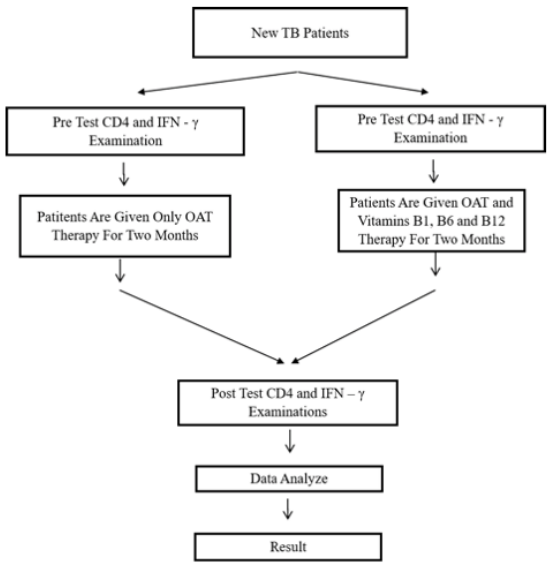

Figure 1. Research Procedure

understanding of the study's objectives, potential risks, and their right to withdraw at any time.

IFN-γ ELISA assay

We prepared all reagents, working standards, samples, and controls for the IFN-γ assay, which was performed using an enzyme-linked immunosorbent assay (ELISA) development kit designed for the quantitative detection of IFN Gamma / Interferon Gamma (17). Briefly, 100 µL of Assay Diluent RD1-51 was added to each well, followed by the addition of 100 µL of standard, control, or sample into each well. The plate was thoroughly mixed and then covered with the provided sealer, incubating at room temperature for 2 hours. After incubation, the contents of each well were discarded, and washing was performed by adding 400 µL of wash buffer into each well, repeating the process three times for a total of four washes. Following the final wash, the excess wash buffer was removed by tapping the plate upside down against a clean paper towel. Next, 200 µL of the conjugate was added into each well, and the plate was once again covered with a new sealer and incubated at room temperature for 2 hours. Another round of washing was performed. Subsequently, 200 µL of substrate solution was added to each well, and the plate was covered and incubated at room temperature for 30 minutes, protected from sunlight. Finally, 50 µL of stop solution was added to each well, leading to a color change from blue to yellow. In cases where the color produced was green or the color change appeared non-uniform, gentle shaking was employed to ensure thorough mixing. The optical density of each well was determined within 30 minutes using the ELISA reader at 450 nm. The examination results were validated by a clinical pathology specialist.

CD4+ T Cell Count

The number of CD4+ T cells was performed by using Flow Cytometry (18). Trucount™ tubes were used for the assay. Briefly, the method consisted, Add 50 µL of blood with EDTA to the tube. Add 20 µL of CD4+ reagent. The tube containing blood with EDTA, and reagents was vortexed for 5 seconds and then incubated for 15 minutes at room temperature. After 15 minutes, add 450 µL Facslyse, which has been diluted with a ratio of 1:10. Vortex for 5 seconds, then incubate for 15 minutes at room temperature. The sample was ready to be analyzed with Fluorescence-Activated Cell Sorting (FACS), which is a technique used in flow cytometry to physically separate cells based on their fluorescent properties. During FACS, the cells are first stained with fluorescent dyes or antibodies that bind to specific molecules on the cell surface. A clinical pathology specialist validated the examination results.

Data Analysis

The data were analyzed as parametric data. Data analysis was performed using the Wilcoxon and Mann-Whitney statistical tests with a p-value < 0.05.

RESULTS

The total respondents were 34 patients. Table 1 shows that patient distribution according to age was in the range of 12-25 years one patient (2.9 %), ages 26-45 years 13 patients (38.4 %), ages 46-65 years 19 patients (55, 8 %) and age> 65 years one patient (2.9 %). The respondents who received the first-line OAT at the Arosbaya Health Center that were male were 19 patients (55.8 %) and female patients 15 (44.2 %). The distribution of patients based on the results of smears before giving vitamins shows that patients with smear +1 results were two patients (5.88 %), smear +2 were 14 patients (41.1 %), and smear +3 were 18 patients (53.02 %).

Table 2 presents a comparison of IFN-γ levels and CD4+ cell counts between the control group and the experimental group in both the pre-test and post-test conditions. In the pre-test phase, there was no statistically significant difference in IFN-γ levels between the control group (99.46 ng/mL) and the experimental group (110.28 ng/mL) with a p-value of 0.07. Similarly, the CD4+ cell counts did not show a statistically significant difference in the pre-test, with the control group at 257.18 cells/mm^3 and the experimental group at 301.41 cells/mm^3 (p-value = 0.12). However, after the intervention, significant changes were

observed. The control group's IFN-γ levels decreased to 95.76 ng/mL (post-test) with a p-value of 0.001, while the experimental group's IFN-γ levels decreased to 90.44 ng/mL (post-test) with a p-value of 0.005, both indicating statistical significance. Moreover, the CD4+ cell counts increased significantly in the post-test for both groups. The control group showed a rise to 260.95 cells/mm^3 with a p-value of 0.003, and the experimental group showed an increase to 332.71 cells/mm^3 with a p-value of 0.002. These findings suggest that the intervention had a significant impact on both IFN-γ levels and CD4+ cell counts in the experimental group, compared to the control group.

Table 1. Patients Distributions characteristics

Characteristics	Frequency	Percentage (%)
Age (Year)		
12-25	1	2.9
26-45	13	38.4
46-65	19	55.8
>65	1	2.9
Total	34	100
Gender		
Male	19	55.8
Female	15	44.2
Total	34	100
BTA test		
+1	2	5.88
+2	14	41.1
+3	18	53.02
Total	34	100

Table 2. IFN-γ levels CD4+ Cell Counts in the control group and the test group

IFN-γ Levels (ng/mL)	Pre -Test	Post-Test	p-value*
Control	99.46	95.76	0.001
Experimental	110.28	90.44	0.005
P-value*	0.077	-	
CD4+ Cell Counts (Cell/mm^3)	Pre-Test	Post-Test	p-value*
Control	257.18	260.95	0.003
Experimental	301.41	332.71	0.002
P-Value*	0.12	-	

*Alpha = 0.05

DISCUSSION

Vitamins are organic compounds and essential nutrients required by an organism in limited amounts. An increasing number of studies have begun to explore the mechanisms by which vitamins regulate immunity and their effects as adjuvant to treat tuberculosis. Vitamin A, D, and E are the most widely studied, and the mechanisms by which they regulate immunity have been partly elucidated (15,16).

Vitamin B1 (thiamine) can produce a protective immune response to limit the survival of *Mycobacterium tuberculosis* in macrophages (19). Thiamine can activate peroxisome proliferator-activated receptor γ (PPAR-γ), part of the lipid-activated nuclear receptor involved in innate immune cells' differentiation and lipid metabolism, including macrophages involved in the inflammatory response (20). Within macrophages, PPAR -γ will integrate signals of metabolic and inflammatory functions that play an essential role in regulating the immune response and nutrient metabolism during infection by *M. tuberculosis* (21). In the regulation of receptors activated by PPAR-γ, thiamine promotes macrophage proliferation to a classically activated phenotype via microbicidal solid activity and increased TNF-alpha and IL-6. In addition, thiamine can enhance mitochondrial respiration and lipid metabolism to integrate metabolic signals (20,22). PPAR-γ is expressed in large quantities in alveolar macrophages and is essential for differentiation. The function of PPAR-γ activation against mycobacterial infection was shown to positively regulate prostaglandin (PG) E2 production in infected macrophages (23). Thus, PPAR-γ activation will increase cyclooxygenase (COX2) expression and PGE2 production in macrophages infected with *M. tuberculosis* so that macrophages will become activated macrophages and can kill *M. tuberculosis more* strongly (24). When macrophages can kill bacteria, the infection will gradually improve, and gamma interferon levels will decrease (25,26).

Vitamin B6 is essential in synthesizing proteins and nucleic acids so that it can affect the immune system because antibodies and cytokines - cytokines are formed from amino acids. Hence, they require vitamin B6 as a coenzyme in their metabolism (16,27). Studies conducted on human subjects it was shown that a deficiency of vitamin B6 could interfere with lymphocyte maturation, growth, antibody production, and T-cell activation. Gamma Interferon levels (22). So, when the intake of B6 is sufficient, the number of immune cells will increase.

Vitamin B12 also plays a role in the metabolism and proliferation of lymphocyte cells. Studies conducted on human subjects found that a lack of vitamin B12 significantly decreased the number of CD4+ T lymphocytes (28,29). In addition, an abnormal ratio of CD4+ T lymphocytes and suppression of NK cells were found. In contrast, other studies have shown that intramuscular supplementation of vitamin B12 (500 μg daily for two weeks) in humans improves the production of CD4+ T lymphocytes and CD8+ T lymphocytes and increases NK cell activity (30,31).

This study had limitations; the researchers did not know about the nutritional status and nutrition of the patients before. Researchers also did not measure vitamin B levels in serum before supplementing with vitamin B. Vitamin B administration using only one dose does not compare with several other doses and does not compare with variations in the duration of vitamin B supplementation. Researchers suggest giving TB patients vitamins as a support for treatment in addition to administering OAT. Administration of vitamins can increase the body's immunity in TB patients, making TB treatment more optimal.

CONCLUSION

According to the findings, adding vitamins B1, B6, and B12 to standard OAT can considerably reduce IFN-γ levels and raise CD4+ T-cell counts in patients. Vitamin supplementation can improve tuberculosis treatment outcomes by increasing immunological response. Tuberculosis patients receiving OAT were advised to include these vitamins as supplemental therapy. Vitamin supplementation should be considered by healthcare providers to improve immune function and aid patient recovery. More research is required to determine the appropriate quantity and duration of vitamin supplementation and any potential interactions or adverse effects. Raising awareness among healthcare providers about the benefits of vitamin supplementation in tuberculosis management is also critical.

REFERENCES

1. Markandan K, Tiong YW, Sankaran R, Subramanian S, Markandan UD, Chaudhary V, et al. Emergence of infectious diseases and role of advanced nanomaterials in point-of-care diagnostics: A review. Biotechnol Genet Eng Rev. 2022.

2. Mboi N, Syailendrawati R, Ostroff SM, Elyazar IR, Glenn SD, Rachmawati T, et al. The state of health in Indonesia's provinces, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet Glob Heal. 2022;10(11):e1632–1645.
3. Ministry of Health. Give Children Complete Routine Immunizations, Here Are the Details. Kementerian Kesehatan. 2018. Available from: https://www.kemkes.go.id/article/view/18043000011/berikan-anak-imunisasi-rutin-lengkap-ini-rinciannya.html
4. WHO. Global tuberculosis report 2018. Geneva PP - Geneva: World Health Organization; 2018. Available from: https://apps.who.int/iris/handle/10665/274453
5. Nasution SD. Malnutrition and Anemia in Patients with Pulmonary Tuberculosis. Majority. 2015;4(8):29-36.
6. Gupta KB, Gupta R, Atreja A, Verma M, Vishvkarma S. Tuberculosis and nutrition. Lung India. 2009;26(1):9-16.
7. Doan TN, Eisen DP, Rose MT, Slack A, Stearnes G, McBryde ES. Interferon-gamma release assay for the diagnosis of latent tuberculosis infection: A latent class analysis. PLoS One. 2017;12(11):e0188631.
8. WHO. Guideline: nutritional care and support for patients with tuberculosis. Geneva PP - Geneva: World Health Organization; 2013. Available from: https://apps.who.int/iris/handle/10665/94836
9. Dass SA, Balakrishnan V, Arifin N, Lim CSY, Nordin F, Tye GJ. The COVID-19/Tuberculosis Syndemic and Potential Antibody Therapy for TB Based on the Lessons Learnt From the Pandemic. Front Immunol. 2022;13.
10. Putra MM, Sari NPWP. Model Theory of Planned Behavior to Improve Adherence to Treatment and the Quality of Life in Tuberculosis Patients. J Ners. 2020;15(2).
11. Hasanah U, Makhfudli M, Ni'Mah L, Efendi F, Aurizki GE, Ni'mah L, et al. Peer Group Support on the Treatment Adherence of Pulmonary Tuberculosis Patients. In: 4th International Conference on Tropical and Coastal Region Eco Development, ICTCRED 2018. Faculty of Nursing, Universitas Airlangga, Surabaya, Indonesia: Institute of Physics Publishing; 2019.p.12033.
12. Yoshii K, Hosomi K, Sawane K, Kunisawa J. Metabolism of Dietary and Microbial Vitamin B Family in the Regulation of Host Immunity. Frontiers in Nutrition. 2019;6.
13. Mikkelsen K, Apostolopoulos V. Vitamin B12, Folic Acid, and the Immune System BT. In: Mahmoudi M, Rezaei N, editors. Nutrition and Immunity. Cham: Springer International Publishing; 2019:103-114.
14. Amagon KI, Awodele O, Akindele AJ. Methionine and vitamin B-complex ameliorate antitubercular drug-induced toxicity in exposed patients. Pharmacol Res Perspect. 2017;5(5).
15. Soeharto DA, Rifai DA, Marsudidjadja S, Roekman AE, Assegaf CK, Louisa M. Vitamin D as an Adjunctive Treatment to Standard Drugs in Pulmonary Tuberculosis Patients: An Evidence-Based Case Report. Adv Prev Med. 2019;2019:5181847.
16. Suprapti B, Suharjono, Raising R, Yulistiani, Izzah Z, Nilamsari WP, et al. Effects of probiotics and Vitamin B supplementation on IFN-γ and IL-12 levels during intensive phase treatment of tuberculosis. Indones J Pharm. 2018;29(2):80-85.
17. Chileshe J, Goosen WJ, Buss PE, van Helden PD, Warren R, Parsons SDC, et al. A commercial ELISA for detection of interferon-gamma in white rhinoceros. J Vet Diagnostic Investig. 2019;31(4):531-536.
18. Day CL, Abrahams DA, Bunjun R, Stone L, de Kock M, Walzl G, et al. PD-1 Expression on Mycobacterium tuberculosis-Specific CD4 T Cells Is Associated With Bacterial Load in Human Tuberculosis. Frontiers in Immunology. 2018;9.
19. Susanty M, Marhanang IA. Correlation between the expression of melanoma-associated antigen-a3 and cytology results on bronchoalveolar lavage on nsclc. Indian J Forensic Med Toxicol. 2020;14(3):2008-2013.
20. Hu S, He W, Du X, Huang Y, Fu Y, Yang Y, et al. Vitamin B1 Helps to Limit Mycobacterium Tuberculosis Growth via Regulating Innate Immunity in a Peroxisome Proliferator-Activated Receptor-γ-Dependent Manner. Frontiers in Immunology. 2018;9.
21. Kusuyama J, Bandow K, Ohnishi T, Amir MS, Shima K, Semba I, et al. CXCL13 is a differentiation- and hypoxia-induced adipocytokine that exacerbates the inflammatory phenotype of adipocytes through PHLPP1 induction. Biochem J. 2019;476(22):3533-3548.
22. Patti G, Pellegrino C, Ricciardi A, Novara R, Cotugno S, Papagni R, et al. Potential Role of Vitamins A, B, C, D and E in TB Treatment and Prevention: A Narrative Review. Antibiotics. 2021;10.
23. Ranuh IGNIR, Putranto JNE, Le A. Curcumin Involve the Myofibrosis Process of Rabbit Valve Interstitial Cells based on Expression Alpha-Smooth Muscle Actin: Experimental Posttest-only Control Group Design. Int J Drug Deliv Technol. 2022;12(4):1757-1762.
24. Aminy RZ, Kholili U. Anti-tuberculosis drug-induced liver injury in patient with hepatitis B and cirrhosis: A case report. Ann Med Surg. 2022;80.
25. Ji Z, Fan Z, Zhang Y, Yu R, Yang H, Zhou C, et al. Thiamine deficiency promotes T cell infiltration in experimental autoimmune encephalomyelitis: The involvement of CCL2. J Immunol. 2014;193(5):2157-2167.
26. Abbas A, Lichtman A, Pillai S. Cellular and Molecular Immunology. 9th edition. Philadelphia: Elsevier; 2018.

27. Suryadinata R V, Wirjatmadi B. The molecular pathways of lung damage by e-cigarettes in male Wistar rats. Sultan Qaboos Univ Med J. 2021;21(3):436-441.
28. Soeters HM, Napravnik S, Patel MR, Eron JJJ, Van Rie A. The effect of tuberculosis treatment on virologic and CD4+ cell count response to combination antiretroviral therapy: A systematic review. AIDS. 2014;28(2):245-255.
29. Adewole O, Ota M, Erhabor G, Owiafe P, Oladimeji A, Obaseki D. Interferon-gamma treatment kinetics among patients with active pulmonary tuberculosis. Niger Med J. 2013;54(6):376-381.
30. Priyanto H, Chua E, Hutchinson P, Nugraha J, Amin M. A decrease in PPD specific CD4 T cell CD38 and HLA-DR expression in pulmonary tuberculosis patients after 8 weeks of therapy correlates with successful anti-tuberculosis treatment. J Clin Tuberc Other Mycobact Dis. 2021;22.
31. Young DB, Comas I, de Carvalho LPS. Phylogenetic analysis of vitamin B12-related metabolism in Mycobacterium tuberculosis. Frontiers in Molecular Biosciences. 2015;2.

ARTÍCULO ORIGINAL

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Temperature and Time Optimization of pGEM-T Plasmid Transformation in *Escherichia coli* JM109

Optimización de Temperatura y Tiempo de Transformación del Plásmido pGEM-T en *Escherichia coli* JM109

Fusvita Merdekawati[1a*], Jesicca Elisabeth Manurung[2a], Betty Nurhayati[3a]

SUMMARY

Introduction: *The widely used method for transformation was the heat shock method, which was influenced by the time and temperature of heat shock treatment. However, there was a lack of research on the optimal temperature for pGEM-T plasmid transformation in Escherichia coli JM109. This study uses the heat shock method to determine the optimum temperature and time for pGEM-T transformation in Escherichia coli JM109.*
Methods: *The research method used was a quasy experimental. The researched unit was the plasmid pGEM-T and Escherichia coli JM109 competent cells, with six treatment groups with temperature variations of 35°C and 42°C, for 30, 60, and 90 seconds and a controlled group that contained DNA insert. The transformed plasmids were cultured and then isolated to assess the intensity of the plasmid bands on agarose gel electrophoresis using ImageJ analysis.*
Results: *The results of the band width measurement obtained the largest value of 44.874-3.380 pixels in the 42°C- 60-second treatment group. At the same time, the results of measuring the intensity of the band obtained the highest value of 2.2235 in the 42°C-60-second treatment group.*
Conclusion: *The results indicate that the optimum condition for pGEM-T transformation in Escherichia coli JM109 was at 42°C for 60 seconds.*

Keywords: *Recombinant, technology, transformation, Escherichia coli JM109, imageJ.*

RESUMEN

Introducción: *El método ampliamente utilizado para la transformación fue el método de choque térmico, que estuvo influenciado por el tiempo y la temperatura del tratamiento de choque térmico. Sin embargo, existe falta de investigación sobre la temperatura óptima para la transformación del plásmido pGEM-T en Escherichia coli JM109. Este estudio tiene como objetivo determinar la temperatura y el tiempo óptimo para la transformación de pGEM-T en Escherichia coli JM109 utilizando el método de choque térmico.*
Métodos: *El método de investigación utilizado fue un cuasi experimental. La unidad investigada fue el plásmido pGEM-T y células competentes de Escherichia coli JM109, con 6 grupos de tratamiento con variaciones de temperatura de 35°C y 42°C por 30, 60 y 90 segundos y un grupo controlado que contiene inserto de ADN. Los plásmidos transformados se*

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ORCID: 0009-0000-9293-9610[1]
ORCID: 0009-0000-9317-3792[2]
ORCID: 0009-0002-5396-9811[3]

[a]Politeknik Kesehatan Kementerian Kesehatan Bandung, Bandung, Indonesia

*Corresponding Author: Fusvita Merdekawati
E-mail: fusvita.tlm@staff.poltekkesbandung.ac.id

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cultivaron y luego se aislaron para evaluar la intensidad de las bandas de plásmidos en la electroforesis en gel de agarosa usando el análisis ImageJ.
Resultados: *Los resultados de la medición del ancho de banda obtuvieron el mayor valor de 44.874 y 3.380 píxeles en el grupo de tratamiento de 42 °C y 60 segundos. Mientras que los resultados de medir la intensidad de la banda obtuvieron el mayor valor de 2,2235 en el grupo de tratamiento a 42°C-60 segundos.*
Conclusión: *Los resultados indican que la condición óptima para la transformación de pGEM-T en Escherichia coli JM109 fue a 42 °C durante 60 segundos.*

Palabras clave: *Recombinante, tecnología, transformación, Escherichia coli JM109, imageJ.*

INTRODUCTION

Gene cloning introduces foreign DNA or genes to a host cell (bacteria, plant, or animal). This process begins by the insertion of the gene into the vector to form a recombinant DNA molecule. Vectors acted as vehicles for inserting genes into host cells to direct the DNA replication process and the genes' proper (protein) expression (1,2). The cloning process consisted of isolating the gene, preparing the target DNA, inserting the target DNA into the plasmid vector, transforming the plasmid into the host cell, and then the host cell produced protein (3). In the cloning stage above, there was a transformation process, namely inserting a plasmid containing the target gene into the host cell. The transformation is the bacterial ability to insert DNA into cells, and this ability is used for the cloning process (4).

Plasmids were used as cloning vectors by inserting target DNA into the plasmid to form recombinant DNA. Cells transformed with recombinant DNA plasmids were called recombinant bacteria (5). Plasmids were extrachromosomal molecules ranging from 1 kb to more than 200 kb, circular, double-stranded, and closed. The plasmid acted as an accessory genetic unit in bacteria but could replicate and pass on its properties separately from the bacterial chromosome (6). Recombinant plasmid transformation can be done using *Escherichia coli* (*E. coli*) host cells. *E. coli* bacteria can quickly replicate and grow with simple or unique media, making it easy to culture (7). Several strains of *E. coli* can be used for transformation, namely *E. coli* DH5a, *E. coli* BL21, *E. coli* JM109, and *E. coli* HB101. The JM109 strain was transformed because it has a high efficiency above 10^8 CFU/ug and sub-cloning efficiency above 10^7 CFU/μg, including white and blue selection (8). While other strains, such as HB101, are used for vectors that do not require white-blue selection, and BL21 (DE3) can be used as protein expression vectors under the control of the T7 promoter, such as the pET vector (9).

The transformation mechanism involves DNA and the cell surface, where the DNA will bind to the membrane surface and pass through the cell wall and membrane complex (10). The transformation can be carried out by several methods, namely heat shock and electroporation (7). The transformation method that is widely used is heat shock by heating at 42°C for 2 minutes so that the plasmid can enter the bacterial cell (4). This method has the principle that the plasmid will enter the bacterial cell by shocking the high temperature for a few seconds (11).

Giving cold and hot temperatures in the heat shock method can disrupt the complexity of the membrane. Low temperatures result in the release of lipids from the bacterial cell membrane. This repeated process results in the formation of pores on the surface of the plasma membrane and increases the transformation efficiency (12). After the pores in the cell wall are open, incubation is carried out with the plasmid, allowing the plasmid to enter the bacterial cell. This process is done by quickly moving the cells previously incubated on ice to a warm temperature of 42°C for 90 seconds. A heat shock incubation time that is too long can cause membrane damage and cell death. This process must be carried out quickly and precisely so that the cells are in shock. Rapid heating at 42°C creates a heat gradient that causes a current to flow into the cell, allowing the plasmid to enter the cell (4).

The transformation efficiency of the heat shock method is affected by the time and temperature of the heat shock treatment. Several studies have shown different temperatures and times depending on the type of plasmid used and the treatment used on competent cells. Some of the optimal temperatures and times are the pUC19 plasmid at 42°C for 30 seconds, and the

second optimal is the treatment at 37°C (13), the pRGEB32 plasmid at 55°C for 30 seconds (14), 42°C for 45 seconds (15), plasmid pUC19 at 35°C for 25 seconds (16). The optimum temperature and time will differ depending on the type of plasmid. However, there has been not enough research on the optimum temperature of pGEM-T plasmid transformation in Escherichia coli JM109. Based on the preceding description, this study aimed at optimizing the temperature and transformation time of pGEM-T using the heat shock method on *E. coli* JM109. The heat shock procedure was implemented with various time and temperature variables to ascertain the optimal temperature and time parameters for successfully transforming the pGEM-T plasmid into *E. coli* JM109 bacteria.

METHODS

Design Study

This research was conducted in the Biology Molecular Laboratory of Polytechnic of the Ministry of Health Bandung. This Study was a form of quasi experimental.

Samples

The researched unit was the pGEM-T plasmid and *E. coli* JM109 competent cells obtained from the Promega pGEM-T easy kit. Two temperature variations were used, namely 42° C and 35° C, and 3-time variations of 30, 60, and 90 seconds. Hence, the treatment groups in this study consisted of 6 treatment groups and a controlled group.

Data Collection

The data used in this study was primary data by conducting pGEM-T plasmid transformation experiments on *E. coli* JM109 with heat shock temperatures of 42° C and 35° C with variations in time of 30, 60, and 90 seconds. There were six treatment groups based on the variation in temperature and time. After the transformation process, the bacterial cells were cultured, and then grown colonies were observed through blue and white selection and then used. Electrophoresis was applied to assess the migration of the transformation results. The quality of the transformation results was evaluated from the bands formed and measured using the ImageJ software to measure the area and intensity of the plasmid bands. Bands were quantified using the ImageJ software by using the "analyze gels" menu, and then lanes were plotted to obtain band width graphs. Then, this graph was connected to obtain the Region of Interest (ROI) section, and the "magic wand tool" menu was selected to quantify the width of the plasmid band. To obtain the intensity value, the percentage of intensity needed to be obtained. This was done by using the "analyze gels" menu and selecting the "label peaks" option. Then, the percentage of intensity for each variation was divided by the control to produce the intensity value. Band intensity describes the optimality of the transformation using a specific temperature and time. A higher band width and intensity will indicate a higher level of optimality.

RESULTS

The experiment utilized the blue and white selection procedure to assess colony appearance. In the control group, white colonies indicated successful DNA insertion, while the treatment group showed blue colonies without DNA inserts. Figure 1 visually presents the distinct colony differentiation between the control and treatment groups. Table 1 quantitatively displays the number of blue colonies, with the treatment group at 42°C for 60 seconds showing the highest count and the group at 42°C for 90 seconds having the lowest count. Thus, it can be concluded that the 42°C for 60 seconds treatment group exhibited the most optimal colony growth.

The isolates obtained after plasmid isolation was then observed for migration using 0.4 % agarose gel electrophoresis. The corresponding results are presented in Figure 2. The treatment group that contained plasmids without DNA inserts migrated faster than the controlled contained DNA inserts. The results of plasmid migration are shown in Figure 2.

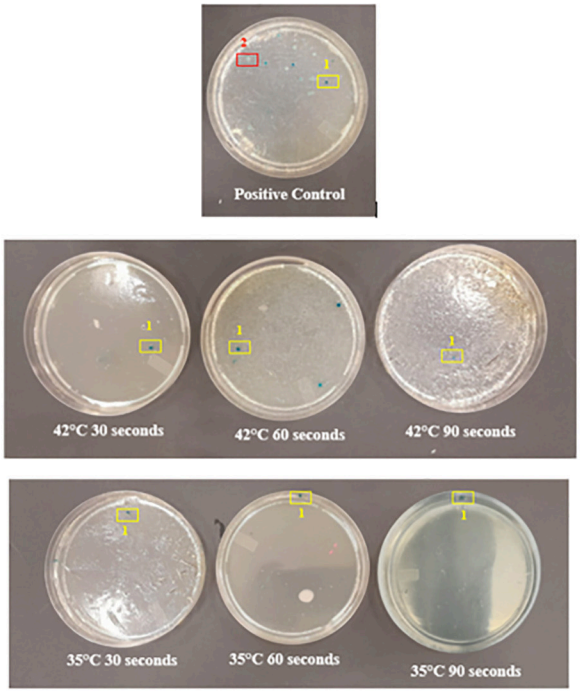

Figure 1. Blue and White Selection Results (1) Blue Colonies, (2) White Colonies.

The control group band was above the treatment group because the migration speed was slower than the treatment group band. This is due to the presence of a 542 bp DNA insert which increased the molecular weight of the plasmid. The migration bands formed were read using electrophoresis and UV transilluminators and then analyzed using ImageJ software. The data obtained from the analysis using ImageJ are in the form of band area and percent band intensity. The data was analyzed using ImageJ, as presented in Table 2.

Table 1. Number of Colonies of Treatment Group

No.	Treatment Group	Total White Colonies	Total Blue Colonies
1	Control	9	5
2	42°C 30 seconds	-	4
3	42°C 60 seconds	-	12
4	42°C 90 seconds	-	2
5	35°C 30 seconds	-	4
6	35°C 60 seconds	-	1
7	35°C 90 seconds	-	1

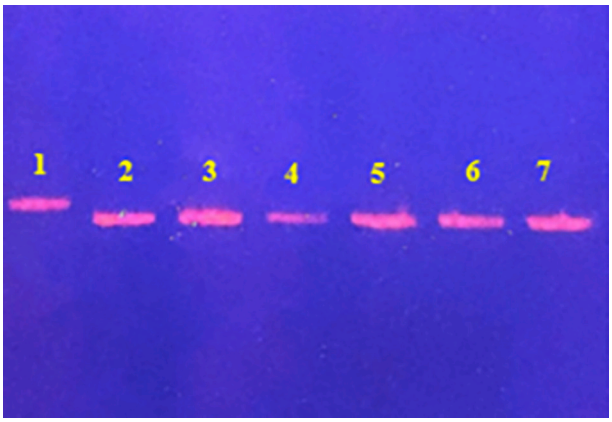

Figure 2. Electrophoresis results with UV transilluminator readings (1) Positive control, (2) Temperature 42°C 30 seconds, (3) Temperature 42°C 60 seconds (4) Temperature 42°C 90 seconds, (5) Temperature 35 °C 30 seconds, (6) Temperature 35°C 60 seconds, (7) Temperature 35°C 90 seconds.

The band's intensity was calculated by comparing the treatment group's intensity with the control groups. Descriptive statistical tests were conducted to determine the largest band width and band intensity. Table 3 presents the results,

Table 2. Results of Agarose Gel Analysis with ImageJ

No	Treatment group	Band Width (pixel)	% Intensity	Intensity
1	Control	20182.388	9.969	1
2	Temperature 42°C 30 seconds	32090.338	15.852	1.590129401
3	Temperature 42°C 60 seconds	44874.338	22.166	2.223492828
4	Temperature 42°C 90 seconds	12158.066	6.006	0.60246765
5	Temperature 35°C 30 seconds	36370.995	17.966	1.802186779
6	Temperature 35°C 60 seconds	26894.409	13.285	1.332631157
7	Temperature 35°C 90 seconds	26894.409	14.475	1.480188585

showing that the treatment group at 42°C for 60 seconds had the largest band width and highest intensity. The maximum band width recorded was 44874.3380 pixels, while the highest band intensity was 2.2235. In contrast, the treatment group at 42°C for 90 seconds had the smallest band width of 12158.0660 pixels and the lowest band intensity of 0.6025.

Table 3. Descriptive Test Results

	Total Treatment	Minimum	Maximum	Mean
Band Width	6	12158.0660	44874.3380	29880.425833
Band Intensity	6	0.6025	2.2235	1.505183

DISCUSSION

Blue-white screening offers a convenient and potent method for distinguishing bacterial colonies or phage plaques with a cloning vector carrying inserted DNA from those harboring empty vectors devoid of insert DNA. The approach relies on developing a blue pigment when beta-galactosidase facilitates the breakdown of the synthetic substrate X-gal through hydrolysis. Hydrolysis of X-gal (5-bromo-4-chloro-3-indolyl-β-D-galactoside) produces galactose and 5-bromo-4-chloro-3-hydroxyindole. *E. coli* colonies lacking DNA inserts will exhibit a blue colour due to the expression of beta-galactosidase. In contrast, colonies carrying DNA inserts will appear white as they lack the production of active enzymes (16). In the study, the control group yielded both blue and white colonies, indicating the presence or absence of DNA inserts. On the other hand, the treatment group produced solely blue colonies, signifying the absence of DNA inserts. The readings obtained using the UV transilluminator revealed bands in all treatment groups, which exhibited faster migration than the control group. Plasmids in the treatment group moved faster because the molecular weight was lighter without a DNA insert. Meanwhile, the positive control had slower migration due to the increased molecular size in the presence of a 542 bp DNA insert. This is because large DNA fragments migrate slower than smaller DNA fragments (17-19).

The obtained readings were analyzed using ImageJ to determine the largest band area and highest band intensity. Following the analysis, the data was acquired regarding band area and percentage of band intensity (20). The band intensity value was obtained by dividing the percentage of band intensity in the treatment group by the percent intensity of the control band. After calculating the intensity, the band intensity data were obtained for the control and each treatment group. Band width and band intensity indicates the DNA quantity, or in this case, the plasmid content within the isolate (21). Descriptive tests were applied to the band area and intensity to identify the largest value, indicating a higher number of plasmids and representing the most optimal treatment group.

The key to successful transformation lies in using chemically treated competent cells, such as $CaCl_2$ treated cells, which enhance the permeability of the *E. coli* cell membrane and facilitate the entry of plasmids into the cells. Previous studies have demonstrated that competent cells of *E. coli* strains BL21 (BE3), JM109, TG1, and HB101 exhibited optimal transformation efficiency when subjected to $CaCl_2$ treatment (22,23). In addition, recombinant plasmid DNA is needed to be transformed into cells. Plasmids usually encode antibiotic-resistant genes to differentiate them from non-recombinant bacterial cells so that *E. coli* that already contains recombinant plasmids will be resistant to antibiotics (24,25). This study used competent cells that had been added with $CaCl_2$ and was the most optimal treatment for competent cells (24). As for the recombinant plasmid, this study used the pGEM-T plasmid, which is resistant to the

antibiotic ampicillin and is observable from the blue and white selection results.

In the heat shock process involving temperature changes, *E. coli* cells responded to heat shock by inducing heat-shock protein (HSP) (26). This protein allowed cells to survive under stress conditions due to temperature (27). Heat shock protein acted as a chaperone which helped fold proteins in cells so that cells were not damaged when exposed to heat. The factor σ32 (sigma-32) controlled this heat shock response, encoded by the rpoH gene. Regulon σ32 could be classified as molecular chaperones and ATP-dependent proteases. Molecular chaperones, including DnaK-DnaJ-GrpE and GroEL-GroES, facilitated better folding of newly synthesized polypeptides and helped repair protein damage due to temperature (28). Heat shock proteases such as CIpP, Lon, and HfIB degraded misfolded proteins, which chaperones could not help (29). HSP chaperones and proteases played a role in protecting cells and protein folding under conditions of increased temperature (30).

DnaK-DnaJ-GrpE and GroEL-GroES were chaperones with the best characteristics found in *E. coli*. Other chaperones were Clp ATPases (ClpB, ClpX, and ClpY), Hsp90 HtpG homologs, and small Hsps (sHsps), IbpA, and IbpB (31). DnaK and GrpE were essential for the growth of *E. coli* at a temperature of around 43°C (32). GrpE allowed *E. coli* to grow at a maximum temperature of 43.5 °C (33). Meanwhile, ClpB was given a temperature of 42°C then grown at a temperature of 30°C, showing the results of growing at a maximum high temperature of 50°C. So, ClpB protected *E. coli* cells from lethal effects due to very high temperatures (31). ClpA could maintain cells up to 46°C, while the chaperone GroES30 could maintain cellular integrity and cell viability at 42-46°C. However, this chaperone could not maintain cell viability at 50°C, causing cell death (34).

This study employed heat shock treatments at 42°C and 35°C to determine the optimal temperature. The assessment was based on parameters such as colony count, band area, and intensity, with the optimal temperature identified as 42°C. At this temperature, the growth of *E. coli* was found to be favorable, primarily due to specific heat shock proteins, including DnaK, GrpE, ClpB, ClpA, and chaperone GroES30. Moreover, the presence of sHsps (small heat shock proteins) and Hsp90s (heat shock protein 90s) played a vital role in maintaining partially folded proteins in a conformation that can be reactivated through their interaction with Hsp70s (35).

It is essential to consider the temperature during the transformation process, as excessively high temperatures can result in cell death (4). At 42°C, forming larger and more membrane pores facilitates the entry of plasmids into bacterial cells. Heat shock induces the release of lipids from the outer membrane and reduces the potential of the inner membrane, allowing plasmids to enter *E. coli* bacteria (12). Moreover, heat shock proteins such as DnaK, GrpE, ClpB, ClpA, and chaperone GroES30 effectively protect *E. coli* cells (35,36). In this study, the treatment group subjected to heat shock at 42°C for 60 seconds demonstrated the highest number of colonies, the largest band area measuring 44874.3380 pixels, and the highest band intensity of 2.2235. Therefore, the treatment group at 42°C represents the optimum temperature for plasmid transformation.

The duration of the transformation process can significantly impact its efficiency. During the heat shock stage, the bacterial cell membrane opens its pores to facilitate the entry of the plasmid. If the duration is too short, the plasmid may not fully enter the *E. coli* cell, resulting in lower efficiency. On the other hand, if the pore opening time is too long, it can lead to membrane damage and cell death (4). In this study, the treatment group subjected to heat shock at 42°C for 60 seconds exhibited the highest number of colonies, the largest band area measuring 44874.3380 pixels, and the highest band intensity of 2.2235. Therefore, the 60-second transformation treatment group proved optimal for allowing the plasmid to enter *E. coli* cells without compromising viability.

CONCLUSIONS

The results indicate that the optimum temperature in this study was 42°C, and the optimal time was 60 seconds. This conclusion was drawn based on the highest number of colonies observed, which amounted to 12 colonies, the largest band

width recorded, measuring 44874.3380 pixels, and the highest intensity observed, reaching 2.2235. Researchers and laboratory technicians should consider this optimal condition to improve plasmid transformation experiments' efficiency and success rate. Further studies can explore variations in other parameters or combinations to optimize the transformation process and validate these findings in different *E. coli* strains or plasmids.

REFERENCES

1. Kalajanti VP, Wahjudi M, Purwantari KE, Nawangsasi P, Oktariza RT, Pradana KA, et al. GABRA6 and SLC6A4 genotypes are correlated with the fasting blood glucose and physical fitness in the seemingly healthy young adults. J Ners. 2023;18(1):80-87.
2. Wong DWS. Cloning Vectors for Introducing Genes into Host Cells. In: The ABCs of Gene Cloning. Springer, Cham. 2018. Available: https://doi.org/10.1007/978-3-319-77982-9_9
3. Choramo A, Debelo M. Recombinant DNA Technology and its Applications. J Mol Genet. 2019;11:1-13.
4. Brown TA. Gene Cloning and DNA Analysis: An Introduction. 8th ed. Wiley Blackwell; 2020.
5. Reece JB, Urry LA, Cain ML, Wasserman SA, Minorsky P V, Jackson RB. Campbell Biology. 9th ed. New York: Pearson; 2019.
6. Walker JM, Rapley R. Molecular biomethods handbook. 2nd edition. 2008:1-1124.
7. Casali N, Preston A. *E. coli* Plasmid Vectors. In: Methods in Molecular Biology. Humana Totowa, NJ; 2003.p.XII, 316.
8. Jubair N, Rajagopal M, Chinnappan S, Abdullah NB, Fatima A. Review on the Antibacterial Mechanism of Plant-Derived Compounds against Multidrug-Resistant Bacteria (MDR). Evidence-based Complement Altern Med. 2021;2021.
9. Inoue H, Nojima H, Okayama H. High-efficiency transformation of *Escherichia coli* with plasmids. Gene. 1990;96(1):23-28.
10. Rahimzadeh M, Sadeghizadeh M, Najafi F, Arab S, Mobasheri H. Impact of heat shock step on bacterial transformation efficiency. Mol Biol Res Commun. 2016;5(4):257-261.
11. Bui LM, Geraldi A, Nguyen TT, Lee JH, Lee JY, Cho B-K, et al. MRNA engineering for the efficient chaperone-mediated co-translational folding of recombinant proteins in *Escherichia coli*. Int J Mol Sci. 2019;20(13).
12. Panja S, Aich P, Jana B, Basu T. How does plasmid DNA penetrate cell membranes in artificial transformation process of *Escherichia coli*? Mol Membr Biol. 2008;25(5):411-422.
13. Singh M, Yadav AS, Ma X, Amoah E. Plasmid DNA transformation in *Escherichia Coli*: Effect of heat shock temperature, duration, and cold incubation of CaCl2 treated cells. Int J Biotechnol Biochem. 2010;6:561-568.
14. Patigu R, Wijayanti P, Sebastian A, Purwestri YA. Optimization of heat shock temperature and time on the transformation of pRGEB32 into *Escherichia coli*. J Biol Trop. 2021;21.
15. Froger A, Hall JE. Transformation of plasmid DNA into *E. coli* using the heat shock method. J Vis Exp. 2007;(6):253.
16. Wang Y, Sun S, Yu L, Hu S, Fan W, Leng F, et al. Optimization and mechanism exploration for Escherichia coli transformed with plasmid pUC19 by the combination with ultrasound treatment and chemical method. Ultrason Sonochem. 2021;74:105552.
17. Sumarsih S, Fatimah, Hadi S, Ni'matuzahroh, Geraldi A, Fitri RD, et al. Expression of Recombinant Lipase from Serratia marcescens LII61 in *Escherichia coli*. Jordan J Biol Sci. 2022;15(2):199–203.
18. Ningsih RRP, Sumarsih S, Hadi S, Retnowati W, Purkan P. Cloning and Expression of Gene Encoding Lipase from Local Isolate Bacillus cereus Isolated from Compost Jambangan Indonesia. Jordan J Biol Sci. 2022;15(5):779-786.
19. Kurniati A, Puspaningsih NNT, Putri KDA, Damayanti M, Purwani NN, Rahmah SA, et al. Heterologous fusion gene expression and characterization of a novel carbohydrate binding module (Cbm36) to laccase (Lcc2). Biocatal Agric Biotechnol. 2022;42.
20. Astuti SD, Ma'rifah ZA, Fitriyah N, Zaidan AH, Arifianto D, Setiawatie EM. c-doxycycline activated by diode laser exposure to reduce S. aureus biofilms: An *in vitro* study. In: T. D, J. P, MX W, editors. Photonic Diagnosis and Treatment of Infections and Inflammatory Diseases II 2019. Biomedical Engineering Postgraduate School, Universitas Airlangga, Surabaya, 60115, Indonesia: SPIE; 2019.
21. Ziraldo R, Shoura MJ, Fire AZ, Levene SD. Deconvolution of nucleic-acid length distributions: a gel electrophoresis analysis tool and applications. Nucleic Acids Res. 2019;47(16):e92.
22. Rosantia S, Higa T, Yagi N, Tokunaga T, Higa S, Yakabi Y, et al. Characterization of CTX-M-type-extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae isolated from Indonesian undergraduate medical students of a university in Surabaya, Indonesia. J Infect Chemother. 2020;26(6):575-581.

23. Liu X, Liu L, Wang Y, Wang X, Ma Y, Li Y. The Study on the factors affecting transformation efficiency of *E. coli* competent cells. Pak J Pharm Sci. 2014;27(3 Suppl):679-684.
24. Sarkar S, Chaudhuri S, Basu T. Mechanism of artificial transformation of *E. coli* with plasmid DNA – Clues from the influence of ethanol. Curr Sci. 200283(11):1376-1380.
25. Mun Teo MY, Ceen Ng JJ, Fong JY, Hwang JS, Song AA-L, Hong Lim RL, et al. Development of a single-chain fragment variable fused-mutant HALT-1 recombinant immunotoxin against G12V mutated KRAS colorectal cancer cells. PeerJ. 2021;9.
26. Bohne J, Sokolovic Z, Goebel W. Transcriptional regulation of prfA and PrfA-regulated virulence genes in Listeria monocytogenes. Mol Microbiol. 1994;11(6):1141-1150.
27. Arsène F, Tomoyasu T, Bukau B. The heat shock response of *Escherichia coli*. Int J Food Microbiol. 2000;55(1-3):3-9.
28. Hartl FU. Molecular chaperones in cellular protein folding. Nature. 1996;381(6583):571-580.
29. Gottesman S. Proteases and their targets in *Escherichia coli*. Annu Rev Genet. 1996;30:465-506.
30. Straus DB, Walter WA, Gross CA. The heat shock response of *E. coli* is regulated by changes in the concentration of sigma 32. Nature. 1987;329(6137):348-351.
31. Squires C, Squires CL. The Clp proteins: proteolysis regulators or molecular chaperones? J Bacteriol. 1992;174(4):1081-1085.
32. Johnson C, Chandrasekhar GN, Georgopoulos C. *Escherichia coli* DnaK and GrpE heat shock proteins interact both in vivo and in vitro. J Bacteriol. 1989;171(3):1590-1596.
33. Ang D, Chandrasekhar GN, Zylicz M, Georgopoulos C. Escherichia coli grpE gene codes for heat shock protein B25.3, essential for both lambda DNA replication at all temperatures and host growth at high temperature. J Bacteriol. 1986;167(1):25-29.
34. Thomas JG, Baneyx F. Roles of the Escherichia coli small heat shock proteins IbpA and IbpB in thermal stress management: comparison with ClpA, ClpB, and HtpG *In vivo*. J Bacteriol. 1998;180(19):5165-5172.
35. VanBogelen RA, Kelley PM, Neidhardt FC. Differential induction of heat shock, SOS, and oxidation stress regulons and accumulation of nucleotides in *Escherichia coli*. J Bacteriol. 1987;169(1):26-32.
36. Squires CL, Pedersen S, Ross BM, Squires C. ClpB is the *Escherichia coli* heat shock protein F84.1. J Bacteriol. 1991;173(14):4254-4262.

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Anti-microbial Activities of Syzigium cumini leaves against Periodontophatic Bacteria (*Porphyromonas gingivalis*)

Actividades antimicrobianas de las hojas de Syzigium cumini contra bacterias periodontopáticas (*Porphyromonas gingivalis*)

Yenni Hendriani Praptiwi[1a], Yonan Heriyanto[2a], Tri Widyastuti[3a], Susi Sukmasari[4b*]

SUMMARY

Introduction*: Syzigium cumini has been known to have an anti-microbial effect and is traditionally used as medicine for some human diseases. However, only a few studies were done on water extracts of these leaves. This study aimed to elucidate the minimum inhibition concentration (MIC) and minimum bactericidal concentration (MBC) of water extract of Syzigium cumini leaves against Porphyromonas gingivalis that represent periodontopathic bacteria.*
Methods: *S. cumini leaves were collected from local farms. The leaves were washed and dried. Water extraction was performed to collect the compound, then was diluted into concentrations of 1 %, 2.5 %, 5 %, 7.5, 10 %, 12.5 %, 15 %, and 20 %. The bacteria were grown in triplicates agar blood and then put in the anaerobic jar to incubate for 48 hours at 37^{0}C. Disc Diffusion test, MIC, and MBC were performed.*
Result: *The anti-microbial disc diffusion test of S. cumini extract against P. gingivalis indicated by the presence of a 6.9 ± 0.14 mm clear area around the extract starting at a concentration of 7.5 %, and 13.6±0.32 mm at a concentration 20 %. The minimum inhibition concentration of S. cumini was 0.156 %. The clear sight starting from the 6th well indicates that there was no growth of bacteria. After incubation for 2x24 hours, there was no growth of bacteria on the agar blood with a 2.5 % concentration of S. cumini extract.*
Conclusion*: Aqueous extract of S. cumini leaves has an anti-microbial potential effect against Periodontophatic bacteria which was represented by Porphyromonas gingivalis. Further research on Syzigium cumini leaves at the molecular level is advisable.*

Keywords: *Syzigium cumini, Porphyromonas gingivalis, Human diseases.*

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ORCID: 0000-0002-0943-6623[1]
ORCID: 0000-0003-4178-7658[2]
ORCID: 0009-0005-4655-5807[3]
ORCID: 0000-0002-1955-0681[4]

[a]Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia.
[b]Paediatric Dentistry and Dental Public Health Department, Kulliyyah of Dentistry, International Islamic University Malaysia, Kuantan, Malaysia

*Corresponding Author: Susi Sukmasarikmasari@iium.edu.my

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RESUMEN

Introducción: *Se sabe que Syzigium cumini tiene un efecto antimicrobiano y se usa tradicionalmente como medicamento para algunas enfermedades humanas. Sin embargo, solo se han realizado unos pocos estudios en los extractos acuosas de estas hojas. Este estudio tuvo como objetivo dilucidar la concentración mínima de inhibición (CMI) y la concentración mínima bactericida (CMB) del extracto acuoso de hojas de Syzigium cumini contra Porphyromonas gingivalis que representan bacterias periodontopáticas.*

Métodos: *Se recolectaron hojas de S. cumini de fincas locales. Las hojas se lavaron y secaron. Se realizó extracción con agua para recolectar el compuesto, luego se diluyó en concentraciones de 1 %, 2,5 %, 5 %, 7,5, 10 %, 12,5 %, 15 % y 20 %. Las bacterias se cultivaron en sangre de agar por triplicado y luego se colocaron en la jarra anaerobia para incubar durante 48 horas a 37^{0}C. Se ha realizado la prueba de difusión en disco, MIC y MBC.*
Resultado: *La prueba de difusión de disco antimicrobiano del extracto de S. cumini contra P. gingivalis indicó la presencia de un área clara de 6,9 ± 0,14 mm alrededor del extracto a partir de una concentración de 7,5 % y de 13,6 ± 0,32 mm a una concentración de 20 %. La concentración mínima de inhibición de S. cumini fue de 0,156 %. La vista clara a partir de los pozos 6, indica que no hubo crecimiento de bacterias. Después de incubar durante 2x24 horas, no hubo crecimiento de bacterias en el agar sangre con una concentración del 2,5 % de extracto de S. cumini.*
Conclusión: *El extracto acuoso de las hojas de S. cumini tiene potencial efecto antimicrobiano contra las bacterias periodontófagas representadas por Porphyromonas gingivalis. Se recomienda realizar más investigaciones sobre las hojas de Syzigium cumini a nivel molecular.*

Palabras clave: *Syzigium cumini, Porphyromonas gingivalis, enfermedades humanas.*

INTRODUCTION

Globally gingivitis is inflammation of the gum that affects more than 90 % of the population and is found in 70.4 % of children ages 5-15 years old (1). According to an Indonesian basic health survey in 2018, the prevalence of periodontitis starting from age 15 to 65 -year-old was more than 67.8 % (2). The inflammation mainly occurs because of dental plaque as bacterial biofilm surrounding the gum. Untreated gingivitis will cause periodontitis, alveolar bone damage and tooth loss. Dental plaque is a biofilm that attaches to the dental surface due to neglect of oral hygiene (3). During the development of gingivitis, the microflora increases in the number of species (4).

To prevent the expansion of biofilm into subgingival, removal of the supragingival biofilm and rebalancing a microflora by adequate home oral hygiene and by professional cleaning will eliminate gingivitis (5). As an adjunct to other oral hygiene measures such as tooth brushing and flossing, antiseptic mouthwash has been used to prevent and treat gingivitis. Some medication against gingivitis bacteria, such as metronidazole gel has been used to treat periodontitis (6).

Black-pigmented anaerobic gram-negative bacilli cause chronic gingivitis (7,8). It is characterized by brown or black pigment on agar blood. As an agent of periodontal disease (periodontopathic organism), one of the black-pigmented anaerobic is *Porphyromonas gingivalis* (5). The main colonization in the oropharynx and found almost solely at subgingival sites (5,6). *P. gingivalis* is non-motile, saccharolytic, and looks cox-shaped until it is short-lived. The initial stage of gingivitis is the colonization of this bacterium in the gingiva sulcus (7). At first, the bacteria colonize the periodontal environment and then attach to the layer of the surface of the tooth. *P. gingivalis* is found in the saliva layer on the surface of the tooth (7). This bacterium plays a very important role in virulence through the adhesion process with the human cells, able to inhibit the production of IL-8 by epithelial cells that can make the microorganisms avoid polymorphonuclear leukocytes, and the bacterial enzymes can facilitate tissue damage (7). There are some drugs to avoid the severity. However, antimicrobial resistance in patients worldwide is a global concern. Traditional medicine is the rising alternative medicine to overcome the hassle.

Eugenia Jambolana (*Syzygium cumini*) belongs to the family Myrtaceace. *Syzigium cumini* is a green tropical plant widely grown in Bangladesh, Pakistan, India, South America, Madagascar, Malaysia, Phlipina, and Indonesia (8). The plant has many names such as Duwet, Jamblang, Java plum, Jamun, Guava rivet, Indian Blackberry, and many more local names. The fruit taste is sweet-sour, and the color is purple when ripped. Based on empirical utilization, most of this plant has long been known as a traditional medicinal plant, especially for diabetes. The leaves are used to strengthen teeth and gums, treat vaginal discharge, abdominal pain, fever, gastropathy, dermopathy, and constipation, and inhibit the disposal of blood in the stool (9). *Syzigium cumini* fruits are edible, but seasonal. The leaves are available in all seasons, then it's easy to have as medicinal ingredients.

Some studies report that the stems, leaves, and fruits of *S. cumini* have activity as antioxidants, anti-inflammatories, antihelminthic, anticancer, antibacterial, and antidiabetic (10). The phytochemical and antioxidant effects of *S. cumini* show the presence of alkaloids, steroids, saponins, cardiac glycosides, carbohydrates, proteins, tannins, and phenols (11). Compared to other solvents in the percolation method, water extraction of these leaves resulted in the highest percentage of phenol and antioxidant capacity (12). *S. cumini* leaves have anti-microbial effects against gram-positive and gram-negative bacteria such as *Pseudomonas aeruginosa, Klebsiella pneumoniae*, and *Staphylococcus aureus* (11,13,14) and some multidrug-resistant pathogenic bacteria (15). This study aimed to assess the minimum inhibition concentration (MIC) and minimum bactericidal concentration (MBC) of the water extract leaves against *Porphyromonas gingivalis* as a periodontophatic microorganism.

METHODS

This *in vitro* study was an experimental study conducted at a microbiology laboratory. The variables were water extraction of *Syzigium cumini* leaves and oral microbiota representing periodontopathic bacteria *Porphyromonas gingivalis*.

Extraction

S. cumini leaves were collected from local farms in Sukorejo, Wonosobo, Central Java, Indonesia. The area longitude is 109.98, latitude -7.14, and elevation 3 527 feet. The leaves were washed under the tap water for 15 minutes to clean up, then dried in the oven at 50°C for 3 days. The dried leaves were crushed into powder.

The dried leaves powder was soaked in water at a concentration of 10 % w/v, equal to 25 g of powder in 250 mL of water in a cone flask, then shaken at 120 rpm, 27°C using an incubator shaker. After 24 hours, the solvent was filtered using Whatman No 1 and vacuumed filter to separate the extract from the solvent. The filtrate was centrifuged at 5 000 rpm for 10 minutes, at 27°C to separate the supernatant completely. The supernatant was then piped out, leaving residue on the bottom of the centrifuge tube. The collected solvents were then dried using a rotary evaporator (IKA RV8 model) until dry. The collected extract was left under the smoke hood for 2 days until the solvent completely evaporated. The yield was then collected and stored at -20°C before further analysis. The extract was diluted into concentrations of 1 %, 2.5 %, 5 %, 7.5 %, 10 %, 12.5 %, 15 % and 20 %.

Anti-microbial Disk Diffusion Test.

Freeze-dried cultures of *P. gingivalis* ATCCA 33277 have been purchased. The bacteria were grown in triplicates of agar blood and then put in the anaerobic jar to incubate for 48 hours at 37°C. The holes were made by punching the prepared agar blood using a sterile tube. Then it was placed each concentration of extract into each hole, then put all covered plates into an anaerobic jar. The agar blood was left in the anaerobic jar for 2 days. The data collection was done by determining the clear area from the bacteria-free around the hole. It was measured the diameter of the free area using a gauge on each plate. The hole with chlorhexidine was used as a control. Zones of microbial growth inhibitions were recorded at 24 and 48 hours.

Minimum inhibitory concentration test (MIC)

The minimum inhibitory concentration (MIC) was performed by microdilution technique using 6 rows on 72 wells of microtiter plates and Mueller Hinton Broth (MHH) as a medium. According to the Clinical & Laboratory Standards Institute (CLSI), 100 mL MHB was added to all wells. On the first to third rows microtiter plates were added 100 mL of extract and then homogenized. The extract concentration on the first wells was 5 %, then reduce a half accordingly until the tenth wells. Therefore, the concentration of the extract was 5 %; 2.5 %; 1.25 %; 0.625 %; 0.3125 %, 0.156 %; 0.078 %, 0.039 %, 0.0195 %, and 0.00975 %, respectively. Next, from the fourth to the sixth rows microtiter plates added 100 mL of chlorhexidine. Inserted bacteria into the well's microtiter plates as much as 10^5

Mc Farland. The microplates were placed in an anaerobic jar and incubated for 48 hours at 37^0C. The visual examination was carried out to determine the MIC that can be seen from the absence of bacterial growth.

Minimum Bactericidal Concentration Test (MBC)

Planting the inoculum from the clear well into MHA and incubating anaerobically for 48 h at 37^0C. MBC was determined by assessing at the minimal concentration of extracts in which there was no growth of bacteria in the MHA.

RESULTS

The activity of *S. cumini* extracts against *P. gingivalis* was indicated by the presence of a 6.9 ±0.14mm clear area around the extract starting at a concentration of 7.5 %. At 20 % concentration, the clear zone was 13.6±0.32 mm. The results of the anti-bacterial test by disk diffusion test method (Kirby Bauer method) are presented in Table 1.

The result of the anti-microbial activity extract *S. cumini* against *P. gingivalis* can be seen in Table 2.

Table 1

The diameter of the clear zone area in response to Syzigium cumini (leaves)

Water extract (%)	R1	R2	R3	Mean	SD	Diameter of clear zone (mm)
1	0	0	0	-	-	-
2.5	0	0	0	-	-	-
5	0	0	0	-	-	-
7.5	7	6.8	0	6.9	0.14	6.9 ±0.14
10	11.2	11.1	11.8	11.4	0.38	11.4 ±0.38
12.5	12.6	12.5	12.9	12.7	0.21	12.7 ±0.21
15	12.9	12.3	13.2	12.8	0.46	12.78±0.46
20	13.8	13.2	13.7	13.6	0.32	13.6 ± 0.32
CHX %	R1	R2	R3	Mean	SD	Diameter of clear zone (mm)
0.2	22.1	20.5	22.8	21.8	1.18	21.8 ± 1.18

Table 2

Minimum Inhibitory Concentration and Minimum Bactericidal Concentration

Bacteria	Test Sample	Concentration (%)													
		C(-)	C(+)	0.00975	0.0195	0.039	0.078125	0.15625	0.3125	0.625	1.25	2.5	5	MIC	MBC
	Water extract	(-)	(+)	(+)	(+)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)		
		(-)	(+)	(+)	(+)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)	0.15	2.5
		(-)	(+)	(+)	(+)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)		
P. Gingivalis	Test Sample	Concentration (%)													
		C(-)	C(+)	9.77 E-05	0.000 195	0.000 391	0.000 781	0.001 563	0.003 125	0.006 25	0.01 25	0.025	0.05	MIC	MBC
	CHX	(-)	(+)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)		
		(-)	(+)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	0.0004	0.0008
		(-)	(+)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)		

(+): bacteria growing.
(-): bacteria do not grow.

DISCUSSION

S. cumini leaves extract has anti-microbial effects on anaerobic bacteria and anaerobic facultative bacteria such as *Staphylococcus aureus* and *Escherichia coli* (15,16). However, the best way to extract *Syzigium cumini* has not been much explored (17-19). The potential water-based extraction was better than methanol extract and petroleum ether against four types of bacteria, such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Bacillus subitils*, and two types of fungi (*Aspergillus niger*, and *Candida albicans*) (17). This is reinforced by the results of Sukmasari et al. (12) which stated that out of some solvents in the percolation method, the water extract of *Sygyzium cumini* leaves has a total phenolic content and better antioxidant capacity. Supporting by a previous study on some oral microbiota (11,15). The aqueous extracts of *S. cumini* leaves in this study demonstrated antibacterial activity against *P. gingivalis* as one of the dominant black-pigmented or periodontopathic bacteria that cause periodontal diseases through the MIC and MBC test.

The extracts used in the disc diffusion test study exhibited antibacterial activity starting at a concentration of 7.5 % and 20 % concentration, the clear zone was 13.6±0.32 mm. To support the disc diffusion test, the broth microdilution test method found out the minimum concentration of *S. cumini* leaf extract against *P. gingivalis* bacteria was 0.156 % and the concentration of bactericide activity at least at a concentration of 2.5 %. Therefore, these results show that *S. cumini* leaves have antibacterial power, especially against anaerobic bacteria. This antibacterial activity may be attributed to the alkaloids, glycosides, steroids, terpenoids, saponins, flavonoids, and perhaps resins since these secondary metabolites were detected in the extracts (10,12,20,21).

The aqueous extract of *S. cumini* leaves has a potential effect to be used as an anti-microbial agent on black pigmented or periodontopathic bacteria which represent by *Porphyromonas gingivalis*, even though chlorhexidine solution presents a wide spectrum anti-microbial action (22). Therefore, further laboratory and clinical studies are required to determine its potency and safety at a molecular level.

CONCLUSION

Aqueous extract of *S. cumini* leaves has the potential effect to be used as an anti-microbial agent on Periodontophatic bacteria which represent by *Porphyromonas gingivalis*.

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REFERENCES

1. Krismariono A, Setiawatie EM, Rachmawati RY, Setiawan YA, Padmarini HN, Apriliyanti NA. Antibacterial Activity of Water Hyacinth (Eichhornia Crassipes) Leaf Extract Against Bacterial Plaque from Gingivitis Patients. J Int Dent Med Res. 2022;15(3):966-971.
2. Nelwan SC, Nugraha RA, Endaryanto A, Dewi F, Nuraini P, Tedjosasongko U, et al. Effect of scaling and root planing on level of immunoglobulin E and immunoglobulin G4 in children with gingivitis and house-dust mite allergy: A pilot randomised controlled trial. Singapore Dent J. 2019;39(1):21-31.
3. Sitanaya R, Lesmana H, Sunariani J, Harjanto JM, Achmad H, Irayani S, et al. The Role of Mastication in Improving TGF-β Levels on the Inhibition of *Streptococcus sanguinis* and *Streptococcus mutans* in Gingivitis. J Int Dent Med Res. 2022;15(1):268-273.
4. Firdaus R, Harryadi CI, Kurnia S, Krismariono A. Inhibitory effect of lemongrass extract (Cymbopogon citratus) in supragingival plaque bacterial growth for gingivitis patient: A research study. J Int Oral Heal. 2022;14(3):324-330.
5. Susilawati, Bramantoro T, Setyowati D, Olivia KL. Research article the miswak (Salvadora persica) chewing stick: Muslim consumer behavior of halal oral hygiene product. Int J Pharm Res. 2020;12(4):2745-2750.
6. Setijanto R, Rahayu M, Bramantoro T, Wening G, Rudhanton R, Ramadhani A. Gingival Inflammation in 2 Phases of Menstrual Cycle and its Relation to Oral Hygiene of Female Dentistry Students. J Int Oral Heal. 2019;11(6):388-392.
7. Acob JRU, Dewi YS, Arifin H. Five Cs as reflective learning attitude among Philippines nursing students. J Ners. 2022;17(2):161-167.

8. How Y-H, Yeo S-K. Oral probiotic and its delivery carriers to improve oral health: A review. Microbiol (United Kingdom). 2021;167(8).
9. Jubair N, Rajagopal M, Chinnappan S, Abdullah NB, Fatima A. Review on the Antibacterial Mechanism of Plant-Derived Compounds against Multidrug-Resistant Bacteria (MDR). Evidence-based Complement Altern Med. 2021;2021.
10. Alam MR, Rahman A Bin, Moniruzzaman M, Kadir MF, Haque MA, Alvi MRUH, et al. Evaluation of antidiabetic phytochemicals in *Syzygium cumini* (L.) Skeels (Family: Myrtaceae). J Appl Pharm Sci. 2012;2(10):094-098.
11. Kumar D, Arora S, Alam M. Pharmacognostical Standardization and Antimicrobial Activity of Leaves of *Syzygium cumini* (Linn.) From Various Region of North India. Int Res J Pharm. 2014;5(2):62-65.
12. Sukmasari S, Mohd FN, Doolaanea AA, Qader OAJA, Rahman MNA. Total phenolic content, flavonoid content, and antioxidant capacity of *Syzygium cumini* (L.) skeels leaves grown in Wonosobo, java, Indonesia and comparison against current findings of *Syzygium cumini* leaves and Syzygium polyanthum (Wight) walp leaves. J Pharm Sci Res. 2018;10(1):31-35.
13. Sharma VK, Chitra D, Charumathy M, Gangadhar L, Anooj ES. Studies on antimicrobial activity of *Syzygium cumini* and *Syzygium alternifolium*. Ann Trop Med Public Heal. 2020;23(7):1168-1173.
14. Prasad R, Swamy VS. Antibacterial Activity of Silver Nanoparticles Synthesized by Bark Extract of *Syzygium cumini*. J Nanoparticles. 2013;2013:1-6.
15. Imran M, Imran M, Khan S. Antibacterial activity of *Syzigium cumini* leaf extracts against multidrug-resistant pathogenic bacteria. J Appl Pharm Sci. 2017;7(3):168-174.
16. De Oliveira GF, Furtado NAJC, Da Silva Filho AA, Martins CHG, Bastos JK, Cunha WR, et al. Antimicrobial activity of Syzygium cumini (Myrtaceae) leaves extract. Brazilian J Microbiol. 2007;38(2):381-384.
17. de Oliveira Brandão TS, Pinho LS, Teshima E, David JM, Rodrigues MI. Optimization of a technique to quantify the total phenolic compounds in jambolan (*Syzygium cumini* Lamark) pulp. Brazilian J Food Technol. 2019;22:1-9.
18. Zhang QW, Lin LG, Ye WC. Techniques for extraction and isolation of natural products: A comprehensive review. Chinese Med (United Kingdom). 2018;13(1):1-26.
19. Eshwarappa RSB, Iyer RS, Subbaramaiah SR, Richard SA, Dhananjaya BL. Antioxidant activity of *Syzygium cumini* leaf gall extracts. BioImpacts. 2014;4(2):101-107.
20. Sukmasari S, Mohd FN, Abdul Qader OAJ, Doolaanea A, Abdul Rahman MN. Phytochemical and antioxidant capacity profiles of *Syzygium cumini* (L.) skeels leaves grown in Telur Bagan Kedah, Malaysia using sequential cold percolation extraction. Int J Pharm Res. 2018;10(2):251-255.
21. Das G, Nath R, Das Talukdar A, Ağagündüz D, Yilmaz B, Capasso R, et al. Major Bioactive Compounds from Java Plum Seeds: An Investigation of Its Extraction Procedures and Clinical Effects. Plants. 2023;12(6):1214.
22. de Castilho AL, Saraceni CHC, Díaz IEC, Paciencia MLB, Suffredini IB. New trends in dentistry: Plant extracts against *Enterococcus faecalis*. The efficacy compared to chlorhexidine. Braz Oral Res. 2013;27(2):109-115.

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Effect of Moderate Intensity Activities and Soymilk Consumption on Decreasing Metabolic Syndrome Parameters

Efecto de las actividades de intensidad moderada y el consumo de leche de soja en la disminución de los indicadores del Síndrome Metabólico

Nandang A Waluya[1a*], Bani Sakti[2a], Yoseph Rohyadi[3a], Parta Suhanda[4b]

SUMMARY

Introduction: *The prevalence of metabolic syndrome (MetS) in Indonesia tends to increase. This MetS has an impact on increasing morbidity and mortality rates due to Non-Communicable Diseases (NCDs) such as coronary heart disease (CHD), stroke, and diabetes mellitus (DM). Monitoring and controlling MetS is an important effort to be made in preventing the increase of NCDs. Simple and easy efforts include maintaining moderate activity in daily living and consuming soymilk while maintaining a healthy lifestyle. The purpose of the study was to analyze the effect of daily moderate-intensity activity and soymilk consumption on MetS parameters.*

Methods: *The research design was quasi-experimental using the One-Group- Pretest -Post-test Non-equivalent Group design. The sample in this study were MetS individuals with a total of 60 respondents consisting of case and control groups. The stages of the study were screening MetS, measuring MetS parameters, performing daily moderate-intensity physical activity for 30 minutes 5 times a week, and consuming 25 mg of milk in 280 mL of water for 14 days. Data analysis was carried out using an independent t-test.*

Results: *Moderate-intensity physical activity and soymilk consumption had a significant effect on systolic blood pressure (p-value 0.042), blood sugar levels (p-value 0.013), and cholesterol levels (p-value 0.007). There was no significant effect on Fasting Blood Glucose (FBG) levels (p-value 0.992).*

Conclusion: *Moderate-intensity physical activity and soymilk consumption can help reduce metabolic syndrome parameters, especially blood pressure, blood glucose levels, and cholesterol levels.*

Keywords: *Metabolic syndrome, physical activity, soymilk, health.*

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ORCID: 0009-0007-0290-6358[1]
ORCID: 0000-0003-3209-4753[2]
ORCID: 0009-0002-2087-4939[3]
ORCID: 0000-0001-6492-3347[4]

[a]Department of Nursing, Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia.
[b]Department of Nursing, Politeknik Kesehatan Kemenkes Banten, Banten, Indonesia.

*Corresponding Author: Nandang A Waluya
E-mail: nandangwaluya@staff.poltekkesbandung.ac.id

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RESUMEN

Introducción: *La prevalencia del síndrome metabólico (MetS) en Indonesia tiende a aumentar. Este MetS tiene un impacto en el aumento de las tasas de morbilidad y mortalidad por Enfermedades No Transmisibles (ENT) como la enfermedad coronaria*

(CHD), el accidente cerebrovascular y la diabetes mellitus (DM). El seguimiento y control del MetS es un esfuerzo importante que se debe realizar para prevenir el aumento de las ENT. Los esfuerzos simples y fáciles incluyen mantener una actividad moderada en la vida diaria y consumir leche de soya mientras se mantiene un estilo de vida saludable. La actividad de intensidad moderada puede reducir el riesgo de Mets. El propósito del estudio fue analizar el efecto de la actividad diaria de intensidad moderada y el consumo de leche de soya en los parámetros MetS.

Métodos: *El diseño de investigación fue cuasi-experimental utilizando el diseño de Grupo Único-Pretest-Postest de Grupo No Equivalente. La muestra en este estudio fueron personas con MetS con un total de 60 encuestados que consisten en grupos de casos y controles. Las etapas del estudio fueron la detección de MetS, la medición de los parámetros de MetS; realizar diariamente actividad física de intensidad moderada durante 30 minutos 5 veces por semana y consumir 25 mg de leche en 280 mL de agua durante 14 días; El análisis de datos se llevó a cabo utilizando una prueba t independiente.*

Resultados: *La actividad física de intensidad moderada y el consumo de leche de soja tuvieron un efecto significativo sobre la presión arterial sistólica (valor de p 0,042), los niveles de azúcar en sangre (valor de p 0,013), los niveles de colesterol (valor de p 0,007). No hubo un efecto significativo sobre los niveles de glucosa en sangre en ayunas (FBG) (valor p 0,992).*

Conclusión: *La actividad física de intensidad moderada y el consumo de leche de soya pueden ayudar a reducir los parámetros del síndrome metabólico, especialmente la presión arterial, los niveles de glucosa en sangre y los niveles de colesterol.*

Palabras clave: *Síndrome metabólico, actividad física, leche de soya, salud.*

INTRODUCTION

12 %-37 % of the Asian population and 12 %-26 % of the European population suffer from metabolic syndrome. Individuals with metabolic syndrome have an increased risk of cardiovascular morbidity and mortality (1,2), as metabolic syndrome is known to be a strong risk factor for type 2 diabetes (3), cardiovascular disease (2), and stroke (4) as a non-communicable disease (NCDs) (5). Metabolic syndrome (MetS) is predicted to cause twice the increase in the risk of heart disease and a five times increase in type 2 diabetes mellitus (6,7). Metabolic syndrome is defined as a group of metabolic abnormalities characterized by at least three of the following criteria: hypertension, high triglyceride (TG) levels, low high-density lipoprotein (HDL-C) levels, abdominal obesity, and high fasting glucose (8). It is estimated that the risk of developing Cardiovascular disease (CVD) over the next 5 - 10 years is higher. In addition, available evidence also suggests that individuals with metabolic syndrome have a 30%-40% higher likelihood of developing Type 2 Diabetes Mellitus (T2DM) or CVD or both, over 20 years (9).

Regular moderate-intensity physical activity for at least 30 minutes continuously at least 5 or 7 days per week can reduce the risk of developing metabolic syndrome (10). Likewise, in patients with metabolic syndrome physical activity correlates with a significantly lower risk of coronary heart disease (about 50 %) (11). Management of MetS is important to prevent cardiovascular disease, T2DM, and stroke. Simple measures that can be taken include moderate-intensity activity and consumption of soymilk. Exercise will help in glucose homeostasis by promoting changes in gene expression (such as increasing GLUT4 expression) and encouraging mitochondrial biogenesis and fiber-type transformation (12).

Soymilk containing soy protein significantly reduces LDL cholesterol (13). Long-term isoflavone supplementation can reduce blood glucose levels. Isoflavones can reduce blood glucose levels. Supplementation with isoflavones is known to suppress gluconeogenic enzyme activity and reduce β-oxidation of fatty acids and lipid accumulation (14,15). The increasing cases of NCDs (cardiovascular disease, T2DM, and stroke) in Indonesia are expected to increase the burden on society and the government. Therefore, a joint commitment is needed to reduce NCDs morbidity, mortality, and disability (16), including through MetS-related research activities. The purpose of the study was to analyze the effect of daily moderate-intensity activity and soymilk consumption on MetS parameters.

METHODS

The research design is a quasi-experimental type using a Non-equivalent Group Pretest-Posttest design. To determine the effect of moderate-intensity activity and soymilk consumption on metabolic syndrome parameters (17). The sample of this study was MetS individuals in the working area of the Puskesmas in Bandung City. The sample size was determined using the quasi-experimental type sample size formula using the Non-equivalent Group Pretest-Posttest design (18).

The sample size was 60 respondents with MetS (30 control group and 30 intervention group). The non-random sampling method was utilized through purposive sampling. Inclusion criteria for individuals with MetS, aged 18 - 64 years. Agree to become a respondent by signing a written informed consent provided by researchers. This study has been approved by the Health Research Ethics Committee of the Bandung Health Polytechnic number 05/KEPK/EC/VIII/2022.

Dependent variables: Blood pressure, fasting and current blood glucose levels, and cholesterol levels. The measuring instruments used were a digital sphygmomanometer, glucometer (Accuheck Guide®), and cholesterol checker (Easytouch GCU®). The independent variable is moderate-intensity physical activity every day for 30 minutes 5 times per week (19). To do brisk walking to work or the market, and leisurely walking, walking during work breaks. Consume/drink 25 grams of soymilk daily (20) after 14 days of physical activity.

Data collection methods for MetS parameters were carried out by direct examination and administration of soymilk and monitoring through a checklist sheet. Data analysis was performed using an independent t-statistical test after the normality test with SPSS 25 version. The data were expressed as the mean ± SD (standard deviation) and p-values < 0.05 were stated to indicate statistical significance.

RESULTS

The data collection for this study was carried out from September to November 2022. The study subjects were metabolic syndrome group, namely waist circumference ≥ 90 cm in men and ≥ 80 cm in women, had a history of hypertension or were on medication, glucose intolerance, namely fasting plasma glucose levels ≥ 100 mg/dL. The intervention group performed moderate activity and consumed soymilk.

The characteristics of respondents were, age variable in the intervention group, the average age was 51.4 years, and the control group was 49.4 years. Body mass index (BMI) variables in the intervention group obtained an average of 27.19, the control group obtained an average BMI of 27.65. The variable abdominal circumference in the intervention group obtained an average of 93.9 cm, the control group obtained an average of 89.77 cm (Table 1).

Table 1

Overview of Respondent Characteristics

Characteristics	Mean (mg/dL)	SD (mg/dL)	Minimum - Maximum	n
Age (years)				
Intervention Group	51.4	6.29	36–60	30
Control Group	49.4	8.68	25 - 60	30
BMI				
Intervention Group	27.19	5.05	20 – 43	30
Control Group	27.65	5.47	15 - 42	30
Abdominal circumference (cm)				
Intervention Group	93.9	9.51	78 – 112	30
Control Group	89.77	14.37	59 - 119	30

The results of the pre-intervention study revealed that in the intervention group, the average Systolic was 159.83 mmHg, Fasting Blood Glucose (FBG) 121.37 mg/dL. Current Blood Glucose (CBG) 139.33 mg/dL. Cholesterol level 230.23 mg/dl. Whereas in the control group, it was known that the systolic average was 146.73 mmHg, FBG 121.37 mg/dL, and CBG 129.63 mg/dL. Cholesterol 224.90 mg/dL. The results of the post-intervention study revealed that in the intervention group, the average Systolic was 139.83 mmHg, FBG 115.13 mg/dL. CBG 114.67 mg/dL. Cholesterol level 214.17 mg/dL. Whereas in the control group, it was known that the Systolic average was 140.20 mmHg, FBG115.07 mg/dL, and CBG 142.80 mg/dL. The average Cholesterol is 232.73 mg/dL (Table 2).

Table 2

Overview of Metabolic Syndrome Parameters

Pre and Post-Intervention Moderate Intensity Activities and Consuming Soy Milk

Variable	pre-intervention		post-intervention	
	Group of Control $\overline{X} \pm SD$	Group of Intervention $\overline{X} \pm SD$	Group of Control $\overline{X} \pm SD$	Group of Intervention $\overline{X} \pm SD$
1. Systolic Blood Pressure (mmHg)	146.73 ± 23.93	159.83 ± 22.75	140.20 ± 20.93	139.83 ± 0.75
2. FBG (mg/dL)	121.37 ± 21.21	121.37 ± 21,21	115.07 ± 29.20	115.13 ± 20.45
3. CBG (mg/dL)	129.63 ± 39.60	139.33 ± 25,62	142.80 ± 58.18	114.67 ± 15.70
4. Cholesterol(mg/dL)	224.90 ± 25.70	230.23 ± 30.80	232.73 ± 22.24	214.17 ± 28.92

FBG: Fasting Blood Glucose. CBG: Current Blood Glucose.

Effect Physical Activity Moderate Intensity and Consumption of soymilk, the results of the statistical test p-value 0.042 show at alpha 0.05 there is a mean significant difference in Systolic Blood Pressure between the intervention group with the control group. Similarly, the intervention of physical activity of moderate intensity and consumption of soymilk effect CBG and Cholesterol levels, p-value of 0.013 and 0.007, respectively. Whereas the effect on FBG was not significantly different when compared to intervention and control groups (p-value of 0.992) (Table 3).

Table 3. Effect Activity Moderate Intensity and Soymilk Consumption To MetS Parameters at the Health Center in Bandung City

MetS indicator	Mean (mg/dL)	SD (mg/dL)	P-value	N
Systolic Blood Pressure				
Control Group	140.20	20.93	0.042	30
Intervention Group	139.83	20.75		30
CBG				
Control Group	142.80	58.18	0.013	30
Intervention Group	114.67	15.70		30
Cholesterol				
Control Group	232.73	22.24	0.007	30
Intervention Group	214.17	28.92		30
FBG				
Control Group	115.07	29.20	0.992	30
Intervention Group	115.13	20.45		30

FBG: Fasting Blood Glucose. CBG: Current Blood Glucose

DISCUSSION

Our results indicate that there was an influence of moderate physical activity intensity and consumption of soy milk on Systolic Blood Pressure, Current Blood Glucose, and levels of cholesterol. Metabolic Syndrome (syndrome X, insulin resistance) is a multifactorial disease with various risk factors that arise from accompanying insulin resistance and abnormal adipose deposition (6). These are risk factors for coronary heart disease, diabetes, fatty liver, and some types of cancer (21).

To diagnose Metabolic Syndrome, the presence of at least three out of five factors is required: abdominal obesity (waist circumference > 90 cm for Asian men and > 80 cm for Asian women), hypertriglyceridemia (triglycerides ≥ 150 mg/dL or use of triglyceride-lowering medication), low High-Density Lipoprotein Cholesterol (HDL < 40 mg/dL for men and < 50 mg/dL for women), hypertension (Systolic ≥ 130 mmHg and/or Diastolic ≥ 85 mmHg or taking antihypertensive medication), and impaired fasting glucose (Fasting Plasma Glucose ≥ 100 mg/dL or taking antidiabetic medication) (22). Metabolic Syndrome is a significant risk factor for cardiovascular diseases (CVD), particularly coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM) (23).

Metabolic Syndrome (MetS) is a multifactorial disease associated with insulin resistance and abnormal adipose deposition, making it a significant risk factor for coronary heart disease and diabetes. Monitoring and controlling MetS is crucial to prevent the development of non-communicable diseases (NCDs). Simple efforts like maintaining moderate physical activity in daily life and incorporating soymilk into a healthy lifestyle can be effective in this regard (24). A recent meta-analysis by Zhang et al. supports the connection between Leisure-Time Physical Activity (LTPA) and MetS, showing a significant relationship between LTPA and the incidence of MetS compared to inactive individuals (25). Soymilk, a nutrient-rich drink with isoflavones, offers several benefits, including lowering cholesterol, controlling blood glucose and pressure, and promoting overall well-being (26). Another study examining the influence of soymilk and ginger administration on cholesterol levels found a significant decrease in cholesterol levels (15).

Moderate-intensity physical activity is known to reduce the risk of MetS. A meta-analysis study by Zhang et al. measured the relationship between leisure-time physical activity (LTPA) and MetS, revealing an inverse relationship between the two. Individuals who engaged in at least 150 minutes of moderate physical activity per week showed a lower incidence of MetS compared to those who were not active (27). According to the World Health Organization (WHO), physical activity refers to any bodily movement that requires energy expenditure, and engaging in regular physical activity has been shown to prevent and treat non-communicable diseases such as heart disease, stroke, diabetes, and certain types of cancer. Moderate-intensity activities like fast walking, cycling, and yoga, among others, have significant health benefits and contribute to overall well-being (25,28-30).

Soymilk is derived from soybeans, which are high in protein and contain isoflavones. Isoflavones are natural compounds found in plants, including peanuts and soy, that mimic estrogen. These isoflavones have various health benefits, such as lowering total cholesterol and LDL cholesterol levels and reducing blood clotting, which can lower the risk of heart attack and stroke. The Food and Drug Administration (FDA) recommends consuming at least 25 grams of soy protein or 500 mL of soymilk daily to reduce total cholesterol levels by 5 % to 6 %. Isoflavones act as antioxidants, inhibiting LDL oxidation and enhancing HDL performance. A study conducted in Semarang found a correlation between the amount of soymilk consumption and the total cholesterol level in women aged 30-45 years. The study demonstrated that higher consumption of soymilk was associated with lower cholesterol levels in these women (31).

CONCLUSION

The findings of this study have significant implications for public health, as moderate-intensity physical activity and soymilk consumption were found to have a positive effect

on reducing SM parameters, including Systolic Blood Pressure, Current Blood Glucose levels, and cholesterol levels. These results suggest that promoting and encouraging these lifestyle interventions could be valuable strategies for managing and preventing metabolic disorders. Healthcare providers and policymakers can use this information to develop targeted interventions and educational programs to raise awareness about the benefits of these lifestyle changes. Further research and longitudinal studies are needed to investigate the long-term effects and optimal dosage of these interventions, providing more precise guidelines for achieving meaningful health outcomes. Overall, incorporating moderate-intensity physical activity and soymilk consumption into daily routines can be a proactive approach toward better metabolic health and overall well-being, contributing to preventive healthcare strategies.

REFERENCES

1. Nurdin NM, Anwar F, Diana R, Riyadi H, Khomsan A. High Prevalence of Metabolic Syndrome among Middle-Aged People in the Rural Area of Cianjur, Indonesia. Malaysian J Med Heal Sci. 2023;19:85-86.
2. Aditiawarman, Zulhijayanti NA, Ernawati E, Akbar MIA. A retrospective cohort study of hypertension, cardiovascular disease, and metabolic syndrome risk in women with history of preterm and term preeclampsia five years after delivery. Pregnancy Hypertens. 2023;32:57-63.
3. Pratama NR, Anastasia ES, Wardhani NP, Budi DS, Wafa IA, Susilo H, et al. Clinical outcomes of opioid administration in acute and chronic heart failure: A meta-analysis. Diabetes Metab Syndr Clin Res Rev. 2022;16(10).
4. Sigit FS, Tahapary DL, Trompet S, Sartono E, Willems Van Dijk K, Rosendaal FR, et al. The prevalence of metabolic syndrome and its association with body fat distribution in middle-aged individuals from Indonesia and the Netherlands: A cross-sectional analysis of two population-based studies. Diabetol Metab Syndr. 2020;12(1):1-11.
5. Mboi N, Syailendrawati R, Ostroff SM, Elyazar IR, Glenn SD, Rachmawati T, et al. The state of health in Indonesia's provinces, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet Glob Heal. 2022;10(11):e1632-645.
6. Widjaja NA, Irawan R, Hanindita MH, Ugrasena IDG, Handajani R. METS-IR vs. HOMA-AD and Metabolic Syndrome in Obese Adolescents. J Med Investig [Internet]. 2023;70(1.2):7-16.
7. Rustika R, Driyah S, Oemiati R, Hartati NS. Predictors of Metabolic Syndrome: A Six-Year Prospective Cohort Study in Bogor, Indonesia. Health Researcher and Development Media. 2019;29(3):215-224.
8. Kim HS, Cho YH. Factors associated with metabolic syndrome among middle-aged women in their 50s: based on national health screening data. Int J Environ Res. 2020.
9. Bhalwar R. Metabolic syndrome: The Indian public health perspective. Med J Armed Forces India. 2020;76(1):8-16.
10. Mahmudiono T, Jasim SA, Karim YS, Bokov DO, Abdelbasset WK, Akhmedov KS, et al. The effect of flaxseed oil consumption on blood pressure among patients with metabolic syndrome and related disorders: A systematic review and meta-analysis of randomized clinical trials. Phyther Res. 2022;36(10):3766-3773.
11. Wang SS. Metabolic syndrome. Curr Atheroscler Rep. 2020;444-447.
12. Constantini N, Hackney AC. Endocrinology of physical activity and sport: Second edition. Endocrinology of Physical Activity and Sport: Second Edition. 2013:1-558.
13. Blanco Mejia S, Messina M, Li SS, Viguiliouk E, Chiavaroli L, Khan TA, et al. A meta-analysis of 46 studies identified by the FDA demonstrates that soy protein decreases circulating LDL and total cholesterol concentrations in adults. J Nutr. 2019;149(6):968-981.
14. Prasetyastuti. The role of isoflavone in reducing blood glucose levels. J thee Med Sci (Berkala Ilmu Kedokteran). 2018;50(4):483-492.
15. Safitri W, Agustin WR. The Effect of Giving Soy Milk and Ginger on Lowering Cholesterol Levels in Ngargoyoso Karanganyar Residents. J Edunursing. 2018;2(1):1-7.
16. P2PTM Directorate. Non-communicable Disease Handbook. RI Ministry of Health. 2019;101.
17. Hasnunidah N. Educational Research Methodology. Akad Media. 2017:1-97.
18. Dahlan S. Sample Size in Medical and Health Research. Jakarta: PT Arkans. 2006;121.
19. Heart Association A. Who's at risk for metabolic syndrome? What Is Metabolic Syndrome? 2021.
20. Gardner Ch, Messina M, Kiazand A, Morris J. Effect of Two Types of Soy Milk and Dai.can College of Nutrition. 2013;26(6).
21. Stanley S Wang. Metabolic Syndrome: Practice Essentials, Background, Pathophysiology. Hear. 2020;40(Suppl 2):2020-2021.
22. Tsao Y-C, Li W-C, Yeh W-C, Ueng SW-N, Chiu SY-H, Chen J-Y. The Association between

Metabolic Syndrome and Related Factors among the Community-Dwelling Indigenous Population in Taiwan. International J Environmental Research and Public Health. MDPI AG. 2020;17:8958.

23. Bhalwar R. Metabolic syndrome: The Indian public health perspective. Med J Armed Forces India. 2020.
24. Dewi RC, Wirjatmadi B. Physical activity, exercise habits, and body mass index of adults. Healthc Low-Resource Settings. 2023;11(S1).
25. Tedyanto EH. Increased Physical Activity Can Prevent Metabolic Syndrome. 2021.
26. Patricia Lucas Guntoro DRR. 15 Benefits of Drinking Protein-Rich Soy Milk. 2022.
27. AHA. Prevention and Treatment of Metabolic Syndrome. American Heart Association. 2021.
28. Kalajanti VP, Wahjudi M, Purwantari KE, Visuddho, Nawangsasi P, Oktariza RT, et al. GABRA6 and SLC6A4 genotypes are correlated with the fasting blood glucose and physical fitness in the seemingly healthy young adults. J Ners. 2023;18(1):80-87.
29. World Health Organisation (WHO). Physical activity. 2021;9.
30. Guentoro PL. Physical Activity - Definition, Types, and Benefits - Hello Sehat.pdf. 2022.
31. Andika M. The Effect of Consumption of Soy Milk on Total Cholesterol in Patients with Hypercholesterolemia in the Work Area of the Lubuk Buaya Health Center, Padang. Science tower. 2019;XIII(3):99-105.

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Factors Related to Parents' Intention in Vaccination of Human Papillomavirus for Their Daughter Aged 11-12 Years

Factores Relacionados con la Intención de los Padres en la Vacunación del Virus del Papiloma Humano para su Hija de 11-12 años

Rahayu Dwikanthi[1a], Mamat Mamat [2a*], Lia Komalasari [3a], Meti Lestari [4b], Sri Agustin[5b]

SUMMARY

Introduction: *The knowledge that persistent Human Papilloma Virus (HPV) infection is the main cause of cervical cancer has resulted in the development of prophylactic vaccines to prevent HPV infection and HPV assays that detect nucleic acids of the virus. Thus, effective protection is to provide HPV vaccination in young women (<12 years). Besides the child wanting to be vaccinated, the intention of the parents is also very important in deciding whether their girls are going to be vaccinated against HPV or not. The purpose of this study was to determine factors related to parents' intention to vaccinate Human Papilloma Virus (HPV) for their daughters aged 11-12 years.*

Methods: *Cross-sectional design, the sample was parents of girls aged 11-12 years (grades 5 – 6 Elementary school) whose schools are in urban and rural areas. The sample size was 169 parents with girls aged 11-12 years. The sampling technique for each class was proportional sampling and the determination of class samples was random.*

Results: *Out of 169 samples, 27.8 % did not intend in vaccinating their daughters with the reason that 14.3 % did not understand HPV vaccination. There was a statistically significant relationship between place of residence (p-value 0.001), the information obtained regarding the HPV vaccine (p-value 0.018), and work (p-value 0.03) on people's intention to vaccinate their daughters.*

Conclusion: *There is a need to intensify targeted information dissemination efforts, specifically towards parents with daughters, regarding the HPV vaccine program in village schools and community settings.*

Keywords: *Human papillomavirus vaccine, intention, human papilloma virus.*

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ORCID: 0000-0001-9261-2546[1]
ORCID: 0000-0003-0572-2478[2]
ORCID: 0000-0002-0040-9389 [3]
ORCID: 0000-0002-0040-9389 [4]
ORCID: 0000-0001-2171-0306[5]

[a]Program Studi Kebidanan Karawang, Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia.
[b]Program Studi Kebidanan Tasikmalaya, Politeknik Kesehatan Kemenkes Tasikmalaya, Tasikmalaya, Indonesia.

*Corresponding Author: Mamat mamat, E-mail: mamat.researcher@gmail.com

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RESUMEN

Introducción: *El conocimiento de que la infección persistente por el virus del papiloma humano (VPH) es la causa principal del cáncer de cuello uterino ha resultado en el desarrollo de vacunas profilácticas para prevenir la infección por VPH y ensayos de VPH que detectan los ácidos nucleicos del virus. Así, una*

protección eficaz es proporcionar la vacuna contra el VPH en mujeres jóvenes (<12 años). Además del deseo de la niña de ser vacunada, la intención de los padres también es muy importante para decidir si sus niñas van a ser vacunadas contra el VPH o no. El propósito de este estudio fue determinar los factores relacionados con la intención de los padres de vacunar contra el Virus del Papiloma Humano (VPH) a su hija de 11 a 12 años.

Métodos: *Diseño transversal, la muestra fueron padres de niñas de 11 a 12 años (grados 5 y 6 de primaria) cuyas escuelas se encuentran en áreas urbanas y rurales. El tamaño de la muestra fue de 169 padres con niñas de 11-12 años. La técnica de muestreo para cada clase fue el muestreo proporcional y la determinación de las muestras de clase es aleatoria.*

Resultados: *De 169 muestras, el 27,8 % no tenía intención de vacunar a sus hijas por lo que el 14,3 % no entendía la vacunación contra el VPH. Hubo una relación estadísticamente significativa entre el lugar de residencia (p-valor 0,001), la información obtenida sobre la vacuna contra el VPH (p-valor 0,018) yel trabajo (p-valor 0,03) sobre la intención de las personas de vacunarse a sus hijas.*

Conclusión: *Existe la necesidad de intensificar los esfuerzos de difusión de información específica, específicamente hacia los padres con hijas, con respecto al programa de vacunación contra el VPH en las escuelas de las aldeas y los entornos comunitarios.*

Palabras clave: *Vacuna contra el Virus del Papiloma Humano, Intención, Virus del Papiloma Humano*

INTRODUCTION

Globally cervical cancer ranks 4th of all cancers currently (1,2). In 2022 the government issued a Human Papilloma Virus (HPV) vaccine policy or cervical cancer vaccine which will start in 8 provinces, and it is hoped that by 2023 all provinces will have been exposed to the cervical cancer vaccination. So, with the HPV vaccine, this program is expected to reduce the incidence of cervical cancer and maternal mortality (3). The free vaccine is targeted at school-aged girls in grades 5-6 (aged 11-12 years). This policy was taken considering the effectiveness of the vaccine. The cervical cancer vaccine is more effective given to girls at a young age who have not had sexual activity (4). In the process of implementing this free vaccine, it requires a certain strategy and time because what is faced is children aged 11-12 years who do not necessarily want to even though it is free, including their parents. The role of parents is very important in supporting and making decisions whataboutery or not to participate in these free vaccine activities. There is a needs to develop education, information, and communication during the implementation of the HPV vaccine (5,6).

One strategy is education about cervical cancer or Human Papilloma Virus (HPV) vaccines which are packaged according to the characteristics and educational level of parents (3,7). Some of the possible low intentions toward vaccination are low knowledge of the HPV vaccine, inadequate provider communication, and negative perceptions about HPV and its vaccines (7,8). This is very important issue due to the high mortality rate of mothers or women caused by cancer, even though this disease is preventable through the early vaccine at the early age of 11-12 years. One of the decision-makers who are targeted for vaccines (children elementary schools 5-6) are parents, thus with the provision of education it is hoped that they support the vaccine program (9).

This research was expected to contribute with government programs and to problems that may arise due to a lack of understanding of cervical cancer vaccines in parents of children. With this it was expected a coverage of the HPV vaccine in 2023-2024 for all girls from grade 5 -6 elementary, and the long-term expectation of cases of morbidity and mortality from cervical cancer in Indonesia has decreased significantly. The purpose of this study was to determine factors related to parents' intention in the vaccination of Human Papillomavirus (HPV) in girls aged 11-12 years.

METHODS

Study Design

The design of this study was cross-sectional, in which all variables, both independent (factors thought to be related) and dependent variable (parents' intention in vaccinating against HPV in children aged 11-12 years), were collected simultaneously. This research has received approval from the ethical commission of the Bandung Ministry of Health Polytechnic.

Sampling technique

This study's population was male parents with female children aged 11-12 years who attend 6 elementary schools in urban areas and 6 elementary schools in villages: total169 samples. The sampling technique was carried out by proportional random sampling. As for the data collection technique in each class, a simple sampling technique was carried out by *systematic random sampling* based on the sequence of data in each class. The names of the selected children were used as samples of their parents.

Data Collections

The instrument used was a questionnaire consisting of demographic variables, information about cervical cancer and the HPV vaccine, and the intentions of parents who have daughters aged 11-12 years. Data was collected indirectly through the homeroom teacher in 6 classes in urban areas and 6 school classes in villages. Through the homeroom teacher the questionnaire was delivered to female students.

Data analysis

After the data was collected, data processing was carried out where all data or categorical data were analyzed by frequency distribution and to assess the factors that were related. The Chi-Square and Logistic Regression tests were used to determine the significance of the independent variable to the dependent with the degree of significance of α 0.05 and the level of confidence 95 %.

RESULTS

Socio-demographic Characteristics

Based on Table 1, the proportion of residence and age group was almost the same, some of the jobs are not permanent (47.2 %) with an education level of 44.4 % in Senior High Schools. Of the respondents who work, the majority earn 2 million – 4 million per month (43.2 %). 86.4 % of his wife had never had a Pap smear. Most (56.8 %) have never received information the HPV vaccine. Most of those who had received information about vaccines came from health workers (29.0 %). The media get the most information from magazines. The intention in giving vaccines to children is quite high, namely 17.2 %, where the most reason is so that their children avoid getting sick. As for those who were not intended in vaccinating their children, most of them did not understand cervical cancer.

Table 2 shows 3 demographic variables that have a statistical relationship between demographic characteristics and parents' intention in carrying out the HPV vaccination for their daughters, namely one residence characteristic which showed those who live in urban areas as much as 85 % have an intention in doing the HPV vaccine for their daughters, while those who live in rural areas were only 60.7 %. The results of the Odds Ratio analysis were obtained at 3.67 which showed that samples residing in urban areas were 3.67 times more intentioned to vaccinate their daughters. The results of the Chi-Square statistical test obtained a p-value of 0.001 (α=0.05) meaning that there is a relationship between place of residence and parents' intention to vaccinate their children. Both information regarding the HPV vaccine and cervical cancer, the results of the analysis showed that they had received as much information about the HPV vaccine 82.2 % had an intention of doing the HPV vaccine for their daughters, while those who had never received any information were 64.6 %. The results of the Odds Ratio analysis were 2.53, which showed that those who had received information about the HPV vaccine had 2.53 times the chance of being intentioned to vaccinate their daughters compared to those who had never received information on the HPV vaccine. The results of the Chi-Square statistical test obtained a p-value of 0.018 (α = 0.05) indicating that there is a relationship between information about vaccines and parents' intention to vaccinate their children. The third is the characteristics of the job, where those who work as much as 57.1 % had an intention of doing the HPV vaccine for their daughters, while 35.8 % did not work. The odds ratio obtained was 2.38 which showed that those who worked were 2.38 times more likely to be intentioned in vaccinating

Table 1. Distribution of respondents' socio-demography

Demographic variables (n=169)	Frequency	Percent (%)
Residence		
- City	80	47.3
- Village	89	52.7
Work		
- Laborer	42	24.9
- Farmer	4	2.4
-Self-employed	33	19.5
- Employee	33	19.5
- Government employees	7	4.1
- ABRI/Police	1	0.6
- Trader	2	1.2
- Doesn't work	47	27.8
Education		
- Elementary school	23	13.6
- Junior High School	45	26.6
- Senior High School	75	44.4
- University	26	15.4
Income		
- < 2 million	57	33.7
- 2 million – 4 million	73	43.2
-> 4 million	39	23.1
Pasmear experience his wife		
- < 3 years	7	4.1
-> 3 years	16	9.5
-Never had a pap smear	146	86.4
Vaccine information		
- Ever	73	43. 2
- Never	96	56.8
Information source		
- Health workers	59	29.0
- Teacher	11	6.5
- Friend	8	4.7
- Others information source	5	3.0
- Never receive information	86	56.8
Media information source		
- Newspaper	8	4.7
- Magazines	29	17.2
- Comic paper	10	5.9
- Other media information	26	15.4
- Never receive information	96	56.8
Vaccine Intention		
- Intention	122	72.2
- No Intention	47	27.8
Reasons of Intention (n=122)		
- Avoid disease	104	85.2
- None	18	14.8
- Follow the program	73	59.8
- None	49	40.2
- Follow parents	33	27.0
- None	89	73.0
Not Intention reason (n=47)		
- Afraid of getting sick	18	38.3
- Fear of complications	22	46.8
- Other reason	7	14.9

their daughters than those who did not work. The results of the Chi-Square statistical test obtained a p-value of 0.036 ($\alpha = 0.05$) indicating there was a relationship between work and parents' intention to vaccinate their children.

Table 2. Factors related to the intention of parents who have daughters aged 11-12 years.

Variable	Intention Intention	Not Intention	F (%)	Odds Ratio (OR) (95 % CI)	*p-value*
Residence		12 (15 %)			
- City	68 (85.0 %)	35(39.3) %)	80 (100)		
-Village	54 (60.7 %)		89 (100)	3.67	0.001
Income		16 (28.1%)		(1.74-7.750)	
- < 2 million	41 (71,9%)	21 (28.8 %)	57 (100)		
- 2 – 4 million	52 (71.2%)	10 (25.6 %)	73 (100)		
-> 4 million	29 (74.4%)		39 (100)	1.29(0.41-4.02)*	0.82
		3(42.9 6 %)		1.62(0.56-4.62)*	0.50
Pap smear experience		1 (6.3 %)			
- < 3 years	4 (57.1 %)	43 (29.5 %)	7 (100)		
- > = 3 years	15 (93.8 %)	13 (17.8 %)	16 (100)		
- Never been vaccinated	103(70.5 %)	34 (35.4 %)	146 (100)	1.32 (0.22-7.76)*	0.34
Information				0.16 (0.01-1.37)*	0.06
- Once	60 (82.2 %)	15 (42.9 %)	73 (100)		
- Never	62 (64.6 %)	86 (64.2 %)	96 (100)	2.53	0.018
Work				(1.21-2-52)	
- Work	20 (57.1%)	61 (60.4 %)	35 (100)		
- Doesn't work	48 (35.8%)	40 (58.8 %)	134 (100)	2,389	0.036
Education				(1.51-17.96)	
- Tall	40 (39.6%)		101 (100)		
- Low	28 (41.2%)		68 (100)	1.14	0.96
				(0.57-2.86)	

DISCUSSION

The results of this study indicate that the reason parents are intentioned to vaccinate was to avoid their child's cancer in the future and to participate in the school program, this is in line with the results of other researchers who found the most common reason reported by parents to vaccinate their children is to protect them from cancer-related to HPV and to get recommendations from healthcare providers (10). This reason is the most important thing for parents because they don't want their children to get cervical cancer in the future. It was found that only intention to vaccinate the HPV had a relationship with the COVID-19 vaccine (11), although the results of other analyzes were not significantly related to some previous studies (12,13). Thus, it can be concluded that intention in reasons of prevention of avoiding disease is very dominant as the reason they want to vaccinate their children.

In contrast to the case of low intention in HPV vaccination which can be detrimental to some students in Kuwait, it requires more intentional health promotion efforts (14). It is also shown that awareness of the HPV vaccine among university students is still relatively low in China compared to European countries (15). Vaccination among university students is an age-based target for HPV vaccination because they are a risk group. Several studies indicate that there has been an ongoing effort to address parental awareness, access, and attitudinal barriers to HPV vaccination (16). This is important to do to increase vaccination coverage.

HPV is a sexually transmitted infection common worldwide, which disrupts normal social life and has dire consequences. Despite some exceptions, the burden of HPV infection and related diseases remains high and factors explaining this high rate include poor living conditions in some developing countries. Genital infection is a risk factor that supports the development of high levels of HPV in developing countries (17). This is also the impact of low socioeconomic status in many cases in several developing countries, as research results show that death from HPV cancer is related to the socioeconomic status in America (18). The biggest factor in the occurrence of cervical cancer was infection with HPV (16,18) with an adjusted odds ratio (of 113.7, 95% CI: 40.8–316.9), meaning it was not due to sexual behaviour (19).

Vaccination programs are the right way to reduce HPV infection and related diseases. In the framework of the effectiveness of vaccines, the government has programmed the provision of free vaccines at the age of 11-12 years or for children in grades 5 and 6 of elementary school. This is in line with the conclusions of research results which state that the HPV vaccine effectively prevents cervical cancer at the population level in several girls under the age of 20 years (4). The results of the study suggest that at least 9 years to get the vaccine. HPV provides statistically significant protection for at least 6 years, with indications of continued effectiveness for up to 8 years (20)

Support for efforts to increase awareness and knowledge related to HPV vaccination as well as strengthening the budget for immunization is urgently needed (17). The results of the study show that there is a correlation between limited knowledge and awareness about HPV infection and willingness to do the HPV(21). The results of other studies also showed that some girls, parents, teachers, and leaders who received interventions showed there was a significant increase in the proportion of knowledge about HPV infection and the HPV vaccine. Communication is a process in which two or more people form or exchange information with each other which in turn will result in mutual understanding (22). Meanwhile, according to Indonesian Wikipedia, information is a message (speech or expression) or a collection of messages consisting of orders sequences of, or interpretable meanings of messages or sets of messages. Information can be recorded or transmitted and Understanding Education (Education) is the learning, and habits of a group of people passed down from one generation to the next through teaching, training, or research (23). The importance of the role of communication and information is closely related to coming to the vaccine, as the results of the study show that there is a strong correlation between the level of information or promotion with the arrival of women to the cervical cancer vaccine (HPV vaccine) (24), proven efforts to increase education, provide assurance and awareness HPV can improve screening outcomes in China (24). In certain circumstances, such as in rural areas, cultural and language approaches need to be considered, as is the conclusion from a study that culture and language are the right things to help newcomers to make decisions about vaccinating. Economic considerations are an important part of considering cancer vaccine programs because in substance they have beneficial effects economically and on public health (25). Involving parents in education is very important because research results show more positive perceptions about the HPV vaccine, which predicts acceptance of the HPV OR 1.90 vaccine (95%CI:1.40–2.57) (26). Based on research results, it is also known that children's knowledge is very low about HPV and HPV (27).

Several strategies can be used to increase the coverage of the HPV vaccine, including involving parents because parents decide whether or not their children may be vaccinated against HPV even though it's free. The role of parents is very important in making decisions for children to get immunity through vaccination. Decisions taken by parents of children in carrying out vaccinations affect the success of the government program for HPV (28).

CONCLUSION

The results of the study show that three characteristic demographic factors have a relationship with intention in the HPV vaccine of parents who have daughters aged 11-12 years, namely the place of residence, information obtained by parents regarding the HPV vaccine, and cervical cancer and occupation. Based on

the conclusion, as a further recommendation, it is necessary to disseminate information in household settings residing in rural areas and special community groups with better intensity and quality of information.

REFERENCES

1 . UICC.org. Targeted-commitments/cervical-cancer-elimination-strategy. UICC.org; 22AD. Available from: https://www.uicc.org/what-we-do/driving-global-impact/targeted-commitments/cervical-cancer-elimination-strategy? gclid=CjwKCAjwp6CkBhB_EiwAlQVyxZ0JKhhSDqMaQxuBrKeFjcIZeU0gFYldZ1fTfUTz8XrT2TlxmVpxoRoCz84QAvD_BwE#_ftn2

2. Tan LF, Rajagopal M, Selvaraja M. Review: An Overview on the Pathogenesis of Cervical Cancer. Curr Trends Biotechnol Pharm. 2023;17(1):717-734.

3. Wondimu A, Postma MJ, van Hulst M. Cost-effectiveness analysis of quadrivalent and nonavalent human papillomavirus vaccines in Ethiopia. Vaccine. 2022;40(14):2161-2167.

4. Kjaer SK, Dehlendorff C, Belmonte F, Baandrup L. Real-World Effectiveness of Human Papillomavirus Vaccination against Cervical Cancer. J Natl Cancer Inst. 2021;113(10):1329-1335.

5. Kinasih SE, Koesbardiati T, Mas'udah S. Women's reproductive rights under marriage contract. J Int Womens Stud. 2019;20(9):132-144.

6. Smith LW, Racey CS, Gondara L, Krajden M, Lee M, Martin RE, et al. Women's acceptability of and experience with primary human papillomavirus testing for cervix screening: HPV FOCAL trial cross-sectional online survey results. BMJ Open. 2021;11(10).

7. Laigle V, Postma MJ, Pavlovic M, Cadeddu C, Beck E, Kapusniak A, et al. Vaccine market access pathways in the EU27 and the United Kingdom – analysis and recommendations for improvements. Vaccine. 2021;39(39):5706.5718.

8. Garcia S, Hopfer S, Amaro H, Tanjasiri S. HPV vaccine delay and refusal among unvaccinated Mexican American young adult women: a qualitative investigation of Mexican-born and US-born HPV vaccine decision narratives. J Behav Med. 2023;46(1-2): 88-99.

9. Perdana RF, Simatupang M V, Herawati S, Yusuf M. Risk factors recurrent respiratory papilloma (RRP) on juvenile and adult type in tertiary hospital, Indonesia. J Glob Pharma Technol. 2020;12(6):409-415.

10. Gopalani SV, Janitz AE, Burkhart M, Campbell JE, Chen S, Martinez SA, et al. HPV vaccination coverage and factors among American Indians in Cherokee Nation. Cancer Causes Control. 2023;34(3):267-275.

11. Das AK, Islam J, Jahan S, Sultana A, Nowshin S. Does COVID-19 and oral, lung cancer have a connection? A insight to future investigation; A literature review. Bangladesh J Med Sci. 2023;22(1):15-21.

12. Harapan H, Sallam M, Fathima R, Kusuma HI, Anwar S, Nalapraya WY, et al. Willingness to Pay (WTP) for COVID-19 Vaccine Booster Dose and Its Determinants in Indonesia. Infect Dis Rep. 2022;14(6):1017-1032.

13. Manganello JA, Chiang SC, Cowlin H, Kearney MD, Massey PM. HPV and COVID-19 vaccines: Social media use, confidence, and intentions among parents living in different community types in the United States. J Behav Med. 2023;46(1-2):212–228.

14. Alsanafi M, Salim N, Sallam M. Willingness to get HPV vaccination among female university students in Kuwait and its relation to vaccine conspiracy beliefs. Hum Vaccin Immunother. 2023;19(1):2194772.

15. Yin G, Zhang Y, Chen C, Ren H, Guo B, Zhang M. Have you ever heard of Human Papillomavirus (HPV) vaccine? The awareness of HPV vaccine for college students in China based on meta-analysis. Hum Vaccines Immunother. 2021;17(8):2736-2747.

16. Zhu X, Jacobson RM, MacLaughlin KL, Sauver JS, Griffin JM, Finney Rutten LJ. Parent-reported Barriers and Parental Beliefs Associated with Intentions to Obtain HPV Vaccination for Children in a Primary care Patient Population in Minnesota, USA. J Community Health. 2023:1-9.

17. Kombe Kombe AJ, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y, et al. Epidemiology and Burden of Human Papillomavirus and Related Diseases, Molecular Pathogenesis, and Vaccine Evaluation. Front Public Heal. 2020;8:552028.

18. Priyadarshini M, Prabhu VS, Snedecor SJ, Corman S, Kuter BJ, Nwankwo C, et al. Economic Value of Lost Productivity Attributable to Human Papillomavirus Cancer Mortality in the United States. Front Public Heal. 2021;8:624092.

19. Yamaguchi M, Sekine M, Hanley SJB, Kudo R, Hara M, Adachi S, et al. Risk factors for HPV infection and high-grade cervical disease in sexually active Japanese women. Sci Rep. 2021;11(1).

20. Kjaer SK, Nygård M, Sundström K, Munk C, Berger S, Dzabic M, et al. Long-term effectiveness of the nine-valent human papillomavirus vaccine in Scandinavian women: Interim analysis after 8 years of follow-up. Hum Vaccines Immunother. 2021;17(4):943-949.

21. Alsous MM, Ali AA, Al-Azzam SI, Abdel Jalil MH, Al-Obaidi HJ, Al-abbadi EI, et al. Knowledge and awareness about human papillomavirus infection and its vaccination among women in Arab communities. Sci Rep. 2021;11(1):786.

22. Nur Intan Safitri Basalama. Definition of communication according to Everett M. Rogers. Gorontalo University. 2016.
23. Wikipedia. The Free Encyclopedia. Information, Education (education). Wikipedia Free Encyclopedia. 2021.
24. Robles C, Bruni L, Acera A, Riera JC, Prats L, Poljak M, et al. Determinants of Human Papillomavirus Vaccine Uptake by Adult Women Attending Cervical Cancer Screening in 9 European Countries. Am J Prev Med. 2021;60(4):478-487.
25. Cody P, Tobe K, Abe M, Elbasha EH. Public health impact and cost effectiveness of routine and catch-up vaccination of girls and women with a nine-valent HPV vaccine in Japan: A model-based study. BMC Infect Dis. 2021;21(1).
26. Sitaresmi MN, Rozanti NM, Simangunsong LB, Wahab A. Improvement of Parent's awareness, knowledge, perception, and acceptability of human papillomavirus vaccination after a structured-educational intervention. BMC Public Health. 2020;20(1).
27. Thanasas I, Lavranos G, Gkogkou P, Paraskevis D. Understanding of Young Adolescents About HPV Infection: How Health Education Can Improve Vaccination Rate. J Cancer Educ. 2020;35(5):850-859.
28. Fauzul Hayat, Nurjaman NK. The Effect of Parental Role on Giving COVID-19 Vaccination at MAN 1 Serang City. J Joubas. 2022:18-2

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Hardiness Personality and Family Support for Women's Quality of Life with Breast Cancer

Personalidad resistente y apoyo familiar para la calidad de vida de las mujeres con cáncer de mama

Supatmi Supatmi[1a]*, Reliani Reliani[2a], Raden Khairiyatul Afiyah[3b], Ernawati Ernawati[4c]

SUMMARY

Introduction*: Breast cancer diagnosis and treatment can lead to psychological changes such as stress and depression, which significantly impact the quality of life. Psychological hardiness and family support are two necessary health-elevating factors that strengthen individuals to remain both psychologically and physically healthy despite encountering negative life events such as breast cancer.*
Objective: *This study investigated the relationship between hardiness personality and family support on the quality of life in women with breast cancer.*

Methods: *The study utilized a correlational design with a cross-sectional approach. Hardiness personality and family support were independent variables, while the quality of life during breast cancer served as the dependent variable. To measure hardiness personality, the Revised Hardiness Health Inventory (RHHI-24) was employed, and family support was measured using the Family Support Scale (FSS). The Quality of Life Breast Cancer (QOL-BC) scale was used to assess the quality of life. The sample size consisted of 43 participants selected through simple random sampling, adhering to specific inclusion and exclusion criteria. The data collected were analyzed statistically using linear regression analysis with a confidence interval of 95 % and an alpha value of 0.05.*
Results: *The study found that a hardy personality positively influenced the quality of life in women with breast cancer. This was indicated by a t statistics value of 3.327, a probability of 0.0024, and a coefficient of 0.260 (positive). Similarly, family support also had a positive effect on the quality of life, as shown by a t statistics value of 2.412, a probability of 0.026, and a coefficient of 0.137 (positive).*
Conclusion: *This study reveals that both hardiness personality and family support play crucial roles in positively impacting the quality of life among women with breast cancer. These factors contribute to their ability to cope effectively with the challenges posed by the disease. Further research should focus on improving psychological adaptation to enhance the quality of life in these individuals.*

Keywords*: Hardiness personality, family support, breast cancer.*

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ORCID: 0000-0002-8013-1961[1]
ORCID: 0000-0003-4904-5720[2]
ORCID: 0000-0002-9416-2646[3]
ORCID: 0000-0003-0023-2234[4]

[a]Department of Nursing, Faculty of Health Sciences, Universitas Muhammadiyah Surabaya, Surabaya, Indonesia.
[b]Department of Professional Nurse Education Program, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia.
[c]Department of Nursing and Health Sciences, Universitas Muhammadiyah Semarang, Semarang, Indonesia.

*Corresponding author: Supatmi Supatmi
E-mail**:** supatmioppi@gmail.com

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RESUMEN

Introducción: *El diagnóstico y tratamiento del cáncer de mama pueden provocar cambios psicológicos como el estrés y la depresión, que afectan significativamente la calidad de vida. La resistencia psicológica y el apoyo familiar son dos factores necesarios para mejorar la salud, que fortalecen a las personas para mantenerse tanto psicológica como físicamente sanas a pesar de enfrentar eventos negativos como el cáncer de mama.*
Objetivo: *Este estudio tuvo como objetivo investigar la relación entre la resistencia psicológica y el apoyo familiar en la calidad de vida de mujeres con cáncer de mama.*
Métodos: *El estudio utilizó un diseño correlacional con un enfoque transversal. La resistencia psicológica y el apoyo familiar fueron variables independientes, mientras que la calidad de vida durante el cáncer de mama fue la variable dependiente. Para medir la resistencia psicológica, se utilizó el Inventario de Salud y Resistencia Revisado (RHHI-24), y para medir el apoyo familiar se utilizó la Escala de Apoyo Familiar (FSS). La Escala de Calidad de Vida del Cáncer de Mama (QOL-BC) se utilizó para evaluar la calidad de vida. El tamaño de la muestra consistió en 43 participantes seleccionadas mediante muestreo aleatorio simple, siguiendo criterios de inclusión y exclusión específicos. Los datos recopilados se analizaron estadísticamente utilizando análisis de regresión lineal con un intervalo de confianza del 95 % y un valor alfa de 0,05.*
Resultados: *El estudio encontró que la resistencia psicológica influyó positivamente en la calidad de vida de las mujeres con cáncer de mama, como lo indican un valor de estadísticas T de 3,327, una probabilidad de 0,0024 y un coeficiente de 0,260 (positivo). Del mismo modo, el apoyo familiar también tuvo un efecto positivo en la calidad de vida, como lo muestra un valor de estadísticas T de 2,412, una probabilidad de 0,026 y un coeficiente de 0,137 (positivo).*
Conclusión: *Este estudio revela que tanto la resistencia psicológica como el apoyo familiar desempeñan papeles cruciales al impactar positivamente la calidad de vida de las mujeres con cáncer de mama. Estos factores contribuyen a su capacidad para hacer frente eficazmente a los desafíos que plantea la enfermedad. Se recomienda que futuras investigaciones se centren en mejorar la adaptación psicológica para mejorar la calidad de vida de estas personas.*

Palabras clave: *Resistencia psicológica, apoyo familiar, cáncer de mama.*

INTRODUCTION

Women who are diagnosed with breast cancer and undergo treatment experience anxiety and even depression, which has an impact on their quality of life (1,2). The most decrease in quality of life in breast cancer patients is a decrease in the psychological dimension (3). Psychological problems faced by women with breast cancer such as feeling fear, thinking about death, and feeling worried when the family knows about the disease (4). Previous studies showed that the symptoms of breast cancer survivors tend to decrease in quality of life (QoL) in the early years of diagnosis (5). Studies have shown that cancer diagnosis and treatment will lead to many somatic problems, reduced life function, and family disintegration (6). Quality of life in breast cancer patients decreased due to several factors, such as personality and lack of support from husbands (7).

The World Health Organization (WHO) indicates that 8 %-9 % of women have breast cancer, reaching 23.6 million in 2020 (4). The results of The Basic Health Research of Indonesia in 2018 showed that the most common cancer cases in Indonesia were 58 256 cases of breast cancer out of a total of 348 809 cancer cases (8). Based on data from the East Java Provincial Health Office in 2019, the number of breast cancer patients reached 12 186 cases. According to Waltrin's research (2017) 85 % with poor quality of life and 15 % with good quality in breast cancer patients. Based on Basic Health Research in 2018, the prevalence of cancer in East Java is 2.2 per 1 000 population. If converted to the population of East Java, the number of cancer patients is 86 000 (10). According to Indotang's research (11) of 30 respondents with breast cancer, 19 respondents (63.3 %) had a very low husband support category. Studies conducted by Mahdian and Ghafari explain that hardiness personality is related to the support and expectations received by cancer patients (12). Hardiness personality it was usually defined as a personality structure comprising the three related general dispositions of commitment, control and challenge that functions as a resistance resource in encounters with stressful conditions.

Cancer affects many aspects of life and can cause many temporary or permanent psychosocial

problems (13). Individuals with hardiness personalities in coping with psychological distress use positive coping strategies and are effective in reducing psychological distress (9,11-13). A person who has strong husband support can increase feelings of calm and give them the strength to heal (14). Research conducted for recovery compared to breast cancer patients who have high husband support, they have the motivation or have the spirit to recover.

Hardiness is a psychological trait that serves as a reliable predictor of good health, even in the face of highly stressful events. It involves two key elements: reduced threat evaluation and increased positive expectations. When dealing with cervical cancer, patients employ various coping strategies to manage their condition (15,16). Prior research has shown that hardiness influences the development of a healthy character (17). It fosters inner attitudes that lead to a more realistic approach to life's challenges and stressors (18). Highly resilient individuals tend to report greater happiness, life satisfaction, and better physical and mental health (19). On the other hand, less resilient individuals are more prone to mental health issues like depression, anxiety, and maladaptive coping styles (20-22). Hardiness acts as a protective factor against stress, mitigating its negative impact on individual health (23). Studies have indicated that a person's quality of life can be predicted based on their level of hardiness personality. Additionally, like perceived social support, hardiness personality positively influences the quality of life in oncology patients (12). Another critical factor affecting the quality of life is the support provided by families, including informational and emotional support through effective family communication patterns (24). Psychological care for oncology patients and their families is of significant importance (25). This study aimed at investigating the relationship between hardiness personality and family support on the quality of life in women with breast cancer.

METHODS

This study used analytical correlation with cross sectional approach. The purpose of the study was to determine the effect of hardiness personality, and family support on quality of life in breast cancer patients in the north Surabaya area. A population of 48 women with breast cancer with a sample of 43 respondents was taken using a simple random sampling technique based on inclusion criteria: 1) breast cancer patients, 2) have and live with a partner, 3) are conscious and able to communicate well. The instrument used in this study to assess the variable hardiness personality was the Revised Hardiness Health Inventory (RHHI-24). This instrument allows participants to respond to five items for each domain using a 4-point Likert-type scale. The reliability scale has been examined with α ranging from 0.6-0.79 by using Cronbach's alpha, 0.76-0.92. The Quality of Life was evaluated using the Quality Of Life Breast Cancer questionnaire (QOL-BC) with 46 question items for physical health, psychological, social, and spiritual dimensions. Before collecting the data, the patients who were recruited for this study were asked to fill out and sign the informed consent, while the researchers explained the aims and procedure of this study. Then, the researchers began to distribute the questionnaire and guided the recruited respondents to answer the questionnaire to obtain a data set for analysis. The collected data was analyzed statistically using the linear regression analysis test (95 % CI: α=0.05) with SPSS 20.0 (SPSS Inc., Chicago, IL).

RESULTS

Most respondents were in the age group of 46 to 55 (41.9 %), with most of them having graduated from Junior school (5 5.8 %). The occupation of respondents was dominated by housewives (62.8 %) and from the Maduranese tribe (51.2 %). Moreover, the monthly revenue of patients was below the regional minimum basic salary (60.5 %). According to the stadium of cancer, stage IB has reached a low level (41.9 %) (Table 1).

Table 2 presents the results of the t-tests, indicating the influence of Hardiness Personality and Family Support on the quality of life. For Hardiness Personality, the t statistics value was 3.327 with a probability of 0.0024, showing a significant effect ($p < 0.05$) with a positive coefficient of 0.260. This suggests that higher

Table 1. Sociodemographic of breast cancer woman

Variable	Frequency	Percentage (%)
Ages		
26-35	2	4.7
36-45	9	20.9
46-55	18	41.9
56-65	14	32.6
Education		
Elementary school	4	9.3
Junior school	24	55.8
Senior high school	15	34.9
Occupation		
Housewife	27	62.8
Worker	12	27.9
Self-employed	4	9.3
Tribe		
Javanese	21	48.8
Madura	22	51.2
Stadium		
SHE	4	9.3
IB	18	41.9
IIA	3	7.0
IIB	7	16.3
III	9	20.9
IV	2	4.7
Revenue		
Above region min basic salary	27	60.5
Average regional min basic salary	16	39.5

levels of Hardiness Personality are associated with an improvement in the quality of life. Similarly, for family support, the t-statistics value was 2.412 with a probability of 0.026, indicating a significant effect ($p < 0.05$) with a positive coefficient of 0.137. This implies that Family Support also has a positive and significant impact on the quality of life.

Table 2. T-test Results for Analysis of Quality of Life, Hardiness Personality, and Family Support in Women with Breast Cancer (n=43)

Variable	Min	Max	Mean	Std. Dev.	Coefficient	t Statistics	Sig.
Quality of life (Constant)	53.00	123.00	89.6	14.7458	1.709	4.192	0.0001
Hardiness personality	59.00	97.00	73.0	9.3886	0.260	3.327	0.0024
Family support	50.00	80.00	72.4	10.8503	0.137	2.412	0.0260

DISCUSSION

Hardiness personality acts as a shield for women diagnosed with cancer in the face of conditions that increase stress in individuals. The result of this study showed a significant relationship between hardiness personality and perceived family support, which prevents psychological distress to deal with stress among

women with breast cancer. It means that the higher the level of perceived family support, the higher the psychological hardiness of women with breast cancer. In effect, our study indicates that respondents had an average hardiness score of 73.0233 with SD = 9.3998, where 51.2 % of respondents were mature and had a hard and resistant culture and character slamming in the face of various situations in life. In line with the resilient theory resilient individuals are more optimistic than individuals who are not strong, are more flexible in the face of adversity, and prefer to use adaptive coping styles, such as control and a personal approach using adaptive (26,27), rather than maladaptive coping, such as avoidance, in the face of conditions stress (28). Hardiness and optimism are two factors needed in dealing with and promoting individuals to remain psychologically healthy even in the face of difficulty (12). Hardiness personality has a positive impact on overcoming cancer and hardiness increases individual adaptation to the disease and acts as an intermediary between stress and disease (29–31). Hardiness people act better in the face of difficulties and cope with life's problems such as when women are diagnosed with breast cancer (32).

These values and beliefs make the subject optimistic in facing problems and independent in his life. On the other hand, individuals learn to be willing to take risks when faced with problems (29). Someone who dares to take risks, has confidence in his abilities, accompanied by a sense of optimism will make himself have good mental readiness when experiencing pressure due to the problems experienced. These things help develop a hardy personality in the individual (33). Family support is needed by patients who are facing chronic diseases or patients with terminal conditions such as patients with breast cancer, because the family can provide positive support to patients and know the patient's condition and expectations (34).

Quality of life in breast cancer patients between early stage and advanced stage show a difference in a long time (35). The patient's treatment as well as physical fatigue and activity, can affect the quality of life of patients with breast cancer (36). Family support is very instrumental in the patient's treatment process because family support can help patients with breast cancer to reduce anxiety (37), stress, or depression while undergoing medical therapy (38). Family involvement during treatment therapy patients plays an important role because by involving the patient's family feel comfortable during therapy or the treatment process, and patients can also be cooperative during treatment therapy (39). Supportive care greatly affects the quality of life of patients with breast cancer (40), patients who undergo treatment regularly can improve their overall quality of life based on dimensions of physical, emotional, and social functioning (41).

CONCLUSION

The findings showed that hardiness personality and family support are two important health factors in women with breast cancer. Hardiness personality and high family support affect the quality of life in women with breast cancer. High personality hardiness will increase adaptation because individuals have confidence in their abilities, accompanied by a sense of optimism will make themselves have good mental readiness when experiencing pressure due to breast cancer. Family support is instrumental in overcoming stress, anxiety, and depression that often occur in women with breast cancer.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Sobri FB, Bachtiar A, Panigoro SS, Ayuningtyas D, Gustada H, Yuswar PW, et al. Factors Affecting Delayed Presentation and Diagnosis of Breast Cancer in Asian Developing Countries Women: A Systematic Review. Asian Pacific J Cancer Prev. 2021;22(10):3081-3092.

2. Carreira H, Williams R, Dempsey H, Stanway S, Smeeth L, Bhaskaran K. Quality of life and mental health in breast cancer survivors compared with non-cancer controls: A study of patient-reported outcomes in the United Kingdom. J Cancer Surviv. 2021;15(4):564-575.
3. Wabula I, Yunitasari E, Wahyudi AS. Supportive Care Needs of Women with Breast Cancer: A Systematic Review. J Ners. 2020;15(2 Special Issue):142-148.
4. Chabirah S, Bujawati E, Habibi H, Azriful A. Impact of posttraumatic growth on the quality of life in woman with breast cancer. Al-sihah Public Heal Sci J. 2020;12(1):48.
5. Khoirunnisa SM, Suryanegara FDA, Setiawan D, Postma MJ. Health-related quality of life in Her2-positive early breast cancer woman using trastuzumab: A systematic review and meta-analysis. Front Pharmacol. 2023;14.
6. Henson E, Chen Y, Gibson S. EGFR Family Members' Regulation of Autophagy Is at a Crossroads of Cell Survival and Death in Cancer. Cancers (Basel). 2017;9(4).
7. Shen A, Qiang W, Wang Y, Chen Y. Quality of life among breast cancer survivors with triple-negative breast cancer--role of hope, self-efficacy and social support. Eur J Oncol Nurs. 2020;46(May):101771.
8. Sari P, Sayuti S, Ridwan M, Rekiaddin LO, Anisa A. The Relationship between Knowledge and Healthcare Personnel Support with Self-Breast Examination Behavio. Perilaku dan Promosi Kesehat Indones J Heal Promot Behav. 2020;2(2):31.
9. Andini W. Overview of Quality of Life in Breast Cancer Patients Who Have Undergone Modified R. Universitas Sumatera Utara; 2017.
10. Badan Penelitian dan Pengembangan Kesehatan - Kemenkes. National Report on basic health research 2018. 2018.
11. Indotang FEF. The Relationship Between Family Support and Coping Mechanisms in Breast Cancer Patients. Sun J. 2015;2(4):55-61.
12. Bahrami M, Mohamadirizi S, Mohamadirizi S. Hardiness and optimism in women with breast cancer. Iran J Nurs Midwifery Res. 2018;23(2):105-110.
13. Haj Hashemi F, Atashzadeh-Shoorideh F, Oujian P, Mofid B, Bazargan M. Relationship between perceived social support and psychological hardiness with family communication patterns and quality of life of oncology patients. Nurs Open. 2021;8(4):1704-1711.
14. Almuhtaseb MIA, Alby F, Zucchermaglio C, Fatigante M. Social support for breast cancer patients in the occupied Palestinian territory. PLoS One. 2021;16(6 June):1-13.
15. Binka C, Nyarko SH, Awusabo-Asare K, Doku DT. I always tried to forget about the condition and pretend I was healed: Coping with cervical cancer in rural Ghana. BMC Palliat Care. 2018;17(1):1-8.
16. Supatmi S, Santoso B, Yunitasari E. The Effect of Spirituality on Psychological Hardiness of Cervical Cancer Patients with Chemotherapy. Stud Ethno-Medicine. 2022;16(1-2):17-23.
17. Levin AO, Carpenter KM, Fowler JM, Brothers BM, Andersen BL, Maxwell GL. Sexual morbidity associated with poorer psychological adjustment among gynecological cancer survivors. Int J Gynecol Cancer. 2010;20(3):461-470.
18. Bukovic D, Silovski H, Silovski T et al. Sexual functioning and body image of patients treated for ovarian cancer. Sex Disabil. 2008;26:63-67.
19. Abdollahi A, Alsaikhan F, Nikolenko DA, Al-Gazally ME, Mahmudiono T, Allen KA, et al. Self-care behaviors mediate the relationship between resilience and quality of life in breast cancer patients. BMC Psychiatry. 2022;22(1).
20. Schreurs B, van Emmerik H, Notelaers G, de Witte H. Job insecurity and employee health: The buffering potential of job control and job self-efficacy. Work Stress. 2010;24(1):56-72.
21. Abdollahi A, Abu Talib M. Hardiness, spirituality, and suicidal ideation among individuals with substance abuse: The moderating role of gender and marital status. J Dual Diagn. 2015;11(1):12-21.
22. Eschleman KJ, Bowling NA, Alarcon GM. A Meta-Analytic Examination of Hardiness. Int J Stress Manag. 2010;17(4):277-307.
23. Talavera-Velasco B, Luceño-Moreno L, Martín-García J, García-Albuerne Y. Psychosocial risk factors, burnout and hardy personality as variables associated with mental health in police officers. Front Psychol. 2018;9(SEP).
24. Epstein N B, Bishop D S, Levin S. The McMaster model of family functioning. J Marital Fam Ther. 1978;4(4):19-31.
25. Sheikhzakaryaee N, Atashzadeh-Shoorideh F, Ahmadi F, Fani M. Psychological limbo as a barrier to spiritual care for parents of children with cancer: A qualitative study. Asian Pacific J Cancer Prev. 2018;19(4):1063-1068.
26. Alharbi TAF, Alqurashi AAB, Mahmud I, Alharbi RJ, Islam SMS, Almustanyir S, et al. COVID-19: Factors Associated with the Psychological Distress, Fear and Resilient Coping Strategies among Community Members in Saudi Arabia. Healthc. 2023;11(8).
27. Erbes CR, Arbisi PA, Kehle SM, Ferrier-Auerbach AG, Barry RA, Polusny MA. The distinctiveness

of hardiness, positive emotionality, and negative emotionality in national guard soldiers. J Res Pers. 2011;45(5):508-512.

28. Delahaij R, Gaillard AWK, van Dam K. Hardiness and the response to stressful situations: Investigating mediating processes. Pers Individ Dif. 2010;49(5):386-390.
29. Saraswati W, Wardani R, Suhatno S, Hartono P, Imandiri A. The effect of electroacupuncture therapy on pain, plasma β-endorphin, and quality of life of stage III cervical cancer patients: A randomized control trial. JAMS J Acupunct Meridian Stud. 2021;14(1):4-12.
30. Naeini EE, Sanaei Zaker B. The Effectiveness of Stress Management Training on Hardiness in Patients with Breast Cancer. Abnorm Behav Psychol. 2016;2(2).
31. Juraskova I, Butow P, Robertson R, Sharpe L, McLeod C, Hacker N. Post-treatment sexual adjustment following cervical and endometrial cancer: A qualitative insight. Psychooncology. 2003;12(3):267-279.
32. Lindau ST, Gavrilova N, Anderson D. Sexual morbidity in very long term survivors of vaginal and cervical cancer: A comparison to national norms. Gynecol Oncol. 2007;106(2):413-418.
33. Winda A, Sudiantara Y. Hardiness in Women with Breast Cancer. Psikodimensia. 2014;13(2).
34. Jacob BM, Horton C, Rance-Ashley S, Field T, Patterson R, Johnson C, et al. Need of patient in ICU with Continuous visitation. Fam Crit Care. 2016;25(2):118-125.
35. Yeong SW, Lee SW, Ong SC. Cost-Effectiveness of Breast Cancer Early Detection Program in Low- and Middle-Income Countries: A Systematic Review. Value Heal Reg Issues. 2023;35:57-68.
36. Canário ACG, Cabral PUL, De Paiva LC, Florencio GLD, Spyrides MH, Da Silveira Gonçalves AK. Physical activity, fatigue and quality of life in breast cancer patients. Rev Assoc Med Bras. 2016;62(1):38-44.
37. Cham CQ, Ibrahim N, Siau CS, Kalaman CR, Ho MC, Yahya AN, et al. Caregiver Burden among Caregivers of Patients with Mental Illness: A Systematic Review and Meta-Analysis. Healthc. 2022;10(12).
38. Banerjee J, Aloysius A, Platonos K, Deierl A. Family-centred care and family delivered care – What are we talking about? J Neonatal Nurs. 2018;24(1):8-12.
39. Al-Mutair AS, Plummer V, Clerehan R, O'Brien A. Needs and experiences of intensive care patients' families: A Saudi qualitative study. Nurs Crit Care. 2014;19(3):135-144.
40. Dewi LC, Pratiwi IN, Nimah L, Ramoo V. Family caregivers, perspective of caring for cancer patients during radiotherapy: A qualitative study. J Pak Med Assoc. 2023;73(2):S18-20.
41. Mackie BR, Mitchell M, Marshall PA. The impact of interventions that promote family involvement in care on adult acute-care wards: An integrative review. Collegian. 2018;25(1):131-140.

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Effect of Crispy Catfish and Red Beans on Increasing the Hemoglobin Level of Young Women with Anemia

Efecto del Bagre Crujiente y Las Judías Rojas en el Aumento del Nivel de Hemoglobina en Mujeres Jóvenes con Anemia

Widi Hastuti[2a], Gurid Pramintarto Eko Mulyo [2a], Mimin Aminah[3a], Widartika Widartika[4a], Syarif Assalam[5b], Shilka Amelia[6a], Muna Nur Aeni[7a]

SUMMARY

Introduction: *Women have the highest risk of sufering anemia, especially young women. One way to prevent anemia in adolescents is to increase the intake of food sources of protein and iron. One of the food sources of protein is catfish. Red beans as a vegetable source that contains iron and is high in fiber. Crispy catfish and red beans are food products that are processed, served attractively, and have a long shelf. The study aimed to determine the effect of crispy catfish and red beans on increasing hemoglobin (Hb) levels in young women with anemia.*
Methods*: This study used a quasi-experimental pre-test – post-test design. The sample of young women was 26 people per group, totaling 52 samples. In both groups, interventions were carried out every day for 21 days with interventions in the form of snacks. The intervention group was given 60 grams of crispy catfish and red beans, while the control group was given 60 grams of crispy without catfish and red beans.*
Results: *Crispy catfish and red beans per serving size of 60 grams contained 128.45 % of energy, 95.5 % of protein, 83.5 % of fat, 154.87 % of carbohydrates, 28.93 % fiber, and 0.39 % of iron. There was no significant difference in the food intake of respondents before the intervention, between the intervention group and the control group, for energy value p=0.681 (p<0.05), protein value p=0.267 (p>0.05), fat value p=0.428 (p>0.05), carbohydrate value p=0.126 (p>0.05), fiber value p=0.139 (p>0.05), and Fe value p=0.122 (p≤0.05). There is a significant difference in protein intake after the intervention (with catfish crispy) value p=0.0001 (p<0.05), while energy intake, carbohydrates, fat, fiber, and Fe there was no difference. There was a significant increase in Hb levels in young women after the intervention, with a p-value of 0.0001 (p <0.05).*
Conclusion: *This product can be an alternative snack for young women with anemia. The highest protein score is the amino acid Lysine. There is an effect on protein intake and an increase in the Hb level of young women with anemia after the intervention of giving crispy catfish and red beans.*

Keywords*: Anemia, hemoglobin level, young women, local food production, malnutrition.*

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ORCID: 0000-0003-1700-5679[1]
ORCID: 0000-0003-4701-9588[2]
ORCID: 0009-0000-9712-0874[3]
ORCID: 0000-0001-9097-5757[4]
ORCID: 0009-0000-0063-2858 [5]
ORCID: 0009-0009-9438-8758 [6]
ORCID: 0009-0002-0170-4221 [7]

[a] Politeknik Kesehatan Kemenkes Bandung, Bandung, Indonesia
[b] Universitas Pasundan Bandung, Bandung, Indonesia

*Corresponding Author: Widi Hastuti
E-mail: widihastuti@staff.poltekkesbandung.ac.id

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RESUMEN

Introducción: *Las mujeres tienen el mayor riesgo de sufrir anemia, especialmente las jóvenes. Una forma de prevenir la anemia en adolescentes es aumentar la*

ingesta de proteínas y hierro de fuentes alimentarias. Una de las fuentes alimentarias de proteínas es el bagre. Las alubias rojas son una fuente vegetal que contiene hierro y es rica en fibra. El bagre crujiente y las alubias rojas son productos alimenticios que se procesan, se sirven de forma atractiva y tienen un largo período de conservación. El objetivo del estudio fue determinar el efecto de la administración de bagre crujiente y alubias rojas sobre los niveles de hemoglobina (Hb) en mujeres jóvenes con anemia. **Métodos:** *Este estudio utilizó un diseño cuasi-experimental pre-test - pos-test. La muestra de mujeres jóvenes fue de 26 personas por grupo, por lo que el total es de 52 muestras. En ambos grupos se realizaron intervenciones diarias durante 21 días con intervenciones en forma de tentempiés. Al grupo de intervención se le dieron 60 gramos de bagre crujiente y alubias rojas, mientras que al grupo de control se le dieron 60 gramos de bagre crujiente sin alubias rojas.* **Resultados:** *El bagre crujiente y las alubias rojas por ración de 60 gramos pueden aportar 128,45 % de energía, 95,5 % de proteínas, 83,5 % de grasas, 154,87 % de hidratos de carbono, 28,93 % de fibra y 0,39 % de hierro. No hubo diferencias significativas en la ingesta de alimentos antes de la intervención entre el grupo de intervención y el grupo de control, para el valor energético p=0,681 (p<0,05), el valor proteico p=0,267 (p>0,05), el valor de grasa p=0,428 (p>0,05), el valor de carbohidratos p=0,126 (p>0,05), el valor de fibra p=0,139 (p>0,05), y el valor de Fe p=0,122 (p≤0,05). Se observó una diferencia significativa en la ingesta de proteínas después de la intervención (con bagre crujiente) p -valor =0.0001 (p<0.05), mientras que en la ingesta de energía, carbohidratos, grasa, fibra y Fe no hubo diferencias. Se obsevó un incremento significativo en los niveles de Hb de las mujeres jóvenes entre el grupo de intervención y el grupo de control, con un valor de p 0,0001 (p <0,05).* **Conclusiones:** *Este producto puede ser un tentempié alternativo para mujeres jóvenes con anemia. La puntuación de proteína más alta es el aminoácido Lisina. Existió un efecto sobre la ingesta de proteínas y un aumento del nivel de Hb de las mujeres jóvenes con anemia tras la administración de bagre crujiente y alubias rojas.*

Palabras clave: *Anemia, nivel de hemoglobina, mujeres jóvenes, producción local de alimentos, malnutrición.*

INTRODUCTION

Anemia is one of the health problems around the world. The global prevalence of anemia in women aged 15-49 years was 29.9 % (1-3). It causes anemia in young women to become a health problem with a prevalence of >15 %. According to Basic Health Research (2013), the prevalence of anemia in Indonesia is 21.7 %, with 26.4 % of anemia patients aged 5-14 years and 18.4 % of patients aged 15-24 years (4,5). Women, especially young women, have the highest risk of anemia (6-8).

Young women are one of the groups at risk of anemia (6,9). Menstruating girls need iron to replace menstrual loss. Iron loss during one menstrual cycle (about 28 days) is approximately 0.56 mg daily. This amount is coupled with a basal loss of 0.8 mg daily, bringing the total iron loss to 1.36 mg daily. According to Lutfiasari, et al. (2023), the limit of hemoglobin (Hb) levels for young women to diagnose anemia is if the Hb level is less than 12 g/dL (10). Anemia causes a reduction of oxygen binding to hemoglobin and transport from the lungs to the rest of the body, which will result in difficulty concentrating and learning. In addition, physical endurance is low, with a decrease in physical activity and with the consequence to get sick easily (12,13).

Iron is required for the synthesis of hemoglobin. Iron deficiency happens because young women experience menstruation every month. Intake of nutrients in the body must be fulfilled, especially in adolescents. Protein intake in the body is beneficial for iron absorption. Besides, vitamin C in the adolescent body must be fulfilled because vitamin C is a reducing agent. Then in the intestine, iron will be maintained in the form of iron so that it is more easily absorbed by consuming food sources of iron (14).

A low intake of protein sources can cause anemia in young women (15). In the population aged 16-18 years, the average adequacy of protein consumption is 64.4 %, and adolescents who consume below the minimum need as much as 35.6 % (16). One of the government programs to overcome anemia in young women is the provision of blood supplement tablets with a national target. Young women get blood tablets with preventive doses, namely once a week and once a day during menstruation. However, the provision of blood supplement tablets only focuses on pregnant women, while for young

women has not been done optimally (17). It causes a high incidence of anemia in young women (18).

Overcoming the problem of anemia that occurs in young women can be done by including supplementary iron in the form of snacks like crispy catfish and red beans. Based on local food, young women's snacks are prioritized in animal and vegetable protein sources. Indonesia has a variety of diverse foods, and local food has great potential to be a functional food source. Good functional food should be a daily consumption pattern, especially locally based, to improve healthy function and health and reduce disease risk.

Catfish is a source of animal protein as one of the local foods that the Indonesian people widely use for food. The benefits of bioactive components in catfish are the content of unsaturated fatty acids that can reduce the risk of disease and improve immune function. Abundant availability of catfish, with total catfish production in Indonesia reaching 116 114 tons in 2022 (19). The price is relatively affordable, making catfish chosen to be a food that is widely used by the Indonesian people to be used as food that somebody can consume daily. Nutrients in 100 g of fresh catfish are energy 135 kcal, protein 17 grams, fat 6.6 grams, carbohydrates 1.1 g, and Iron 1.6 mg (20). The nutritional content of catfish is higher than snakehead fish, as the protein content in snakehead fish is only 16.2 g, and iron content is only 0.1 mg. Catfish is good local food for people with anemia because of its high iron content (20).

Research conducted by Hastuti (2022) resulted in the product crispy catfish (20). This product contains protein but lacks fiber content. If we want a crispy product that contains protein and fiber, then the product needs to add fiber-source food, namely red beans, with a fiber content of 4.0 g/100 g. Red beans have a relatively high iron content compared to other beans. Red beans have an iron content of 10.3 mg/100 g (21). Iron in red beans is high compared to other legumes such as mung beans, which contain as much as 7.5 mg/100 g, soybeans 6.9 mg/100 g, cashew nuts 3.8 mg/100 g, and peanuts 4,1 mg/100 g (21). Total red bean production in Indonesia reached 66.210 tons (22).

Crispy catfish is a processed product liked by people of various ages, such as children, adolescents, and adults. This product is preferred because it has a crunchy texture and is easy to digest. Based on the results of other studies, the group of adolescents studied was given an intervention by giving high iron (Fe) food products such as snack bars, cookies, biscuits, and muffins (10,23-25). Crispy products can innovate in making high-protein and iron food products (21). This processed product is highly nutritional because it contains carbohydrates, protein, fat, iron, and high fiber.

The high protein and iron content in catfish and red beans is expected to increase protein and iron intake for young women with anemia. The study aimed to determine the effect of crispy catfish and red beans on increasing hemoglobin (Hb) levels in young women with anemia.

METHODS

This study used a quasi-experimental pre–test–post–test design. The study design compared the incidence of anemia among young women before and after the intervention. This research received approval for an ethical review from the Health Research Ethics Commission of the Health Polytechnic of the Ministry of Health Bandung No. 09/KEPK/EC/VIII/2021, dated August 10, 2021.

Sampling was carried out using purposive sampling techniques. The criteria for inclusion of the sample were adolescents aged 10-15 years, had menstruation, did not suffer from chronic diseases such as pulmonary tuberculosis and hepatitis, did not eat foods containing iron inhibitors, namely tannins, and students were willing to participate in the study by filling out informed consent. The sample size was determined based on calculations using the formula Lameshow, 1990, and considered the addition of subjects who dropped out by 10 %. From the analysis of the formula, a minimum sample of 26 young women (intervention group) and 26 young women (control group) was obtained so that the total sample was 52 young women.

This study used instruments in the form of interview questioners to determine the

characteristics of samples (age, Hb level) and respondents (age, education level, occupation), SFFQ (Semiquantitative Food Frequency Questioner) forms and 1 x 24-h recall forms for measured food intake. The independent variable was the intervention of giving crispy catfish and red beans. The dependent variable is the hemoglobin level of young women (26).

The interventions were carried out every day for 21 days in the form of snacks. The intervention group was given 60 grams of crispy catfish and red beans, with an energy content of 253.72 kcal and protein of 5.68 g; while the control group was given 60 grams of crispy , with an energy content of 197.50 kcal, protein 6.00 g (Recommended Nutritional Adequacy Rate for Young Women, Ministry of Health, 2019). This intervention was carried out at school and accompanied by their respective teachers. After intervention, Hb levels and food intake was assessed using the 2 x 24-hours recall method on days 5 and 15 (26).

This study used univariate analysis to categorize sample characteristics (age), respondent characteristics (age, education level, occupation), and nutritional status presented in a frequency distribution table and analyzed descriptively. This study used bivariate analysis to determine the relationship between variables. Bivariate analysis was used for the dependent t-statistical Test to determine differences in food intake and Hb values before and after the intervention. The limit of significance used a 95 % confidence level with a p-value <0.05.

Protein score is the arrangement and number of amino acids contained in protein molecules because the efficiency of using protein in the body will depend on the smallest number of essential amino acids (27). The quality of protein is determined by the amount and the arrangement of amino acids in the protein. Protein is said to be of high quality if it has an amino acid arrangement that matches the arrangement of amino acids in human body tissues (28). The quality of the new product's amino acids is determined to be compared with egg amino acids, considered the standard of amino acid perfection. The value of one amino acid, e.g., tryptophan, is compared to the total number of amino acids of the whole product, then a percentage is produced. The formula to get a protein score on a product is by comparing the percentage of one amino acid with the percentage amino acid of the egg so that it can be said to be a protein score, with a unit of "score."

$$\text{Protein score: } \frac{\%\ \textit{amino acid of produc}}{\%\ \textit{standard of amino acid (egg)}}$$

RESULTS

The characteristics of the sample according to the father's education, father's occupation, mother's education, and mother's occupation are presented in Table 1.

Table 1 shows that most of the father's education level was a senior high school in both the intervention and control groups. The father type of work was partly self-employed in both the intervention and control groups. The mother's education level in the intervention and control groups was mostly senior high school. The level of education was a factor that affects the quality and quantity of food because, with a high level of education, it was expected that the knowledge and information about nutrition will be better. The mother's work was significant as a housewife in the intervention and control groups.

The results of testing the nutritional value of crispy catfish and red beans per 100 grams are presented in Table 2.

Table 2 shows that 100 g of crispy catfish and red beans contain an energy of 514.15 Kcal and a protein calorie percent of 46 %. The results of testing the nutritional value of crispy catfish and red beans per serving size of 60 grams are presented in Table 3 below.

Table 3 shows that crispy catfish and red beans per serving size of 60 grams can contribute 128.45 % of energy, 95.5 % of protein, 83.5 % of fat, 154.87 % carbohydrates, 28.93 % fiber, and 0.39 % of iron. The type of protein score crispy catfish and red beans can be seen in Figure 1. It shows that lysin was the highest type of amino acid in crispy catfish and red beans.

Table 1

Sample Characteristics According to Father's Education, Father's Occupation, Mother's Education, and Mother's Occupation

Variable	Intervention Group		Control Group	
	n (26)	%	n (26)	%
Father's education				
Junior High School	0	00.0	0	00.0
Senior High School	20	76.9	15	57.7
Diploma	6	23.1	7	26.9
Bachelor	0	00.0	4	15.4
Father's occupation				
Civil Servants	0	0.0	0	00.0
Private employees	2	7.7	3	11.5
Self-employed	23	88.5	23	88.5
Laborer	1	3.8	0	00.0
Mother's education				
Junior High School	0	00.0	0	00.0
Senior High School	20	76.9	18	69.2
Diploma	4	15.4	3	11.5
Bachelor	2	7.7	5	19.2
Mother's occupation				
Civil Servants	1	3.8	0	0.0
Private employees	2	7.7	2	7.7
Self-employed	9	34.6	2	7.7
Housewives	14	53.8	22	84.6

Table 2

The Nutritional Value of Crispy Catfish and Red Beans per 100 g

Groceries	Net weight (g)	Gross weight (g)	Energy (Kcal)	Protein (g)	Fat (g)	Carbohydrate (g)
Catfish Flour	40	308	406.15	52.31	20.31	3.38
Red Bean Flour	60	63	108.00	6.95	1.39	17.68
	Total		514.15	59.26	21.70	21.07
	BMC requirements		360.00	46 % (≥16 %)		

Table 3

The Nutritional Value of Crispy Catfish and Red Beans per Serving Size of 60 grams compared to the Daily Value (RDA)

Test Type	Lab Test Results	Average DV Snack Age 10 - 15 years	% DV
Energy	253.72 kcal	197.50	128.46
Protein	5.73 g	6.00	95.50
Fat	5.68 g	6.80	83.50
Carbohydrates	44.92 g	29.00	154.87
Fiber	0.81 mg	2.80	28.93
Iron	0.47 mg/kg	1.20	0.39

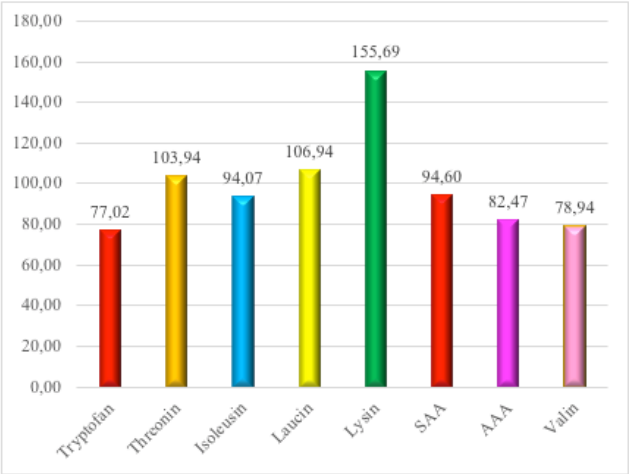

Figure 1. Protein Score Crispy Catfish and Red Bean (The unit of the protein score is the "score")

Table 4 shows the results of statistical tests using the Independent T-test at a 95 % confidence level, indicating that there was no significant difference in the food intake of respondents before the intervention between the intervention group and the control group for energy value p=0.681 (p<0.05), protein value p=0.267 (p>0.05), fat value p=0.428 (p>0.05), carbohydrate value p=0.126 (p>0.05), fiber value p=0.139 (p>0.05), and Fe value of p=0.122 (p≤0.05).

Table 4

Food Intake of Respondents Before Intervention Between the Intervention Group and the Control Group

Variable	Intervention Group (n=26)			Control Group (n=26)			Value of p*
	Min-Max	Average	SD	Min-Max	Average	SD	
Energy	1 515.20 –1 691.55	1 609.77	51.22	1 648.6 – 1 982.4	1 782.26	89.00	0.681
Protein	48.15 – 51.81	49.54	1.02	46.39 – 51.24	49.41	1.23	0.267
Fat	54.54 – 57.60	55.79	0.94	53.27 – 59.87	57.02	1.64	0.428
Carbohydrate	231.72 – 242.33	238.68	3.13	249.47 – 290.15	259.74	10.23	0.126
Fiber	19.19 – 23.81	22.08	1.50	19.27 – 22.83	21.10	1.03	0.139
Iron	7.43 – 9.45	8.91	0.44	7.01 – 8.99	8.06	0.56	0.122

*Independent Test

Table 5 shows the results of statistical tests using the Independent T-test at a 95 % confidence level, showing that there was a significant difference in protein intake after the intervention (with catfish crispy) value p=0.0001 (p<0.05) while energy intake, carbohydrates, fat, fiber, and Fe there was no difference.

Table 5

Food Intake of Respondents After Intervention (with Crispy Catfish and Red Beans Between Intervention Group and Control Group

Variable	Intervention Group (n=26)			Control Group (n=26)			Value of p*
	Min-Max	Average	SD	Min-Max	Average	SD	
Energy	1 750.38 – 1 935.26	1 851.26	52.11	1 712.26 –1 945.27	1 842.96	61.10	0.600
Protein	54.26 – 56.78	55.39	1.11	50.02 – 50.66	50.21	0.14	0.0001
Fat	59.24 – 63.23	61.04	0.89	54.25 – 63.28	60.74	1.52	0.397
Carbohydrate	272.24 – 287.25	282.18	4.25	266.24 – 287.25	280.19	6.62	0.204
Fiber	20.00 – 24.62	22.66	1.51	19.96 – 24.52	1.18	1.03	0.286
Iron	8.20 – 9.55	8.93	0.39	8.12 – 9.45	8.82	0.42	0.313

*Independent Test

Table 6 shows that there was a significant difference in change in food intake before and after intervention between the intervention group and the control group with a value of P = 0.025. This result showed that giving crispy catfish and kidney beans is effective in increasing protein intake.

Table 6

Comparison of Changes in Food Intake Before and After Intervention in Intervention Group and Control Group

Variable	Intervention Group (n=26)		Control Group (n=26)		Value of P
	Mean	SD	Mean	SD	
Energy	234.75	96.81	218.14	135.23	0.082
Protein	8.97	3.62	3.21	8.33	0.025
Lemak	11.45	4.36	10.01	4.02	0.939
Carbohydrate	39.65	20.52	35.18	18.26	0.799
Fiber	5.99	2.32	5.01	2.64	0.436
Iron	1.76	0.98	1.43	1.16	0.242

*Independent Test

Table 7 shows that the mean Hb level in the intervention group was higher than the control group, which is 12.45 g/dL in the intervention group and 11.86 g/dL in the control group.

Table 7

Hb Levels of the Intervention Group and Control Group Before and After the Intervention

Variable	Intervention Group (n=26)		Control Group (n=26)		p-value	95 % CI
	Mean	SD	Mean	SD		
Hb Levels Before	11.87	0.99	11.56	1.42	0.357	-0.37;0.99
Hb Levels After	12.45	0.48	11.86	0.39	0.0001	0.36;0.83

DISCUSSION

The results showed that there was no significant difference in the young women's food intake before the intervention between the intervention group and the control group for energy, carbohydrate, fat, fiber, and iron intake. There was a significant difference in protein intake after the intervention. At the same time, there were no differences in energy, carbohydrate, fat, fiber, and iron intake after the intervention with crispy catfish and red beans. This study is in line with other studies, which stated a significant difference in protein intake after giving red bean, banana, and tuna-based cookies (29).

100 g of crispy catfish and red beans contain 514.15 Kcal of energy and 46 % of protein calories. The highest protein score was the amino acid lysine, with a protein score value of 155.69. Lysine is important for adequate growth, and it plays an essential role in the production of carnitine, a nutrient responsible for converting fatty acids into energy and helping lower cholesterol. Humans synthesize L-carnitine from the amino acids lysine and methionine in a multi-step process occurring across several cell compartments. It can increase β-oxidation so that somebody can reduce the accumulation of body fat. In addition, lysine can increase the activities of antioxidant enzymes by upregulating Nrf2 and upregulating the expression of antioxidant enzyme genes, thereby increasing the ability of free radical scavenging to protect against oxidative damage (30).

An adequate energy and protein diet is necessary to reduce inflammation and increase iron absorption. Malnutrition of protein and energy stimulates increased cytokine production with inflammation, immune deficiency, and anemia (31). There is a mechanism to increase iron absorption in people with iron deficiency. The form of iron entering the duodenum affects its absorption. Heme iron derived from animal foods is more easily absorbed, does not depend on duodenal pH, and is not affected by inhibitory substances such as phytate and polyphenols (32). Therefore, catfish, one of the animal source foods, can be an excellent source of iron.

After the intervention, hemoglobin levels in the intervention group were higher than in the control group with crispy catfish and red beans. This study aligns with other studies that state that fried catfish cakes effectively increase hemoglobin levels and blood oxygen saturation (33).

Bioavailable heme iron is 15 %-35 %, and bioavailable non-heme iron is 2 %-20 % (34). Despite its lower bioavailability, the amount of non-heme iron in legume foods can be more significant than heme iron in most foods, so non-heme iron generally contributes more than heme iron (35). Red beans are non-heme iron. Vitamin C can help increase iron absorption because of its ability to reduce ferric to ferrous iron and its ability to chelate iron (36). The combination of catfish and red beans is recommended for snacks for anemic young women. These crispy catfish and red bean products can contribute to the nutritional adequacy of snacks for the age group of 10-15 years. This research aligns with Hastuti et al. (35), which states that red bean catfish-based products can be used as an alternative snack because they contain high protein and iron, suitable for young women with anemia.

CONCLUSION

Crispy catfish and red bean products can be alternative snacks for young women with anemia. The highest protein score is the amino acid Lysine. There is an effect on protein intake and an increase in the Hb level of young women with anemia after the intervention of giving crispy catfish and red beans.

REFERENCES

1. Puspitasari HZG, Armini NKA, Pradanie R, Triharini M. Anemia prevention behavior in female adolescents and related factors based on Theory of Planned Behavior: A cross-sectional study. J Ners. 2022;17(1):25-30.
2. WHO. World Health Statistics 2022 (Monitoring Health of the SDGs). Geneva : World Health Organization: World Health Organization. 2022:1-131. Available from: http://apps.who.int/bookorders.

3. Kinyoki D, Osgood-Zimmerman AE, Bhattacharjee N V, Schaeffer LE, Lazzar-Atwood A, Lu D, et al. Anemia prevalence in women of reproductive age in low- and middle-income countries between 2000 and 2018. Nat Med. 2021;27(10):1761-1782.
4. Kementrian Kesehatan RI. Basic Health Research. Jakarta - Indonesia; 2013.
5. Balitbang Kementrian Kesehatan RI. Riset Kesehatan Dasar 2013. Jakarta; 2013.
6. Triharini M, Mar'Ah Has EM, Nofita G. Determinant factors of anemia in pregnancy based on health belief model: A correlational study. J Ners. 2023;18(1):50-56.
7. Kaimudin N, Lestari H, Afa J. Screening and Determinants of Anemia Incidence in Young Girls at State Senior High School 3 Kendari in 2017. J Ilm Student of Health, Community Health, Unsyiah. 2017;2(6):185793.
8. Efendi F, Israfil I, Ramadhan K, McKenna L, Alem AZ, Malini H. Factors associated with receiving iron supplements during pregnancy among women in Indonesia. Electron J Gen Med. 2023;20(5).
9. Shara F El, Wahid I, Semiarti R. The relationship between nutritional status and the incidence of anemia in young women at SMAN 2 Sawahlunto. J Health Andalas. 2014;6(1):202.
10. Lutfiasari D, Martini S, Widati S. The effectiveness of peer group on adolescent anemia prevention behavior: A systematic review. J Public Health Africa. 2023;14(S2)(2542):1-5.
11. Silitonga HTH, Salim LA, Nurmala I, Hargono R, Purwandini S. Knowledge, attitude, intention, and program implementation of iron supplementation among adolescent girls in Sidoarjo, Indonesia. J Public Health Africa. 2023;14(S2):1-5.
12. Zainiyah H, Khoirul Y. Examination of Hb Levels and Counseling About Anemia and Anticipation for Al Hidayah High School Students. J Paradig. 2019;1(2):16-25.
13. Suryani D, Hafiani R, Junita R. Analysis of Diet and Iron Nutrition Anemia in Young Girls in Bengkulu City. J Health Masy Andalas. 2017;10(1):11-18.
14. Farahdiba D. Correlation between Consumption Levels of Fe, Protein and Vitamin C with Hemoglobin Levels in Students at MTSN Ngemplak, Boyolali Farahdiba Regency, Desti. Solo. Nutrition Study Program, Faculty of Health Sciences, University of Muhammadiyah Surakarta. 2018. Muhammadiyah University of Surakarta; 2018.
15. Triharini M, Armini NKA, Pitaloka SA. The correlation between family role and anemia prevention in pregnancy. Healthc Low-Resource Settings. 2023;11(S1):1-5.
16. Ministry of Health of the Republic of Indonesia. Basic Health Research. Balitbang Ministry of Health RI. 2018. Available from: https://www.kemkes.go.id/article/view/19093000001/ penyakit-jantung-penyebab-kematian-terbanyak-ke-2-di-indonesia.html
17. Sarsam SM, Al-Samarraie H, Alzahrani AI, Shibghatullah AS. A non-invasive machine learning mechanism for early disease recognition on Twitter: The case of anemia. Artif Intell Med. 2022;134(102428):1-12.
18. Sholicha, Almaratus C, Muniroh L. Correlation Between Intake of Iron, Protein, Vitamin C and Menstruation Pattern with Haemoglobin Concentration among Adolescent Girl in Senior High School 1 Manyan Gresik. Media Gizi Indonesia. 2019;14(2):147.
19. Damanti RR, Rahadian DAS, Rahadian R. Release of Quarterly 2022 Marine and Fisheries Data. Ministry of Maritime Affairs and Fisheries in 2022. 2022.
20. Ministry of Health of the Republic of Indonesia. Indonesian Food Composition Table (TKPI). 2017.
21. Hastuti W, Aminah M, Moviana Y, Amelia S, Aeni MN. Community Empowerment Through Making Crispy Red Beans for Business Actors In Cinunuk Village, Bandung Regency. 2022;000(November):16-17.
22. Central Bureau of Statistics. Vegetable Plant Production 2020. 2020. Available from: https://www.bps.go.id/indicator/55/61/2/production-tanaman-sayuran.html
23. Rahmadona, Mardiah, Rullyni NT, Respatiningrum, Harianja RR. Effect of Temvita Cookies as a Healthy Snack on Hemoglobin Levels of Young Women with Anemia. Phot J Science and Health. 2022;12(2):103-110.
24. Riana A. The Effect of Providing Iron Source Cookies on Hemoglobin Levels of Female Students at Stik Immanuel Bandung. J Immanuel Health Sciences. 2020;14(1):21-26.
25. Dewita, Syahrul, Isnaini. Utilization of Catfish Protein Concentrate (Pangasius hypopthalmus) For Biscuits and Snacks. J Indonesian Fishery Hash Processor. 2011;14(1):30-34.
26. Pakpahan C, Darmadi D, Agustinus A, Rezano A. Framing and understanding the whole aspect of oral sex from social and health perspectives: A narrative review. F1000Research. 2022;11(177):1-21.
27. Nuraini D. Ketersediaan Lisin sebagai Indikator Mutu Protein. War II/J Agro-based Ind. 1991;8(2):36-45.
28. Winarno FG, Rahman A. Protein: Sumber dan Peranannya. Bogor: FATEMETA-IPB; 1974.
29. Hastuti W, Aminah M, Mulyono GP. Interventions for Providing Cookies Based on Red Nuts, Banana, and Snakehead Fish as an Emergency Food AlternativeTowards Nutritional Status of Children. Sapporo Med J. 2020;54(10):1-11.

30. Saputra IPGAJ, Astawa IPA, Sudiastra IW. The Effect of Lysine and Methionine Amino Acids on the Percentage of Carcasses and Commercial Cuts of Broiler Carcass Aged 32 Days. J Trop Breeders. 2021;9(3):569-587.
31. Bianchi VE. Role of nutrition on anemia in elderly. Clin Nutr Espen. 2015;11(E):1-11.
32. Abbaspour N, Hurrell R, Kelishadi R. Review on Iron and its Importance for Human Health. J Res Med Sci. 2014;19(2):164-174.
33. Suryani IS, Jamil MU, Amalia NR, Pratiwi AM. The Effectiveness of Fried Catfish Cake in Increasing Hemoglobin Levels and Oxygen Saturation in Blood in Pregnant Women. PLACENTUM J Ilm Kesehat dan Apl. 2021;9(3):33.
34. Hurrell R, Egli I. Iron bioavailability and dietary reference values. Am J Clin Nutr. 2010;91(5):1461S-1467S.
35. E R Monsen, L Hallberg, M Layrisse, D M Hegsted, J D Cook, W Mertz CAF. Estimation of Available Dietary Iron. J Clin Nutr. 1978;1(1):134-141.
36. Krisnanda R. Vitamin C helps in the absorption of iron in iron deficiency anemia. J Nurse Researcher Prof. 2020;2(3):279-286.

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Multi-Dimensional Impact of Cyber Gender-Based Violence: Examining Physical, Mental, Social, Cultural, and Economic Consequences

Impacto multidimensional de la violencia de género cibernética: examen de las consecuencias físicas, mentales, sociales, culturales y económicas

A'im Matun Nadhiroh[1a], Eko Winarti[2b], Annisa' Wigati Rozifa[3a*], Noer Saudah[4c]

SUMMARY

Background: *The Internet, especially social media, is also at risk of being misused and triggering violence against humans. Gender-based violence (GBV) facilitated by new technologies is a phenomenon that increasingly affects the privacy and safety of women and girls in and out of cyberspace. This study aimed to describe the physical, mental, social, cultural, and economic impacts of gender-based violence of cyber.*
Methods*: This study used a descriptive survey. The population of this study was adolescents in the East Java region; the sample size was 480 adolescents selected using a purposive sampling technique, with the following criteria: adolescents aged 12-25 years and willing to be respondents. The variables in this study include the characteristics of the respondents, cyber-based gender violence, and the impacts experienced. Data was collected using a questionnaire using Google Forms, which consisted of; gender, gender-based violence, cyber gender-based violence, and questions about the impact of cyber-based violence. The research questionnaire has been tested for validity and reliability. The research process was carried out according to ethical principles.*
Results: *This research shows that more than 50 % of respondents are aged 17-25 years, more than 75 % are female, almost 50 % have a high school education, and most are unmarried. As many as 308 (64 %) have received threats, insults, insults, harassment, sending pornographic photos, pornographic videos, and indecent sentences. The most significant impact of Cyber Gender-Based Violence on adolescent psychology is 265 (55 %).*
Conclusion: *Based on this research, the most dominant impact of gender-based violence in cyberspace is the psychological impact, in addition to the physical, social, cultural, and economic effects. Good education, especially for children, must be carried out intensively to prevent children from potentially falling into cybercrime. The government must formulate a strategy to address cyber violence against women.*

Keywords*: Factor, cyber, gender-based, violence.*

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ORCID: 0000-0002-1848-0458[1]
ORCID: 0000-0002-4443-5490[2]
ORCID: 0000-0002-9088-6524[3]
ORCID: 0000-0002-6638-0996[4]

[a]Faculty of Health Science, Universitas Muhammadiyah Surabaya, Surabaya, Indonesia.
[b]Faculty of Health Science, Universitas Kadiri, Kediri, Indonesia.
[c]Faculty of Health, Universitas Bina Sehat PPNI, Mojokerto, Indonesia.

*Corresponding Authors: A'im Matun Nadhiroh
E-mail: a'immatunnadhiroh@um-surabaya.ac.id

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RESUMEN

Antecedentes: *Internet, especialmente las redes sociales, también corre el riesgo de ser mal utilizada y desencadenar violencia contra los humanos. La violencia basada en género (VBG) facilitada por las nuevas tecnologías es un fenómeno que afecta cada vez más la privacidad y seguridad de mujeres y niñas dentro y fuera del ciberespacio. Este estudio tiene como objetivo describir los impactos físicos, mentales, sociales, culturales y económicos de la violencia de género en cibernética.*

Métodos: *Este estudio utilizó una encuesta descriptiva. La población de este estudio fueron adolescentes en la región de Java Oriental; el tamaño de la muestra fue de 480 adolescentes seleccionadas utilizando una técnica de muestreo intencional, con los siguientes criterios: adolescentes de 12 a 25 años y dispuestos a ser encuestados. Las variables de este estudio incluyen las características de los encuestados, la violencia de género cibernética y también los impactos experimentados. Los datos se recopilaron mediante un cuestionario utilizando Google Forms, que consistió en género, violencia de género, ciberviolencia de género y preguntas sobre el impacto de la ciberviolencia. El cuestionario de investigación fue probado en cuanto a validez y confiabilidad. El proceso de investigación se llevó a cabo de acuerdo con principios éticos.*

Resultados: *Esta investigación muestra que más del 50 % tiene entre 17 y 25 años, más del 75 % son mujeres, casi el 50 % tiene educación secundaria y la mayoría no está casada. Hasta 308 (64 %) han recibido amenazas, insultos, insultos, hostigamientos, envío de fotos pornográficas, videos pornográficos y frases obscenas. El impacto más significativo de la Ciberviolencia de Género en la psicología del adolescente es 265 (55 %).*

Conclusión: *Con base en esta investigación, el impacto más dominante de la violencia de género en el ciberespacio es el impacto psicológico, además de los efectos físicos, sociales, culturales y económicos. La buena educación, especialmente para los niños, debe llevarse a cabo de manera intensiva para evitar que los niños caigan potencialmente en el ciberdelito. El gobierno debe formular una estrategia para abordar la violencia cibernética contra las mujeres.*

Palabra clave: *Factor, cibernético, basado en el género, violencia.*

INTRODUCTION

Along with modern technology's emergence, access to the Internet has become easier and faster. The Internet has spread and is an integral part of everyday life, both for work and leisure activities, to communicate thoughts and information, and to build connections beyond geographic boundaries (1,2). Apart from being a medium for expression, the Internet, especially social media, is also at risk of being misused and triggering violence against humans (3,4). Although it looks democratic, the virtual world suffers from violence and gender inequality, similar to the offline world (5). Some acts that fall under cyber violence include harassment, invasion of privacy, sexual exploitation, sexual harassment, and online threats (6,7). Gender-based violence (GBV) is experienced by many women and girls online (8-10). Women are victims of cyber violence in many instances. A study shows that one in four women experience cyber violence (11).

The United Nations (1993) defines GBV as an act of violence in public or private life that may result in physical, sexual, or psychological harm. One study explains that women are more at risk of becoming victims of online sexual harassment than men (12). UNESCO (2015) (13) notes that most women have experienced cyber violence incidents. Additionally, Amnesty International (2017) (14) in their survey of 4 000 women in 8 countries, found that a quarter of their respondents had experienced online harassment at least once, with some incidents threatening their safety. In Indonesia, the National Commission on Violence Against Women, in its 2020 Annual Report, revealed a 300 % increase in Online Gender-Based Violence *(OGBV)* cases compared to the previous year (15). Even during the pandemic, there was a 400 % increase in OGBV cases compared to 2019 (16).

There are various forms of cyberviolence against women, including cyberstalking, nonconsensual pornography (or 'revenge porn'), gender-based insults and harassment, 'slut-shaming' unsolicited pornography, 'sextortion,' rape and death threats, 'doxing' and trafficking, which electronically activated. The risk of cyberviolence increases in adolescents (17,18). Adolescents are genuine users of digital media platforms, especially social media, essential in increasing social connections, self-discovery, and self-esteem. Therefore, adolescents are at risk of engaging in cyberbullying and using age-appropriate content through social media (19).

If left unchecked, female-based cyber violence has social, physical, psychological, and economic impacts on women (20). A study in Sweden found the effects of cyber-based violence on adolescents. 84 % of adolescents reported behavioural results, 80 % social impacts, 56 % cognitive impacts, and 12 % experienced physical impacts (21). Other studies support this statement and find psychological implications, including anxiety and damaged self-image, women's rights and dignity violations, and gender justice and equality (22).

This study aimed to describe the physical, mental, social, cultural and economic impacts of gender-based violence in cyber. Besides, this study aimed to address issues related to gender equality amidst the challenges of gender-based cyber violence that have damaged Indonesian society and weakened efforts to realize gender-based equality. This study required concrete policies to prevent online gender-based violence and the participation of social media platforms to increase awareness campaigns in building an environment of gender equality and respecting one another's gender.

METHODS

This study used a descriptive survey. The population of this study was adolescence in the East Java region, with a total sample of 480 adolescents. This research was conducted from November to December 2022 with the inclusion criteria of adolescents aged 12-25 years and willing to be respondents.

The variables in this study include the characteristics of the respondents, cyber-based gender violence, and the impacts experienced. Data collection used a questionnaire distributed via Google Form, which consisted of gender 3 question items, gender-based violence 10 question items, cyber gender-based violence 14 question items, and 3 question items about the impact of cyber-based violence. The questionnaire in this study has gone through the validity and reliability test stages. The implementation of the research process complies with ethical principles such as informed consent, anonymity, and confidentiality.

This descriptive research collected data using a frequency distribution based on the variables studied. The method of presentation was in the form of tables, diagrams, presentations, and narration.

RESULTS

Data collection through youth data collection in the East Java region consisted of 480 young people, both early and late. The results of this research were descriptive by collecting data using a frequency distribution based on the variables studied.

Table 1 shows the Respondents characteristics, were more than 50 % are aged 17-25 years, more than 75 % are female, and almost 50 % have a high school education. All respondents who participated in this study came from 29 districts in East Java.

Table 1. Characteristics of Respondents

Criteria	Amount (n)	Percentage (%)
Age		
1. Early Adolescents (12 – 16 years)	198	41
2. Late Adolescents (17 – 25 years)	282	59
Gender		
1. Boy	109	23
2. Girls	371	77
Education		
1. Middle school	49	10
2. High school	235	49
3. College	162	34
4. Graduated D3	9	2
5. Graduated Bachelor	25	5
Marital status		
1. Not married	469	97.7
2. Married	10	2.08
3. Divorced life	0	0
4. Divorced dead	1	0.22

Figure 1 was a form of cyber gender-based violence, where out of 480 adolescents who have received threats, insults, insults, harassment, sending pornographic photos, pornographic videos, and obscene sentences, as many as 308 (64 %).

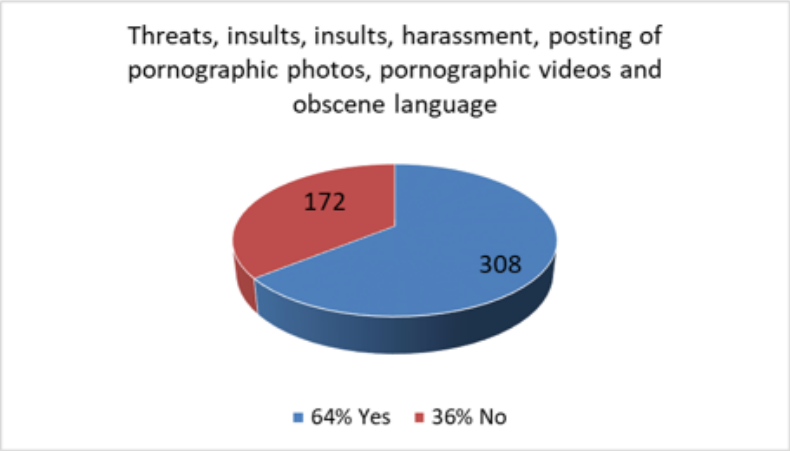

Figure 1. Forms of Cyber Gender-Based Violence

Figure 2 show that there are three impacts of cyber gender-based violence, namely Physical, Psychological, Social, Cultural, and Economic effects. Cyber gender-based violence had the most significant impact on adolescent psychology, namely 265 (55 %).

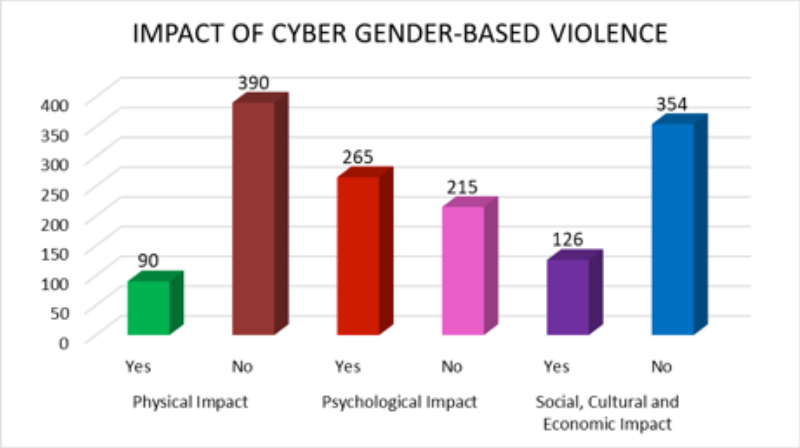

Figure 2. Impact of Cyber Gender-Based Violence

DISCUSSION

Based on the characteristics of the respondents, most respondents were aged 17-25 years or are called late adolescents. The United Nations Broad Commission (2015) (23) showed that women aged 18-24 experience several forms of cyber violence. In this study, most respondents were female. According to WHO (2017), around 35 percent of women worldwide have been victims of GBV at some point. However, several studies in the Middle East and Africa indicate that up to 70 percent of women have experienced physical and sexual violence from an intimate partner during their lifetime. As many as 87,000 women were intentionally killed in 2017 globally, more than half (58 percent) were killed by an intimate partner or family member, meaning that 137 women worldwide were killed by their family members each year day (24).

In addition, most respondents in this study were people with unmarried status. The evidence states that available female students in the study area are more than three times more affected by GBV at school than divorced and married students (25). In this study, most incidents of gender-based violence occurred in women. Previous research explained a statistically significant positive correlation between society's patriarchal ideology (male dominance) in increasing GBV and the education level of the respondents. The survey results also show that student household income is related to their level of education. An increase in household income reduces the propensity of a daughter's family to negotiate gender-based violence (26,27).

Conversely, lower household income makes women vulnerable to unwanted marriages and other acts of violence by male perpetrators. According to them, there are many forms of gender-discriminatory violence in developing countries due to patriarchal ideology, which must make men more substantial and have supremacy over women in society (28). These practices start at home and are followed in schools, creating more challenges to girls' educational attainment. School-going young women are often involved in unwanted violence caused by male perpetrators. These cultural practices imply unequal gender roles that expose women to gender-based violence (29-31).

Covert social practices have tremendously affected the overall level of GBV. Another implication is that the supremacy of men over women stems from gender-selective societal norms. This practice then makes women vulnerable or oppressed by gender-based violence. Consequently, these findings confirm that school-related gender-based violence is caused by hidden social customs, implying that it is a problem strongly related to the socioeconomic background of vulnerable women.

WHO (32) defines violence as an overarching term, including neglect and physical, sexual, and psychological abuse. This scope reflects the broad spectrum of violence that can be experienced in today's society. Women are recognized as very vulnerable to experiencing violence in its various forms. European Union Agency For Fundamental Rights (FRA) (2014) reports that violence against women is a widespread human rights violation that significantly threatens women's safety. In their report based on 42 000 women in 28 European Union (EU) member states, the FRA indicated that violence against women is extensive harassment that systematically remains unreported (9). GBV is violence directed against a person based on sex or gender, including acts that cause emotional, physical, mental, or sexual harm or suffering, threats of such acts, coercion, and other deprivations of liberty. It is psychological, physical, and sexual violence committed or allowed in the family, the general public, or by the state and its institutions (33).

Although cyber violence can affect both men and women, women experience it differently and are more traumatic forms of cyber violence (34). The evidence provides various forms of cyber violence against women, such as cyberstalking, cyber harassment, cyberbullying, online sexual harassment, and nonconsensual pornography (35). The United Nations Broad Commission (2015) (23) shows that women aged 18-24 experience several forms of cyber violence. They suffer disproportionately from cyberbullying, cyber harassment, cyberstalking, or online sexual harassment. The report further shows that in the EU 28 membership, 18% of women have experienced cyber violence in the form of online hatred, harassment, cyberstalking, and others since the age of 15. This prevalence figure represents 28 million women (23). Sargent et al.

(2016) (36) found that more than 50% of girls aged over 13 years in Slovenia experienced some form of cyber violence.

Online violence is direct or indirect online communication expressed in an aggressive, exploitative, manipulative, threatening or obscene manner and designed to cause fear, emotional or psychological, upset, distress, alarm or feelings of inferiority (37). There is a clear emphasis on emotional impact in this definition. Experiencing GBV online can be very damaging and demoralizing. Another study observed that online harassment can cause harm to the victim in powerful ways; it can expose a woman to symptoms of post-traumatic stress disorder, mainly if the abuse occurs frequently (5).

In addition, evidence shows that women who experience GBV report higher rates of depression, having abortions, and contracting HIV, compared to women who do not share it (38). Research also shows that this violence results in immediate and long-term physical, mental, and sexual health problems. The poor health outcomes associated with this violence are compared in importance to those arising from many other, more well-known health risk factors (39,40). For example, a study using the disease burden method in Australia found that among women aged 18 to 44 years, GBV is associated with 7% of the disease burden. This violence is more important than the factors usually considered, such as high blood pressure (hypertension), smoking, and being overweight (41).

GBV has been found to have adverse effects on women, including injury, sexual and reproductive health problems, mental health disorders, sexually transmitted infections, gynecological disorders, adverse pregnancy outcomes, increased risk of non-communicable diseases, and impact on health, and the welfare of their children (42). Another health effect of GBV is improving women's risk of several other health problems, including chronic pain, physical disability, drug and alcohol abuse, and depression (43). GBV also has a negative W-gate impact on a country's human, social, and economic development and is an underlying obstacle to eliminate poverty and build peace (44).

In this study, cyber gender-based violence had the most significant impact on adolescent psychology, namely 265 (55%). Victims or survivors experience depression, anxiety, and fear. In addition, there are also specific points where some victims or survivors express suicidal thoughts due to the danger they face (45). According to Yaya et al. (2021) and Wondimu (2019), social and psychological effects impact on social relationships. Social and psychological impacts in the form of decreased academic achievement, reduced self-esteem, health problems, and mental problems (anxiety and depression) are the results that are most felt (46,47).

CONCLUSION

Based on this research, the most dominant impact of gender-based violence on cyber is the psychological, physical, social, cultural, and economic impacts. Good education, especially for children, must be carried out intensively so that children are kept away from the potential to fall into cybercrime. The Ministry of Communication and Informatics, schools, and families can carry out education. The government must formulate a strategy to address cyber violence against women. Governments, civil society, and other private actors should advocate for awareness-raising campaigns for women about cyber violence. This awareness and training can help women be empowered and decide where to seek social or legal support if they have been abused online. The Internet and other online platforms, such as Facebook, should make clear options for removing online images or abusive content. They must also respond promptly and effectively to complaints from victims of online abuse and finally make genuine agreements to terms of use.

Conflict of Interest

The researcher declares that there is no conflict of interest in this study so that the research is guaranteed to have no problems between members and the article's authorship.

REFERENCES

1 . Hughes DJ, Rowe M, Batey M, Lee A. A tale of two sites: Twitter vs. Facebook and the personality predictors of social media usage. Comput Human Behav. 2012;28(2):561-569.

2. Reyns BW, Henson B, Fisher BS. Being pursued online: Applying cyber lifestyle–routine activities theory to cyberstalking victimization. Crim Justice Behav. 2011;38(11):1149-1169.

3. Litchfield C, Kavanagh E. Twitter, Team GB and the Australian Olympic Team: representations of gender in social media spaces. Sport Soc. 2019;22(7):1148-1164.

4. Sharma MK, Anand N, Thakur PC, Suma N, Biswas A, Archana R, et al. Cyber violence: Case report evidence of an emerging public health concern. Asian J Psychiatr. 2021;57:102017.

5. Lewis R, Rowe M, Wiper C. Online abuse of feminists as an emerging form of violence against women and girls. Br J Criminol. 2017;57(6):1462-1481.

6. Hinduja S, Patchin JW. Personal information of adolescents on the Internet: A quantitative content analysis of MySpace. J Adolesc. 2008;31(1):125-146.

7. Lim SS, Chan YH, Vadrevu S, Basnyat I. Managing peer relationships online–Investigating the use of Facebook by juvenile delinquents and youths-at-risk. Comput Human Behav. 2013;29(1):8-15.

8. Ging D, Siapera E. Special issue on online misogyny. Feminist media studies. Taylor & Francis; 2018;18:515-524.

9. Kavanagh E, Brown L. Towards a research agenda for examining online gender-based violence against women academics. J Furth High Educ. 2020;44(10):1379-1387.

10. Moloney ME, Love TP. Assessing online misogyny: Perspectives from sociology and feminist media studies. Sociol Compass. 2018;12(5):e12577.

11. Mayor Buzón V, García Pérez R, Rebollo Catalán M de los Á. Explorando factores predictores de la competencia digital en las redes sociales virtuales. Pixel-Bit. 2019.

12. Vickery JR, Everbach T. Mediating misogyny. Gender Technol. 2018.

13. UNESCO. Cyber Violence Against Women And Girls: A World-wide Wake-up Call. 2015.

14. Amnesty International. Amnesty reveals alarming impact of online abuse against women. 2017. Available from: https://www.amnesty.org/en/latest/press-release/2017/11/amnesty-reveals-alarming-impact-of-online-abuse-against-women/

15. Komnas Perempuan. Violence on the rise " Policies to eliminate sexual violence to built safe spaces for women and girls. Annu Rec violence against women. 2020:1-109.

16. Ratnasari E, Sumartias S, Romli R. Social Media, Digital Activism, and Online Gender-Based Violence in Indonesia. Nyimak J Commun. 2021;5(1):97-116.

17. Yusuf A, Habibie AN, Efendi F, Kurnia ID, Kurniati A. Prevalence and correlates of being bullied among adolescents in Indonesia: Results from the 2015 Global School-based Student Health Survey. Int J Adolesc Med Health. 2022;34(1).

18. Charlton C, Mani RR, Chinnappan S, Balaraman AK, Muthusamy T, Paranjothy C, et al. Bibliometric and Density Visualisation Mapping Analysis of Domestic Violence in Australia Research Output 1984–2019. Int J Environ Res Public Health. 2022;19(8).

19. Sharma E, Seshadri SP. Adolescence: contemporary issues in the clinic and beyond. Asian J Psychiatr. 2020;47:101803.

20. Ooi K-B, Lee V-H, Hew J-J, Lin B. Mobile Social Cyberbullying: Why are Keyboard Warriors Raging? J Comput Inf Syst. 2021;61(4):371-382.

21. Dredge R, Gleeson J, de la Piedad Garcia X. Cyberbullying in social networking sites: An adolescent victim's perspective. Comput Human Behav. 2014;36:13-20.

22. West J. Cyber-violence against women. Battered Women's Support Services; 2014.

23. UN Women. Urgent action needed to combat online violence against women and girls, says new UN report. 2015. Available from: https://www.unwomen.org/en/news/stories/2015/9/cyber-violence-report-press-release

24. WHO. Violence against women. World Health Organisation. 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/violence-against-women

25. Rohmana DY, Estelina K, Iskandar I. The Bullying Phenomenon and Handling Efforts in Reducing Cases of Bullying: A Systematic Review. J Ners. 2020;15(1 Special Issue):557-562.

26. Laksono A, Wulandari R, Matahari R, Suharmiati. Socioeconomic differences of intimate partner violence among married women in Indonesia: Does poverty matter? Indian J Community Med. 2023;48(2):304-309.

27. Fanani FDN, Fatah MZ. Identification of social support for children as survivors of domestic violence at the Surabaya Embun Foundation. Indones J Public Heal. 2022;17(1):52-60.

28. Sutinah, Kinuthia KM. Trafficking of women and children in East Java, Indonesia. J Int Womens Stud. 2019;20(9):94-106.

29. Banda BM. Socio-cultural factors associated with gender-based violence in Chipata city, Zambia. Texila Int J Publ Heal. 2019;7(4):232-243.
30. Beyene AS, Chojenta CL, Loxton DJ. Consequences of gender-based violence on female high school students in eastern Ethiopia. Afr J Reprod Health. 2021;25(4):22-33.
31. Sikweyiya Y, Addo-Lartey AA, Alangea DO, Dako-Gyeke P, Chirwa ED, Coker-Appiah D, et al. Patriarchy and gender-inequitable attitudes as drivers of intimate partner violence against women in the central region of Ghana. BMC Public Health. 2020;20:1-11.
32. WHO. World report on violence and health. Geneva: World Health Organisation; 2002.
33. Ellis E. Gender-based violence is South Africa's second pandemic, says Ramaphosa. Dly Maverick. 2020;18.
34. Friesen J, Kay A, Eibach R, Galinsky A. Seeking Structure in Social Organization: Compensatory Control and the Psychological Advantages of Hierarchy. J Pers Soc Psychol. 2014;106(4):590-609.
35. West J. Cyber-Violence Against Women Prepared for Battered Women's Support Services. 2014; Available from: http://www.apc.org/en/system/files/APCWNSP_MDG3advocacypaper_full_2011_EN_0.pdf
36. Sargent KS, Krauss A, Jouriles EN, McDonald R. Cyber Victimization, Psychological Intimate Partner Violence, and Problematic Mental Health Outcomes Among First-Year College Students. Cyberpsychol Behav Soc Netw. 2016;19(9):545-550.
37. Kavanagh E, Jones I, Sheppard-Marks L. Towards typologies of virtual maltreatment: Sport, digital cultures & dark leisure. In: Re-thinking leisure in a digital age. Routledge; 2020.p.75-88.
38. United Nations. UN Women Annual Report 2018-2019. UN Women. 2018.
39. Mas'udah S. Power Relations of Husbands and Wives Experiencing Domestic Violence in Dual-Career Families in Indonesia. Millenn Asia. 2023;14(1):5-27.
40. Kusuma MSE, Purwanti T. Children death with child abuse: A case report at bhayangkara hospital, kediri indonesia. Indian J Forensic Med Toxicol. 2020;14(4):3544-3549.
41. Hegarty KL, Andrews S, Tarzia L. Transforming health settings to address gender-based violence in Australia. Med J Aust. 2022;217(3):159-166.
42. Tristiana RD, Pratiwi IN, Wulansari D, Yusuf A, Sulistyono RE. Adolescences experience of gender-based violence: A qualitative study. Int J Public Heal Sci. 2023;12(2):822-830.
43. Zengenene M, Susanti E. Violence against women and girls in Harare, Zimbabwe. J Int Womens Stud. 2019;20(9):83-93.
44. Murhula PBB, Singh SB, Myende SM. The COVID-19 pandemic and its impact on gender-based violence: A global review and analysis. Int J Crim Justice Sci. 2021;16(1):84-96.
45. Kusuma E, Arum NS. Memahami dan Menyikapi Kekerasan Berbasis Gender Online: Sebuah Panduan. Retrieved June. 2019;10:2021.
46. Yaya S, Hudani A, Buh A, Bishwajit G. Prevalence and predictors of intimate partner violence among married women in Egypt. J Interpers Violence. 2021;36(21-22):10686-10704.
47. Wondimu H. The implication of gender-0ased violence on the academic achievement of female students, in the case of Aba Fransua High School of Wolkite Town. Ann Soc Sci Manag Stud. 2019;4(2):47-54.

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Effect of ACTH4-10pro8-gly9-pro10 on malondialdehyde and F2-isoprostane 15(S)-8-iso-PGF2a expression in rat spinal cord injury

Efecto del ACTH4-10pro8-gly9-pro10 en la expresión de malondialdehído y F2-isoprostano 15(S)-8-iso-PGF2a en ratas con lesión de médula espinal

Rifqi Aulia Destiansyah[1a], Eko Agus Subagio[2a*], Muhammad Arifin Parenrengi[3a], Budi Utomo[4b], Muhammad Faris[5a], Abdul Hafid Bajamal[6a], Diaz Syafrie Abdillah[7c]

SUMMARY

Background: *Spinal cord injury (SCI) is damage to the spinal cord caused mainly by trauma resulting in major motor, sensory, and autonomic dysfunctions. This experimental study aims to assess the effect of ACTH4-10Pro8-Gly9-Pro10 administration in rats with mild and severe compression injuries on the levels of malondialdehyde and F2-isoprostane 15(S)-8-iso-PGF2α levels.*
Methods: *Mild and severe spinal cord compression was performed on 27 subjects. They were divided into three groups of samples with control included, 3 and 6 h after the injury. Spinal cord tissue was taken to determine MDA and F2-isoprostane expression under the microscope, and control samples were compared to samples given ACTH4-10Pro8-Gly9-Pro10.*
Results: *In 3- and 6-h-mild ASCI that $ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10} is given, MDA expression was lower (8.40 ± 1.94 and 8.60 ± 1.67) than the control group (12.60 ± 2.6 and 14.40 ± 1.81). Meanwhile, severe ASCI that $ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10} also exhibited lower MDA expression (9.8 ± 2.16 and 12.2 ± 1.92) than the control group (16.2 ± 1.6 and 16.40 ± 2.07). This is in line with the lower expression of F2-isoprostane in acute myelin injuries with mild (5.0 ± 2.0 and 7.6 ± 1.34) and severe (8.0 ± 2.23 and 11.8 ± 1.84) compression. 1.64) compared to controls (mild: 12.8 ± 3.03 and 13.8 ± 2.58; severe: 15.4 ± 2.60 and 16.4 ± 2.30) at 3- and 6-hours post-wound.*
Conclusion: *Administration of $ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10} decreased MDA and F2 isoprostane expression in mild and severe spinal cord compression models. Thus, it might become adjuvant therapy for spinal cord injury to prevent further secondary injury.*

Keywords: *$ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10}, spinal cord injury, reactive oxygen species, malondialdehyde, F2-isoprostane.*

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ORCID: 0000-0001-8933-8785[1]
ORCID: 0000-0002-6790-3779[2]
ORCID: 0000-0002-1327-8955[3]
ORCID: 0000-0001-6060-9190[4]
ORCID: 0000-0002-8377-6773[5]
ORCID: 0000-0003-3824-6973[6]
ORCID: 0000-0001-8387-1052[7]

[a]Department of Neurosurgery, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

[b]Department of Public Health and Preventive Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[c]Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia

*Corresponding author: eko.agus@fk.unair.ac.id

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RESUMEN

Antecedentes: *Lesión de la médula espinal es un daño a la médula espinal causado principalmente por traumatismos que resultan en disfunciones motoras, sensoriales y autónomas importantes. Este estudio experimental tiene como objetivo evaluar el efecto de la administración de ACTH4-10Pro8-Gly9-Pro10 en ratas con lesiones por compresión leves y graves en los niveles de malondialdehído y los niveles de F2-isoprostanos 15(S)-8-iso-PGF2α.*

Métodos: *Se realizaron compresiones medulares leves y graves en 27 sujetos, que luego fueron divididos en tres grupos de muestras con control incluido, 3 y 6 horas tras la lesión. Se tomaron muestras de tejido medular para determinar la expresión de MDA y F2-isoprostano en el microscopio, y se compararon con muestras de control a las que se había suministrado ACTH410Pro8-Gly9-Pro10.*

Resultados: *En las muestras de lesiones leves 3 y 6 horas a las que se había administrado $ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10}, la expresión de MDA fue menor (8,40 ± 1,94 and 8,60 ± 1,67) que en el grupo de control (12,60 ± 2,6 and 14,40 ± 1,81). Por otro lado, en las lesiones graves con $ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10} también se halló una expresión de MDA menor (9,8 ± 2,16 and 12,2 ± 1.92) que en el grupo de control (16,2 ±1,6 and 16,40 ± 2,07). Esto es coherente con la expresión menor de F2isoprostano en las lesiones agudas de mielina con compresión leve (5,0 ± 2,0 and 7,6 ± 1,34) y grave (8,0 ± 2,23 and 11,8 ± 1,84) comparada con las muestras de control (leve: 12,8 ± 3,03 y 13,8 ± 2,58; grave: 15,4 ± 2,60 y 16,4 ± 2,30) 3 y 6 horas tras la lesión.*

Conclusión: *La administración de ACTH4-10Pro8-Gly9-Pro10 disminuyó la expresión de MDA y los isoprostanos F2 en el modelo de compresión de la médula espinal leve y grave. Por lo tanto, podría convertirse en una terapia coadyuvante para lesiones de la médula espinal, con el fin de prevenir lesiones secundarias adicionales.*

Palabras clave: *$ACTH_{4-10}Pro^{8}$-Gly^{9}-Pro^{10}, lesión medular, especies reactivas del oxígeno, malondialdehído, F2-isoprostano.*

INTRODUCTION

Spinal cord injury (SCI), also known as myelin injury, is a medical condition with a high morbidity rate due to the limited capacity of central axon regeneration. This limitation arises from the distinctive properties of glial cells in the central nervous system (CNS), preventing them from adapting to an environment conducive to localized healing (1). Myelin injury represents a significant contributor to human morbidity, presenting a formidable challenge in terms of treatment. When examining the progress achieved in terms of outcomes, it becomes apparent that advancements in palliative care and functional recovery have been relatively stagnant in comparison to other significant developments witnessed in the history of modern medicine (2).

In the United States, more than one million individuals experience paralysis because of spinal cord injuries. Among healthy individuals aged 19 to 29 years, acute spinal cord injury (ASCI) represents the most prevalent type of injury, leading to many patients suffering from significantly diminished quality of life for extended periods following the injury (3). According to data from Fatmawati General Hospital, Jakarta, Indonesia in 2014, out of 104 cases, 37 were attributable to traumatic causes, while 67 were non-traumatic in nature (4). Similarly, data obtained from Dr. Soetomo General Academic Hospital in Surabaya for the period 2013-2017 revealed 442 patients with spinal fractures, with a higher incidence among males compared to females, with a ratio of 3.3:1 (5).

Since the discovery of antibiotics, the prevention of complications, and the introduction of unique treatment methods, developments in the treatment of spinal injury patients have made significant progress (6). Several studies of spinal injuries in mammals show that injury recovery is supported by compensatory anatomical plasticity of the entire nervous system, so the survival rate of spinal injury patients has increased rapidly. However, to date, no effective therapy that improves sufferers' neurological and functional conditions is reported (7).

The development of surgical techniques has made it possible to decompress the spinal nerves, restore normal spinal curvature, and stabilize and/or fusion. The primary objective of these interventions is to alleviate pain, promote early mobilization and rehabilitation, minimize the duration of treatment, and prevent secondary complications associated with disability (8).

ACTH4-10 (ACTH4-10Pro8-Gly9-Pro10) is a neuroprotective agent commonly used in stroke, head injury, and Alzheimer's patients. Its

structure is similar to melanocortin, which can bind to melanocortin receptors and provide anti-inflammatory effects. To date, no data or reports regarding serious side effects from its use (9). ACTH4-10 administration is known to reduce the apoptosis rate of neuron cells in acute spinal cord compression injury in Sprague-Dawley rats by increasing the Bcl-2/HSP70 ratio (10). Other studies show that giving ACTH4-10 can also reduce pro-inflammatory mediators TLR-2, NF-kB, IL-8, and TNF-α in Sprague-Dawley rats treated with acute spinal cord compression injury (11).

Spinal cord injury pathology is influenced by an intricate cascade process, one of the most significant is oxidative stress, which is caused by the formation of free radicals and lipid peroxidation (12). Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxidation in the cells. An increase in free radicals causes the overproduction of MDA. Malondialdehyde level is commonly known as a marker of oxidative stress (13). F2-isoprostane 8-iso-$PGF_{2\alpha}$ is a thromboxane A_2 (TXA_2) receptor agonist, which is a stable biomarker of oxidative stress (14). Therefore, understanding ACTH4-10Pro8-Gly9-Pro10's influence to reduce oxidative stress markers, such as malondialdehyde (MDA) and F2-isoprostane, could provide valuable insights into potential therapeutic strategies for spinal cord injury (15).

This study used Sprague-Dawley rats as a spinal injury model, clamped with clips to produce light and heavy compression. The experimental animals were then given intranasal ACTH4-10Pro8-Gly9-Pro10. Myelin was taken for immunohistochemical examination to identify malondialdehyde (MDA) and F2-Isoprostan 15(S)-8-iso-PGF2α to determine its effect.

MATERIALS AND METHODS

Animals

Twenty-seven white male Sprague-Dawley rats aged 12 weeks (250-300 g) were randomly selected and divided into the control and treatment groups. The rats were acclimatized for two weeks for adaptation in the rearing facility. The rat food was given in the form of pellets. Food and drink for experimental animals were given ad libitum, and the cage temperature was maintained at around 25°C, with dark- light cycle every 12 h. Each group of rats was placed in a separate cage and kept so that they did not interact with each other.

Anesthesia was carried out by administering ketamine combined with xylazine. Ketamine was injected intraperitoneally using a 10 mL syringe containing 10 mL of ketamine (100 mg/mL) and 1 mL of xylazine (100 mg/mL). The drug mixture was injected as much as 0.1 mL/100 g of rat body weight. The drug mixture contains 91 mg/kg of ketamine and 9.1 mg/kg of xylazine. The loss of the carpopedal reflex served as an indicator that the anesthetic agent had been adequately administered, signaling that the surgical procedure could commence immediately. The duration of the anesthetic agent's effect was approximately 60-80 min. Following the injection, the hemodynamic function was monitored. This included observing the mucous membranes, which should appear pink and moist, as well as assessing the capillary refill time, which should be less than 2 seconds (16).

For the compression procedure, modified aneurysm clips were employed as compression devices, calibrated to exert clamping forces of 20 g and 35 g. After performing a laminectomy and exposing the dura, the aneurysm clip was affixed to the myelin. Compression was applied for 1 minute, then released and closed again using sutures (17).

Fabrication of tissue block paraffin

The myelin tissue underwent an initial washing step with PBS (Phosphate Buffered Saline) for 3-5 cycles to eliminate contaminants. Subsequently, the tissue was fixed in 10 % formalin. Dehydration of the tissue was then carried out using a series of graded ethanol solutions, where each concentration (30 %, 50 %, 70 %, 80 %, 96 %, and absolute) was applied for 60 minutes. Following dehydration, a clearing process was performed, involving two immersions of 60 min each in xylene. Subsequent infiltration was achieved by subjecting the tissue to soft paraffin at a temperature of 48°C for 60 min. A block was then created using hard paraffin in a mold, allowing it to solidify over a day. On the following

day, the block was sectioned into slices measuring 4-6 μm in thickness using a rotary microtome. These sections were subsequently mounted on glass slides using 5 % gelatin. To process the slides obtained from the paraffin block, they were immersed in xylene twice, with each immersion lasting 5 min. Subsequently, rehydration was carried out by exposing the slides to a series of sequential alcohol solutions (absolute, 96 %, 80 %, 70 %, 50 %, and 30 %) for 5 min each. Finally, the slides were rinsed in H_2O for 5 min.

Determination of MDA and F2-isoprostane expression

The slides underwent a 5-min washing step with PBS pH 7.4. The blocking procedure was performed using 3 % H_2O_2 for 20 min. The subsequent washing procedure consisted of three repetitions, each lasting 5 min, employing PBS pH 7.4. A 5 % FBS and 0.25 % Triton X-100 solution were employed for protein unspecific blocking. The washing process was repeated three times, each lasting 5 min, employing PBS pH 7.4. Incubation with anti-MDA and anti-F2 isoprostane polyclonal rabbit antibody was conducted for 60 minutes. The washing process, consisting of three repetitions lasting 5 minutes each, was carried out using PBS pH 7.4. Subsequently, the slides were treated with Diaminobenzidine (DAB), incubated for 10 minutes, and subjected to a three-time washing process, each lasting 5 minutes, utilizing PBS pH 7.4. Counterstaining was performed using Mayer Hematoxylin, with a set duration of 10 minutes, followed by washing with tap water, rinsing with H_2O, air-drying, and subsequent observation under a light microscope.

Data Analysis

Data normality analysis was performed using Kolmogorov-Smirnov. Data on levels of MDA and F2-Isoprostan were analyzed using the Paired T-test and ANOVA.

RESULTS

MDA Expression on Paraffin Block IHC Staining Animal Model of Acute Spinal Cord Compression Injury

In this study, a total of three samples were collected from each control group and treatment group, specifically observing the effects of distilled water and ACTH4-10Pro8-Gly9-Pro10 at 3 and 6 h. The samples were obtained from rats subjected to both light and heavy compression injuries, aiming to evaluate the expression of immunoreactivity to MDA staining, which serves as an indicator of the response to ACTH4-10 in the spinal cord injury (SCI) model. To assess the effects of ACTH4-10, cross-sections of the rat spinal cord were obtained from rats treated with mild acute spinal cord compression injury (ASCI). These sections were then dripped with 0.9 % NaCl solution and sacrificed after 3 hours (K+1.1). Subsequently, the sections were examined under a microscope at a magnification of 400x.

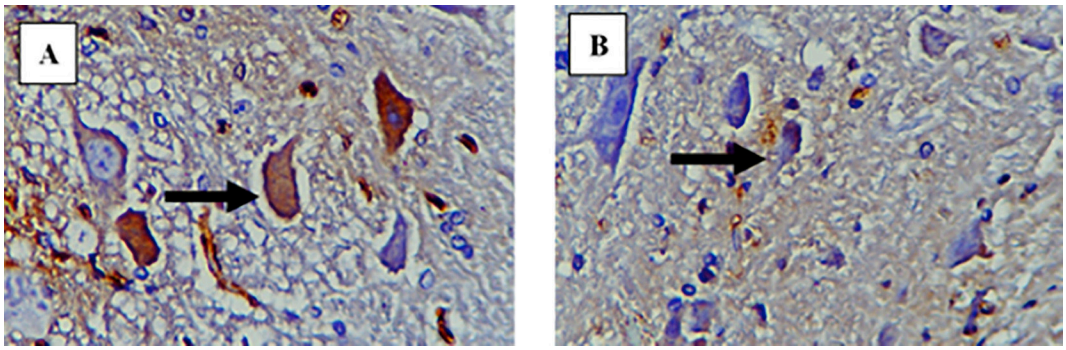

Figure 1. Cross-section of the spinal cord of rats treated with mild ASCI and sacrificed after 3 hours of staining with IHC MDA (A) dripped with 0.9 % NaCl (B) dripped with ACTH4-10Pro8-Gly9-Pro10

Positive neuronal responses expressing MDA were identified using black arrows (Figure 1. A). It was observed that the preparation dripped with ACTH4-10Pro8-Gly9-Pro10 drops significantly reduced the response of neurons expressing MDA (Figure 1. B).

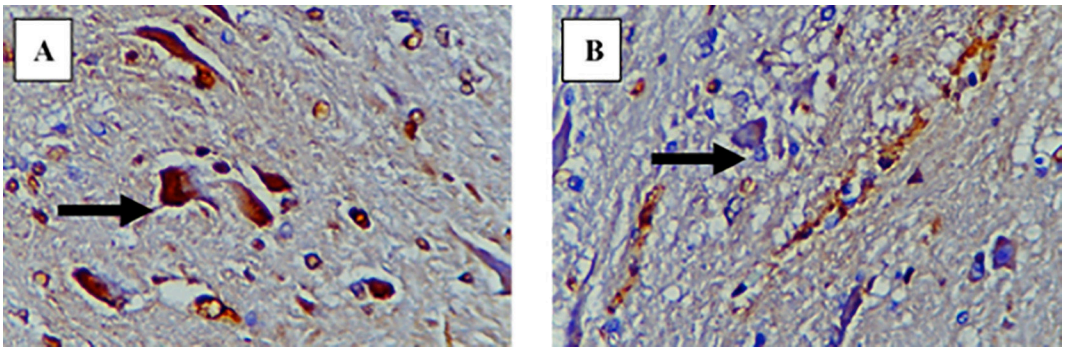

Figure 2. Cross-section of the spinal cord of rats treated with severe ASCI and sacrificed after 6 hours of staining with IHC MDA (A) dripped with 0.9 % NaCl (B) dripped with ACTH4-10Pro8-Gly9-Pro10.

Figure 2A illustrates a cross-section of the spinal cord from rats subjected to severe acute spinal cord injury. The section was treated with 0.9 % NaCl solution and sacrificed after 6 h. The image was captured using a microscope at a magnification of 400x. Positive neuronal responses expressing MDA are indicated by black arrows. In Figure 2B, it can be observed that the response of neurons expressing MDA was significantly reduced when the preparation with ACTH4-10Pro8-Gly9-Pro10 drops was administered.

F2-Isoprostane Expression on Paraffin Block IHC Staining Animal Model of Acute Spinal Cord Compression Injury

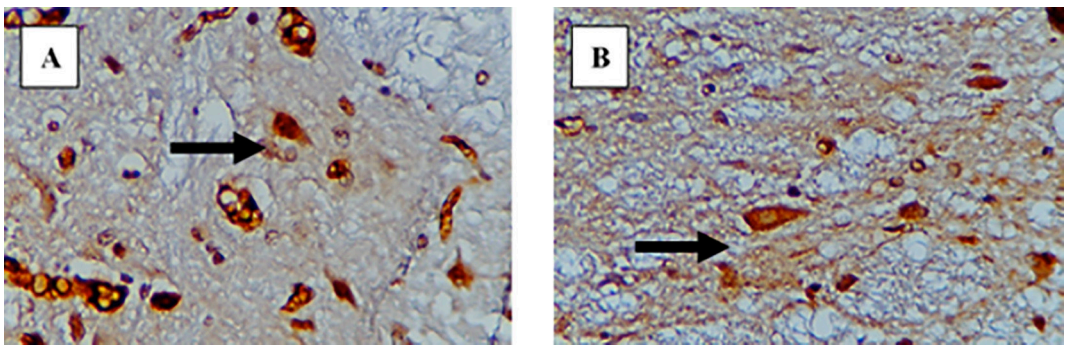

Figure 3. Cross-section of the spinal cord of rats treated with mild ASCI and sacrificed after 3 h of staining with IHC F2 Isoprostane (A) dripped with 0.9 % NaCl (B) dripped with ACTH4-10Pro8-Gly9-Pro10

Figure 3A presents a cross-section of the spinal cord from rats treated with mild acute spinal cord injury. The section was dripped with 0.9 % NaCl solution and sacrificed after 3 hours (K+1.1). The image was captured using a microscope at a magnification of 400x. Positive neuronal responses expressing F2-isoprostane are indicated by black arrows. In Figure 3B, it

can be observed that the preparation given with ACTH4-10Pro8-Gly9-Pro10 drops significantly reduced the response of neurons expressing F2-isoprostane.

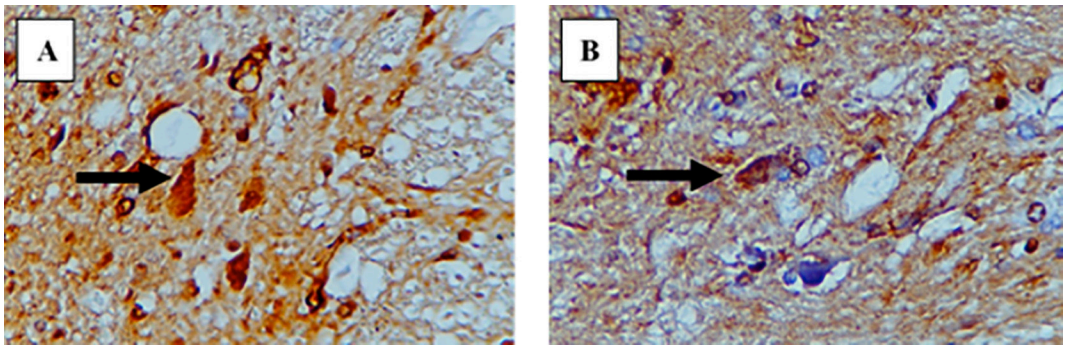

Figure 4. Cross-section of the spinal cord of rats treated with severe ASCI and sacrificed after 6 hours of staining with IHC F2 Isoprostane (A) dripped with 0.9 % NaCl (B) dripped with ACTH4-10Pro8-Gly9-Pro10.

Figure 4. A illustrates a cross-section of the spinal cord from rats subjected to severe acute spinal cord injury. The section was treated with 0.9 % NaCl solution and sacrificed after 6 h. The image was captured using a microscope at a magnification of 400x. Positive neuronal responses expressing F2-isoprostane are indicated by black arrows. Similarly, in Figure 4. B it can be observed that the preparation with ACTH4-10Pro8-Gly9-Pro10 drops led to a significant reduction in the response of neurons expressing F2-isoprostane.

The Results of The Expression of MDA and F2-isoprostane in Each Group

Table 1. MDA Expression in The Mild and Severe ASCI Group

Group	MDA Expression		
	Mean	Standard deviation	P
Mild ASCI NaCl 0.9 % 3 h	12.60	2.60	-
Mild ASCI NaCl 0.9 % 6 h	14.40	2.45	-
Mild ASCI ACTH4-10Pro8-Gly9-Pro10 3 h	8.40	1.4	0.022
Mild ASCI ACTH4-10Pro8-Gly9-Pro10 6 h	8.60	1.67	0.003
Severe ASCI NaCl 0.9 % 3 h	16.20	2.16	-
Severe ASCI NaCl 0.9 % 6 h	16.40	2.07	-
Severe ASCI ACTH4-10Pro8-Gly9-Pro10 3 h	9.80	2.16	0.002
Severe ASCI ACTH4-10Pro8-Gly9-Pro10 6 h	12.20	1.92	0.011

Regarding the expression of MDA in each respective group, it was observed that the group receiving ACTH4-10Pro8-Gly9-Pro10 and sacrificed at 3 and 6 h exhibited a significant reduction in the mean value compared to the group that did not receive ACTH4-10Pro8-Gly9-Pro10 (Table 1).

Table 2. F2 Isoprostane Expression in The Mild and Severe ASCI Group

Group	F2 Isoprostane Expression		
	Mean	Standard deviation	P
Mild ASCI NaCl 0.9% 3 hours	12.80	3.03	-
Mild ASCI NaCl 0.9% 6 hours	13.80	2.58	-
Mild ASCI ACTH4-10Pro8-Gly9-Pro10 3 h	5.0	2.0	0.002
Mild ASCI ACTH4-10Pro8-Gly9-Pro10 6 h	7.60	1.34	0.003
Severe ASCI NaCl 0.9% 3 h	15.40	2.60	-
Severe ASCI NaCl 0.9% 6 h	16.40	2.30	-
Severe ASCI ACTH4-10Pro8-Gly9-Pro10 3 h	8.0	2.23	0.001
Severe ASCI ACTH4-10Pro8-Gly9-Pro10 6 h	11.80	1.64	0.008

Likewise, in terms of F2-isoprostane expression, the group subjected to ACTH4-10Pro8-Gly9-Pro10 administration and sacrificed at 3 and 6 h demonstrated a notable decrease in the mean value in comparison to the group without ACTH4-10Pro8-Gly9-Pro10 administration (Table 2).

DISCUSSION

The findings of this study revealed that rat with mild acute spinal cord injury (ASCI), who received ACTH4-10Pro8-Gly9-Pro10 and were sacrificed at 3 h and 6 h post-treatment, exhibited a decreased expression of MDA compared to the group treated with 0.9 % NaCl. Specifically, in the treatment group of mild ASCI rats administered with ACTH4-10Pro8-Gly9-Pro10, the MDA expression was measured at 8.60 (1.67), which was significantly lower than the group treated with 0.9 % NaCl, measuring 12.60 (2.60). These results were statistically significant between the two groups, with p-values after 3 h and 6 h being 0.022 and 0.003, respectively.

In the severe ASCI treatment group given ACTH4-10Pro8-Gly9-Pro10 and sacrificed after 3 and 6 h, the MDA expressions were 9.80 (2.16) and 12.20 (1.92), respectively, lower than the group given 0.9 % NaCl, namely 16.20 (2.16) and 16.40 (2.07). These results were also statistically significant, with p values after 3 h and 6 h of 0.002 and 0.011. From the above data, the mild and severe ASCI given ACTH4-10Pro8-Gly9-Pro10 showed a decrease in the expression of MDA, which was lower and statistically significant compared to the group given 0.9 % NaCl. This finding supports Puspita et al., who reported that administration of ACTH4-10Pro8-Gly9-Pro10 could reduce MDA levels from 86.31 % from 3.11 ± 0.028 μg/mL to 40.46 % from 1.85 ± 0.020 μg/mL. This is possibly accounted for by the transformation mechanism of the metabolic chain that reduces inflammatory factors and increases anti-inflammatory factors. Where ACTH4-10 peptides induce this mechanism, this reaction also reduces lipid peroxidation. ACTH4-10 peptides act as antioxidants that inhibit the formation of free radicals and prevent or inhibit lipid peroxidation. The hydroxyl group (OH) on the ACTH4-10 peptide may serve as an antioxidant. The mechanism of inhibition of free radicals by ACTH4-10 is by covering the hydroxyl groups and donating hydrogen atoms to lipid radicals. ACTH4-10 peptide suppresses the activity of the lipooxygenase enzyme, resulting in damage due to oxidative stress. The radicals from ACTH4-10 peptides are relatively more stable than lipid radicals, so the radicals from ACTH4-10 peptides do not have enough energy to react with other lipid molecules to form new lipid radicals. Thus, the ACTH4-10 peptide can reduce MDA levels (18).

The F2-isoprostane 8-iso-$PGF_{2\alpha}$, a TXA2 agonist is a stable biomarker of oxidative stress. In the mild ASCI treatment group given ACTH4-10Pro8-Gly9-Pro10 and sacrificed after 3 and 6 h, the expression of F2-isoprostane was lower compared to the group treated with

0.9 % NaCl. The expression of F2-isoprostane in the ACTH4-10Pro8-Gly9-Pro10 group was 5.0 (2.0), whereas, in the 0.9 % NaCl group, it was 12.80 (3.03). These differences in F2-isoprostane expression between the two groups were statistically significant, with p-values of 0.002 and 0.003 after 3 h and 6 h, respectively.

In the severe ASCI treatment group given ACTH4-10Pro8-Gly9-Pro10, the expression of F2-isoprostane was lower compared to the group treated with 0.9 % NaCl. After 3 h and 6 h, the expression of F2-isoprostane in the ACTH4-10Pro8-Gly9-Pro10 group was 8.0 (2.23) and 11.80 (1.64), respectively, while in the 0.9 % NaCl group, it was 15.40 (2.60) and 16.40 (2.30). From the above data, the mild and severe ASCI given ACTH4-10Pro8-Gly9-Pro10 showed a decreased F2-isoprostane expression, which was lower and statistically significant compared to the group given 0.9 % NaCl. The findings from our study support the previous research by Erny et al., which demonstrated that ACTH4-10 administration can reduce the level of prostaglandin E2 associated with NFkB caused by transcription factors (19).

In previous studies, ACTH4-10Pro8-Gly9-Pro10 has been utilized for the treatment and prevention of brain injury complications (20). Although ACTH4-10Pro8-Gly9-Pro10 application in spinal cord injury (SCI) remains limited, it holds promising potential as a therapeutic intervention. The timing of ACTH4-10Pro8-Gly9-Pro10 administration was selected within the initial 3 hours following SCI. This decision is based on considerations from glial cell cultures derived from newborn rat brains, which demonstrated that ACTH4-10Pro8-Gly9-Pro10 led to a rapid reduction in MDA and F2-isoprostane mRNA levels within a maximum duration of 40-60 minutes. Therefore, it can be inferred that alterations in protein levels are likely to be evident within a short duration of approximately 3 hours following the administration of ACTH4-10Pro8-Gly9-Pro10. Furthermore, the main goal of this study is to determine the optimal time window for administering ACTH4-10Pro8-Gly9-Pro10 in spinal cord injury (SCI) cases. The primary objective of administering ACTH4-10Pro8-Gly9-Pro10 is to alleviate secondary injury processes that hinder nerve regeneration, typically occurring within 24 h of the primary injury. Numerous factors influence the development of secondary injury, including hypoxia, ischemia, oxidative stress, and inflammatory mediators. It is worth noting that the characteristics of these factors may differ between humans and other mammals. In this study, rats were used. Furthermore, the clinical administration of ACTH4-10Pro8-Gly9-Pro10 serves as a neuroprotective agent with the potential to modulate neurotransmitters, thereby inhibiting apoptosis and stimulating the production of neuronal protective substrates. In Filipenkov et al. study that used transient occlusion of the middle cerebral artery (MCA), administration of ACTH4-10Pro8-Gly9-Pro10 after 24 h after the injury affected 394 differentially expressed genes (DEGs), both upregulated and downregulated genes, specifically indicating a suppressive effect on inflammatory genes and roles in activating neurotransmitters and initiating the expression of mRNAs that are naturally impaired in ischemia (21).

In another study conducted by Loe et al. in 2020 using a brain injury model, ACTH4-10 Pro8-Gly9-Pro10 was reported to increase neuronal progenitor stem cells (NPSCs) in the subgranular zone of the hippocampal dentate gyrus (20). The results of this study can be used as the basis for further research on the effect of ACTH4-10 Pro8-Gly9-Pro10 administration on stem cell expression levels in models of acute myelin compression injury.

CONCLUSIONS

Administration of ACTH4-10Pro8-Gly9-Pro10 decreases MDA and F2-isoprostane expression in mild and severe spinal cord compression models. Thus, it might become adjuvant therapy for spinal cord injury to prevent further secondary injury.

REFERENCES

1. Ardananurdin A, Subagio EA, Utomo B. Spinal Cord ' s IL-1 , TNF-α and NF-ϰB Expression in Sprague-Dawley Rat on Acute Spinal Cord Injury. Indonesian J Neurosurg. 2020;3:109-114.
2. McGrath R, Hall O, Peterson M, DeVivo M, Heinemann A, Kalpakjian C. The association between the

etiology of a spinal cord injury and time to mortality in the United States: A 44-year investigation. J Spinal Cord Med. 2019; 42:444-452.

3. Ahuja CS, Mothe A, Khazaei M, Badhiwala JH, Gilbert EA, Kooy D, et al. The leading edge: Emerging neuroprotective and neuroregenerative cell-based therapies for spinal cord injury. Stem Cells Transl Med. 2020;9:1509-1530.
4, Tulaar ABM, Karyana M, Karunia Wahyuni L, Paulus AFS, Tinduh D, Anestherita F, et al. People with Spinal Cord Injury in Indonesia. Am J Phys Med Rehabil. 2017; 96:S74-77.
5. Martiana IK, Permana D, Widhiyanto L. Traumatic cervical spinal cord injury. is urgent intervention superior to delayed intervention? A meta-analysis evaluation. J Orthop Traumatol Surabaya. 2019;8:12.
6. Kreydin E, Welk B, Chung D, Clemens Q, Yang C, Danforth T, et al. Surveillance and management of urologic complications after spinal cord injury. World J Urol. 2018;36:1545-1553.
7. Brown A, Martinez M. From cortex to cord: motor circuit plasticity after spinal cord injury. Neural Regen Res. 2019;14:2054.
8. Bryce T, Huang V, Escalo M. Spinal Cord Injury, in Braddom's Physical Medicine and Rehabilitation, ed 6. Elsevier Inc, 2020.p.1049–1100.
8. Asadullah A, Bajamal AH, Parenrengi MA, Turchan A, Utomo B, Sudiana IK, et al. Effect of ACTH4-10Pro8-Gly9-Pro10 on anti-inflammatory cytokine (IL-4, IL-10, IL-13) expression in acute spinal cord injury models (male Sprague Dawley rats). F1000Research. 2023;12:194.
10. Erny E, Prawiro SR, Saharso D, Santoso MI, HMS CK. The Effect of ACTH4-10 Synthetic on separated junction formation and CSF leukocyte number in LPS-induced Meningitis. IOSR J Pharm Biol Sci. 2013;5:40-46.
11. Faris M. The Effect of ACTH4-10Pro8Gly9Pro10 on the Proinflammatory Mediators TLR, NF-Kb, IL-8, TNF-α, and Neutrophils in Spinal Cord Tissues Experiencing Acute Compression Injury Experimental Studies in Sprague-Dawley Mice Model Spinal Cord Injury. 2020. Available in: https://repository.unair.ac.id/103057/1/1.%20HALAMAN%20JUDUL.pdf
12. Anjum A, Yazid MD, Daud MF, Idris J, Hwei Ng AM, Naicker AS, et al. Spinal Cord Injury: Pathophysiology, Multimolecular Interactions, and Underlying Recovery Mechanisms. International J Molecular Sciences. 2020;21(20):7533.
13. Gaweł S, Wardas M, Niedworok E, Wardas P. Malondialdehyde (MDA) as a lipid peroxidation marker. Wiad Lek. 2004;57(9-10):453-455.
14. Thatcher TH, Peters-Golden M. From Biomarker to Mechanism? F2-isoprostanes in Pulmonary Fibrosis. Am J Respir Crit Care Med. 2022;206(5):530-532.
15. Comporti M, Signorini C, Arezzini B, Vecchio D, Monaco B, Gardi C. F2-isoprostanes are not just markers of oxidative stress. Free Radic Biol Med. 2008;44(3):247-256.
16. Institutional Animal Care & Use Committee. IACUC Policies and Procedures. Rosalind Franklin Univ 2018; Available: https://www.rosalindfranklin.edu/ research/ centers/research-support-offices/institutional-animal-care-and-use/.
17. Poon PC, Gupta D, Shoichet MS, Tator CH. Clip Compression Model is Useful for Thoracic Spinal Cord Injuries. Spine (Phila Pa 1976) 2007; 32:2853-2859.
18. Puspita R, Pratamastuti D, Safitri A, Aulanni'am A. The Potency of Semax Peptide Therapy toward MDA Level and Protein Profile in Epilepsy Rats (Rattus norvegicus), in Proceedings of the 1st International Conference in One Health (ICOH 2017). Atlantis Press: Paris, France, 2018.
19. Erny E, Prawiro SR, Saharso D, Santoso MI, HMS CK. The Effect of ACTH4-10 Synthetic on separated junction formation and CSF leukocyte number in LPS-induced Meningitis. IOSR J Pharm Biol Sci. 2013;5:40-46.
20. Loe ML, Indharty RS, Siahaan AM, Tandean S, Riawan W. The Effect of Intranasal Administration of ACTH Analogue Toward Neural Progenitor/Stem Cells Proliferation after Traumatic Brain Injury. Sains Malaysiana. 2020;49:375-382.
21. Filippenkov IB, Stavchansky VV, Denisova AE, Yuzhakov VV, Sevan'kaeva LE, Sudarkina OY, et al. Novel Insights into the Protective Properties of ACTH(4-7)PGP (Semax) Peptide at the Transcriptome Level Following Cerebral Ischaemia–Reperfusion in Rats. Genes (Basel). 2020;11:681.

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Profile of Nasopharyngeal Carcinoma in Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021

Perfil del carcinoma nasofaríngeo en el Hospital Dr. Wahidin Sudirohusodo Makassar 2011 - 2021

Cita Nurinsani Akhmad[1], Nova Audrey Luetta Pieter[2], Sutji Pratiwi Rahardjo[3]

SUMMARY

Background: *Nasopharyngeal carcinoma (NPC) is Indonesia's most common head and neck malignancy. NPC presents non-specific signs and symptoms, which lead to a late or missed diagnosis. Early detection and prevention are essential based on the NPC profile.*
Objective: *This study aimed to assess NPC's sociodemographic and clinical characteristics in Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021.*
Method: *Observational descriptive study with a cross-sectional design was conducted by using secondary data collecting medical records of all NPC patients in Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021.*
Results: *Out of 1 096 patients, 70.3 % of the patients were male, and most of them were from Makassar and Bugis. A palpable lump in the neck is the most common complaint in presentation (28.8 %), followed by nasal congestion (18.6 %). Salted fish consumption was the most prevalent risk factor (28.1 %).* **Conclusion:** *Studying the sociodemographic and clinical characteristics of NPC patients is the most critical factor that causes NPC problems.*
Keywords: *Nasopharyngeal carcinoma, characteristic.*

RESUMEN

Antecedentes: *El carcinoma nasofaríngeo (NPC, por sus siglas en inglés) es la neoplasia maligna de cabeza y cuello más común en Indonesia. NPC presenta signos y síntomas inespecíficos, que conducen a un diagnóstico tardío o erróneo. La detección temprana y la prevención son importantes según el perfil de NPC.*
Objetivo: *Este estudio tuvo como objetivo evaluar las características sociodemográficas y clínicas de NPC en el Hospital Dr. Wahidin Sudirohusodo Makassar 2011 - 2021.*
Método: *Se realizó un estudio descriptivo observacional con un diseño transversal utilizando datos secundarios que recopilan registros médicos de todos los pacientes de NPC en Dr. Wahidin Sudirohusodo Hospital Makassar 2011 - 2021.*
Resultados: *de 1 096 pacientes, el 70,3 % de los pacientes son hombres y la mayoría de ellos son de Makassar y Bugis. Un bulto palpable en el cuello es la queja más común en la presentación (28,8 %), seguido de la congestión nasal (18,6 %). El consumo de pescado salado fue el factor de riesgo más prevalente (28,1 %).* **Conclusión:** *Estudiar las características sociodemográficas y clínicas de los pacientes de NPC es el factor más importante que causa problemas de NPC.*
Palabras clave: *Carcinoma nasofaríngeo característico.*

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ORCID: https://orcid.org/0009-0004-3144-1447[1]
ORCID: https://orcid.org/0000-0002-7639-6000[2]
ORCID: https://orcid.org/0000-0002-8861-1476[3]

Department of Otorhinolaryngology-Head and Neck Surgery, Medical Faculty of Hasanuddin University, Makassar, Indonesia

Corresponding author: Cita Nurinsani Akhmad,
E-mail: cita_melodious@yahoo.com

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface and line the nasopharynx and is the most common head and neck malignancy in Indonesia (1,2). NPC is generally more common in Southeast Asia (1). It remains a health burden in Indonesia, with an overall incidence estimated at 6.2/100 000 or 12 000 new cases yearly. Unfortunately, many of these cases are unregistered in Indonesia due to several factors (1,3).

Based on GLOBOCAN (2020), it was reported that the incidence of new cases of nasopharyngeal carcinoma in Indonesia was 19 943 cases. Deaths from the nasopharynx in Indonesia reached 13 399 cases (4).

The detection of nuclear antigen associated with Epstein-Barr virus (EBV) and viral DNA in NPC type 2 and 3, has revealed that EBV can infect epithelial cells and is associated with their transformation. The etiology of NPC, particularly the endemic form, seems to follow a multi-step process, in which EBV, ethnic background, and environmental carcinogens all seem to play an important role. However, only a small proportion of individuals infected with EBV develop nasopharyngeal carcinoma. This indicates that EBV alone is not a sufficient cause for this malignancy. In adults, other likely etiological factors include genetic susceptibility, consumption of food, in particular salted fish, containing carcinogenic volatile nitrosamines, and as in children, EBV. Environmental exposures and or genetic risk factors likely also play a role in the pathogenesis of NPC (5,6). Therefore, the family of NPC patients is a high-risk group for the occurrence of NPC. This finding supports the genetic factor hypothesis, so it is important to do early screening and detection for family members of NPC patients (6).

NPC presents numerous challenges that go beyond simply treating the disease. The malignancy is manifested with various non-specific signs and symptoms, and despite its high incidence, general practitioners' awareness of NPC is inadequate, potentially leading to many late or missed diagnoses, so they come to health services at an advanced stage (7,8). Saraswati et al (2019) reported that the incidence of NPC in Sanglah Hospital Denpasar increased every year and is more often known in the advanced stage (9). Hibatullah et al. (2021) reported that the characteristics found in NPC patients are caused by non-specific symptoms so they come to health services at an advanced stage (8).

Given that NPC has a considerable impact on health, early detection, and prevention are proposed as the best way to overcome this problem. To do that, we must have data on the population's risk factors and intervention targets. Based on this, was conducted this study to obtain statistical data from the Department of Otorhinolaryngology-Head and Neck Surgery, continuing the previous data in the range of 10 years.

METHOD

This research is a descriptive observational study with a cross-sectional design in a retrospective manner. It analyzes the sociodemographic and clinical characteristics of NPC patients. The sampling technique was total sampling by using secondary data collecting medical records. The research subjects were all NPC patients in Dr. Wahidin Sudirohusodo Hospital Makassar in 2011 – 2021 who fulfilled the inclusion criteria and exclusion criteria incomplete medical record data. The confidentiality of the subject identity was guaranteed. The ethical clearance number is 505/UN4.6.4.5.31/ PP36/ 2022.

RESULTS

Data extraction showed that from 2011 – 2021 there were 1.096 medical records of NPC patients in Dr. Wahidin Sudirohusodo Hospital Makassar.

Table 1 indicates that 771 cases (70.3 %) of NPC patients are male, and most of them (88.8 %) are older than 30 years. In the 1-15-year age group, the highest number of 15 years old was found in 5 cases (0.5 %). The youngest age is found at 9 years. The patients come from various ethnicities in Indonesia, and the most common are Makassar

(42.2 %) and Bugis (27.1 %). Among the known environmental risk factors, the most prevalent is salted fish consumption, identified in 28.1 % of patients. Betel consumption and passive smokers are identified as the two lowest risk factors (8.7 % and 4.8 %, respectively) (Table 1).

Table 1. Sociodemographic Characteristics and Risk Factors of NPC in Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021

Characteristics and risk factors	n	%
Characteristics		
Sex		
Male	771	70.3
Female	325	29.7
Age		
1-15	13	1.2
16-30	110	10.0
31-45	372	34.0
46-60	452	41.2
>60	149	13.6
Ethnicity		
Makassar	463	42.2
Bugis	297	27.1
Toraja	184	16.8
Mandar	110	10.1
Others	42	3.8
Risk factors		
Family		
Yes	242	22.1
No	173	15.8
Active smokers		
Yes	273	24.9
No	197	17.9
Passive smokers		
Yes	53	4.8
No	48	4.4
Betel consumption		
Yes	96	8.7
No	87	7.9
Alcohol consumption		
Yes	107	9.8
No	98	8.9
Salt fish consumption		
Yes	308	28.1
No	206	18.8
Sunlight exposure		
Yes	121	11.0
No	114	10.4

As shown in Table 2, a palpable lump in the neck is the most common complaint at presentation, found in (28.8 %) of patients, followed by nasal congestion (18.6 %) and unilateral hearing defect unilateral (18.1 %). Most patients have felt these complaints for 6 months or less. However, some patients tolerated the complaints for more than a year before going to a doctor.

Table 2. Symptoms and Duration of NPC in Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021

Symptoms and Durations	n	%
Neck lump		
Yes	316	28.8
≤ 6 months	173	15.8
7-12 months	89	8.1
> 1 year	54	4.9
No	115	10.5
Nasal congestion		
Yes	204	18.6
≤ 6 months	132	12.0
7-12 months	47	4.3
> 1 year	25	2.3
No	106	9.7
Bloody discharge		
Yes	74	6.7
≤ 6 months	49	4.5
7-12 months	15	1.4
> 1 year	10	0.9
No	59	5.4
Epistaxis		
Yes	87	7.9
≤ 6 months	53	4.8
7-12 months	21	1.9
> 1 year	13	1.2
No	65	5.9
Postnasal drip		
Yes	49	4.5
≤ 6 months	23	2.1
7-12 months	15	1.4
> 1 year	11	1.0
No	36	3.3
Diplopia		
Yes	67	6.1
≤ 6 months	32	2.9
7-12 months	21	1.9
> 1 year	14	1.3
No	55	5.0

Continued in page S611…

…continuation Table 2 from page S610.

Symptoms and Durations	n	%
Hearing defect (unilateral)		
Yes	198	18.1
≤ 6 months	87	7.9
7-12 months	70	6.4
> 1 year	41	3.7
No	76	6.9
Hearing defect (bilateral)		
Yes	173	15.8
≤ 6 months	71	6.5
7-12 months	63	5.7
> 1 year	39	3.5
No	70	6.4
Tinnitus		
Yes	95	8.7
≤ 6 months	41	3.7
7-12 months	34	3.1
> 1 year	20	1.8
No	68	6.2

DISCUSSION

This study provides benefits in adding scientific references to the profile of NPC patients and in clinical applications can be used as input for NPC profile data in Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021 obtained for further research on nasopharyngeal carcinoma.

Characteristics of the Patients

This research was held at the medical record installation of Dr. Wahidin Sudirohusodo Hospital Makassar 2011 – 2021 with a total sample of 1.096 cases. The characteristics studied were sex, age, and ethnicity. The characteristic of the gender in this study is 70.3 % were male, similar to Asnir et al. (2020) studies which reported that most sufferers of NPC are men (69.3 %). Saraswati et al. (2019) also reported that the highest gender was found in the male gender as many as 75 people (65.79 %) (1,9). Besides that, based on GLOBOCAN (2020), it was reported that in Indonesia, NPC occurs 5.6 times greater in men than women and is the 5th highest cancer in men with a total case of 10.7/100 000 population and women 3.00/100 000 population (4).

In this study, the incidence of NPC based on age was most commonly found in the age group 46-60 years (41.2 %). This finding follows the general age trend of NPC that starts to rise after age 30 years old. The characteristic age of the patient in this study is similar to the reported by Dawolo et al. (2017) who indicated that most NPC patients are from the age group between 46-55 years (30.91 %). In addition, Bachri et al. (2020) reported that the highest number of cases was over 50 years, namely 116 cases (42 %), followed by 68 cases (24 %) aged 41-50 years, 62 cases (22 %) aged 31-40 years, 21-30 years old were 25 cases (25 %), and less than 20 years old were 7 cases (3 %). Saraswati et al. (2019) research showed that the highest periods were in the age group of productive age (36-55 years). According to Asnir et al. (2020), the peak incidence is from the age group 38-47 years (31.6 %) (9-11).

The majority of patients' ethnicity in this study are Makassar (42.2 %), Bugis (27.1 %), Toraja (16.8 %), and Mandar (10.1 %). Compared to other ethnicities, these ethnicities have the largest population in South Sulawesi hence, this distribution may simply reflect the general population and not the genetic risk factor. People of Makassar descent are most prevalent in NPC cases. Nevertheless, other ethnicities are also affected by NPC and thus, there might be no strong relation between the risk factors of NPC and ethnicities. Bachri et al. (2020) also reported that the most original nasopharyngeal carcinoma patients were from the Bugis-Makassar tribe 178 cases (63.57 %) (11).

Risk Factors

Increased risk of NPC has been associated with numerous factors. Having a multifactorial etiology, there are several factors related to NPC, such as salted fish consumption and smoking (7).

In this study, the most prevalent risk was salted fish consumption identified in 28.1 % of patients. In line with our results are the Jayalie et al. (2016) data who stated that salted fish consumption was the most prevalent risk factor (29.9 %). Furthermore, Kasim, et al. (2020) found that there is a significant correlation between the consumption of salted fish and the occurrence of NPC. Kurniasari (2020) also showed that

there is an association between salted fish consumption and nasopharyngeal incidence at the otolaryngeal-head and neck department in RSUP Dr. Mohammad Hoesin Palembang (7,12). The involvement of salted fish and the development of NPC is believed to be related to its component that is nitrosamine (13). In this study, active smokers were identified in 27.3 %. Aini et al. (2022) found that there is a content in cigarettes (nicotine) that can affect several mechanisms of cancer cell formation (14).

In this study, we found that betel consumption was one of the lowest risk factors. Therefore, even though betel consumption might be strongly associated with NPC in some countries, its clear involvement in Indonesia especially in South Sulawesi is still yet to be studied.

Sign and Symptoms

NPC usually originates in the lateral wall of the nasopharynx, which includes the fossa of Rosenmuller. It can then extend within or out of the nasopharynx to the other lateral wall and/or posterosuperiorly to the base of the skull or the palate, nasal cavity, or oropharynx. It then typically metastases to cervical lymph nodes. Distant metastases may occur in bone, lung, mediastinum, and, more rarely, the liver (15).

Cervical lymphadenopathy is the initial presentation in many patients, and the diagnosis of NPC is often made by lymph node biopsy. Symptoms related to the primary tumor include trismus, pain, otitis media, nasal regurgitation due to paresis of the soft palate, hearing loss, and cranial nerve palsies. Larger growths may produce nasal obstruction or bleeding and a "nasal twang". Metastatic spread may result in bone pain or organ dysfunction. Rarely, a paraneoplastic syndrome of osteoarthropathy may occur with widespread disease (15).

In the present study, the most developed symptom was a palpable lump in the neck (28.8 %). Nafisa et al. (2022) reported that the main common complaint was an enlargement of neck lymph nodes (55.1 %). Similarly, Hibatullah et al. (2021) stated that the main complaint is the masses in the neck (38.89 %). Moreover, the second most complaint was nasal congestion (23.5 %) (2,8). Jayalie et al. (2016) stated that a palpable lump in the neck is the most common complaint in presentation (58.1 %), followed by nasal congestion (49.1 %). Faiza et al. (2016) indicated that clinical symptoms were neck mass (93,17 %), followed by nasal obstruction (79,55 %) (7,16).

Most patients come to seek a medical advisor when the duration of the symptoms is 6 months or less, but unfortunately, there were still a lot of patients who came to seek medical advice after more than 6 months, even years. A combination of lack of awareness, knowledge about NPC, and unspecific early signs and symptoms often lead to worsened prognosis. Therefore, the role of a health professional is to be an educator about an early detection system and ensure that patients perform healthy behavior in their daily lives (7).

In conclusion, the characteristic of 1.096 patients who came to Dr. Wahidin Sudirohusodo Hospital Makassar in 2011 – 2021 showed the same sex and age distribution compared with other studies. In this study, most of the NPC patients complained of neck lumps and nasal congestion. We also found that the medical-seeking behavior of NPC patients in Indonesia especially in South Sulawesi is still low as many patients were diagnosed after 6 months of symptoms. In addition, the most prominent risk factor is salted fish consumption. In addition, it was found that the most ethnic groups were Makassar and Bugis.

The limitation of this study is the lack of data with adequate quality. We found that several medical records data were filled incompletely thus creating a problem in data extraction, so some data must be excluded. Therefore, medical records should be filled as completely as possible and should be computerized for the next researcher it is expected to complete the limitation of this study by adding more variable variations.

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The author realized that in writing this research article, there are limitations and shortcomings. Hopefully, this research article is useful.

REFERENCES

1. Asnir RA, Yudhistira A, Friliandita N. Profile of Nasopharyngeal Cancer Patients in Otorhinolaryngology-HNS Department Haji Adam Malik General Hospital Medan During 2014-2016. Int J Nasopharyngeal Carcinoma. 2020;02(03):79-81.
2. Nafisa IM, Utama MS, Sunardi MA, Abel A. Profile of Nasopharyngeal Cancer Patients who Underwent Radiotherapy in Dr . Hasan Sadikin General Hospital Bandung. Indones J Cancer. 2022;16(2):88-93.
3. Gondhowiardjo S, Meidania L, Senoaji F, Sekarutami SM. Nasopharyngeal Carcinoma Profile in Dr. Cipto Mangunkusumo Hospital Year 2013. Radioter Onkol Indones. 2019;10(1):8-11.
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. A Cancer J Clin. 2021;71(3):209-249.
5. Wu L, Li C, Pan L. Nasopharyngeal carcinoma: A review of current updates. Experimental and Therapeutic Medicine. 22018;15:3687-3692.
6. Pieter NAL. Profile Iga (Vca-P18+Ebna1) and Viral Load Ebv Dna As a Risk Factor Among Relatives of Nasopharynx Carcinoma Patient With Ebv Positive At Dr. Wahidin Sudirohusodo Hospital in Makassar. Int J Nasopharyngeal Carcinoma. 2019;1(02):78-82.
7. Jayalie VF, Paramitha MS, Jessica J, Liu CA, Ramadianto AS, Trimartani T, et al. Profile of Nasopharyngeal Carcinoma in Dr. Cipto Mangunkusumo National Hospital, 2010. eJournal Kedokt Indones. 2017;4(3).
8. Hibatullah H, Mohamad PB, Heriady Y. Characteristics of Nasopharyngeal Carcinoma Patients at Al-Ihsan Bandung Regional General Hospital 2017-2019 Period. Pros Kedokt. 2021;7(1):54-62.
9. Saraswati IGA, Nuaba IGA, Suanda IK. Characteristics of Nasopharyngeal Carcinoma Patients at Sanglah General Hospital Denpasar in 2014-2016. 2019; 8(1):56-60.
10. Dawolo AP, Utama DS, Kasim BI. Clinical Profile of Nasopharyngeal Carcinoma in the ENT-HNS Department of Dr. Mohammad Hoesin Hospital Palembang 2014-2015. Maj Kedokt Sriwij. 2017;49(1):1-9.
11. Bachri A, Jufri NI. Retrospective Review of Nasofaring Carcinoma in Wahidin Sudirohusodo General Hospital on 2011-2019 Period. Int J Nasopharyngeal Carcinoma. 2020;02(03):82-84.
12. Kurniasari I. The Relationship between Salted Fish Consumption Habits and the Incidence of Nasopharyngeal Carcinoma in the ENT-HNS Department of Palembang General Hospital; 2020.
13. Putera I, Ramadhan MG, Anindya S, Sutanto NR, Kurniawan A, Hosea FN, et al. Relationship Between Salted Fish Consumption and Nasopharyngeal Carcinoma: An Evidence-based Case Report. Acta Med Indones. 2015;47(1):72-77.
14. Aini PNI, Hassan AH, Rahim TH. Scoping Review: Analysis of the Effect of Cigarette Smoking on Risk Factors for the Occurrence of Nasopharyngeal Carcinoma. Bandung Conf Ser Med Sci. 2022;2(1):847-856.
15. Brennan B. Nasopharyngeal carcinoma. Orphanet J Rare Dis. 2006;1:23.
16. Faiza S, Rahman S, Asri A. Clinical and Pathological Characteristics of Nasopharyngeal Carcinoma in the ENT-KL Section of Dr. M. Djamil Hospital Padang. J Kesehat Andalas. 2016;5(1):90-96.

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Correlation of HbA1c with Ratio of Total Cholesterol/HDL, LDL/HDL, TG/HDL and Apolipoprotein B / Apolipoprotein A-1 Ratio in Patients with Type 2 Diabetes Mellitus

Correlación de HbA1c con el cociente Colesterol Total/HDL, LDL/HDL, TG/HDL y el cociente Apolipoproteína B/Apolipoproteína A en pacientes con Diabetes Mellitus tipo 2

*Irmawati[1], Liong Boy Kurniawan[2], Uleng Bahrun[2], Himawan Sanusi[3], Nursin Abdul Kadir[2], Burhanuddin Bahar[4]

SUMMARY

Background: *The lipid and Apo B/Apo A-1 ratios may be considered additional risk factor assessments, especially in patients with a high risk of cardiovascular diseases, such as diabetes. Blood glucose level can be assessed by measuring glycated hemoglobin (HbA1c), which is used as a long-term control and monitoring.*
Objective: *This study aimed to determine the relationship between HbA1c with lipid ratio and Apolipoprotein B/Apolipoprotein A-1 ratio in patients with type 2 diabetes mellitus.*
Methods: *A cross-sectional study was employed, and there were 60 subjects with type 2 diabetes involved, comprising 26 males and 34 females.*
Results: *The statistical analysis results revealed significant differences in CHOL/HDL, LDL/HDL, and Apo B/Apo A-1 between controlled and uncontrolled type 2 DM subjects (p=0.037; p=0.006; p=0.004), but no significant difference was found in TG/HDL (p=0.244). Meanwhile, the Spearman correlation test displayed a significant correlation between HbA1c levels and CHOL/HDL (p=0.021; r=0.298), LDL/HDL (p=0.002; r=0.393), and Apo B / Apo A-1 (p=0.017; r=0.308) in patients with type 2 diabetes mellitus. However, no significant correlation was observed between HbA1c levels and TG/HDL (p=0.165; r=0.181).*
Conclusions: *There is a significant correlation between HbA1c levels, CHOL/HDL, LDL/HDL, and Apo B/Apo A-1, while HbA1c levels with TG/HDL have no significant correlation.*

Keywords: *Type 2 Diabetes Mellitus, HbA1c, lipid ratio, Apo B/Apo A-1 ratio.*

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[1]Magister of Biomedical Sciences, Graduate School of Hasanuddin University, Makassar, South Sulawesi, Indonesia
[2]Department of Clinical Pathology, Medical Faculty, Hasanuddin University, Makassar, South Sulawesi, Indonesia
[3]Department of Internal Medicine, Medical Faculty, Hasanuddin University, Makassar, South Sulawesi, Indonesia
[4]Department of Public Health, Hasanuddin University, Makassar, South Sulawesi, Indonesia

*Corresponding author: Irmawati
E-mail: im.irmawati28@gmail.com
Phone: +6285399241009
Address: Jalan. Perintis Kemerdekaan Km 10, Makassar, South Sulawesi, Indonesia.

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RESUMEN

Antecedentes: *Los índices de lípidos y Apo B/Apo A-1 pueden considerarse evaluaciones de factor de riesgo adicionales, especialmente en pacientes con alto riesgo de enfermedades cardiovasculares, como la diabetes. El nivel de glucosa en sangre se puede*

evaluar midiendo la hemoglobina glicosilada (HbA1c), que se utiliza como control y seguimiento a largo plazo.
Objetivo: *Este estudio tiene como objetivo determinar la relación entre la HbA1c y el cociente lipídico y el cociente Apolipoproteína B/Apolipoproteína A-1 en pacientes con diabetes mellitus tipo 2.*
Métodos: *Se empleó un estudio transversal, y hubo 60 sujetos con diabetes tipo 2 involucrados, que consisten en 26 hombres y 34 mujeres.*
Resultados: *Los resultados del análisis estadístico revelaron diferencias significativas en CHOL/HDL, LDL/HDL y Apo B/Apo A-1 entre sujetos con DM tipo 2 controlados y no controlados (p=0,037; p=0,006; p=0,004), pero no se encontró diferencia significativa en TG/HDL (p=0,244). Por su parte, la prueba de correlación de Spearman mostró una correlación significativa entre los niveles de HbA1c y CHOL/HDL (p=0,021; r=0,298), LDL/HDL (p=0,002; r=0,393) y Apo B / Apo A-1 (p =0,017; r=0,308) en pacientes con diabetes mellitus tipo 2. Sin embargo, no se observó una correlación significativa entre los niveles de HbA1c y TG/HDL (p=0,165; r=0,181).*
Conclusiones: *Existe una correlación significativa entre los niveles de HbA1c, CHOL/HDL, LDL/HDL y Apo B/Apo A-1, mientras que los niveles de HbA1c con TG/HDL no tienen correlación significativa.*

Palabras clave: *Diabetes Mellitus tipo 2, HbA1c, relación lípidos, relación Apo B/Apo A-1.*

INTRODUCTION

Diabetes is considered the most common metabolic disorder. This disease has clinically become a global pandemic in recent decades and a major healthcare burden worldwide. The occurrence of diabetes continues to rise. The World Health Organization (WHO) defines diabetes as a "metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbance of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The most common form of diabetes is type 2 diabetes (DM). WHO estimates that >590 million patients will be diagnosed with diabetes by 2035 (2).

Rather than caused by the insufficient secretion of the insulin hormone, type 2 diabetes mellitus occurs due to the failure of the body's cells to respond to the hormone. This condition is commonly called "insulin resistance" (3). Insulin resistance is mainly caused by obesity, aging, and lack of physical activity. Insulin resistance plays a significant role in the development of atherogenic dyslipidemia, which involves increased levels of total cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol, and decreased levels of high-density lipoprotein (HDL) cholesterol (4).

Individuals with diabetes mellitus may experience lipid abnormalities or conditions commonly called dyslipidemia. Serum lipid abnormalities (dyslipidemia) are frequently observed in the diabetic population regardless of whether they have insulin deficiency or insulin resistance. Type 2 diabetes mellitus patients are susceptible to developing diabetic dyslipidemia, which increases the likelihood of complications related to cardiovascular disease (5). Lipid toxicity can trigger the process of atherogenesis to become more progressive. Lipoproteins will change due to metabolic changes in DM, such as glycation and oxidation processes (6). This may lead to a higher risk of insulin resistance, resulting in type 2 DM (7).

Lipid metabolism dysfunction in DM is directly associated with a risk for atherosclerotic cardiovascular events. There is evidence showing that death in DM patients is mostly caused by atherosclerosis, accounting for approximately 80 % of cases. As many as 75 % are caused by coronary heart disease (CHD), and the remaining 25 % are caused by stroke (8). Cardiovascular diseases like coronary heart disease largely cause mortality and morbidity in diabetic patients. One of the risk factors for coronary heart disease in patients with type 2 diabetes mellitus is the lipid profile characterized by an increase in total cholesterol, LDL, or triglycerides and a decrease in HDL (4).

Apolipoproteins, also called apoproteins, are important components of lipoprotein clusters found in the lipoproteins (9). Apolipoprotein B is a protein component that is the most important atherogenic element in VLDL, IDL, and LDL (10). In a previous study about Apolipoprotein related mortality risk (AMORIS), the Apo B/Apo A-1 ratio was also investigated; the result indicated that apolipoprotein B (Apo B) and apolipoprotein A-1 (Apo A-1) concentrations, as well as the Apo B/Apo A-1 ratio, were able to enhance the prediction of cardiovascular disease risk (11).

The measurement of glycated hemoglobin (HbA1c) can be utilized to determine the blood glucose levels for long-term control and monitoring; HbA1c reflects average plasma glucose over the previous eight to 12 weeks and can serve as a basis for assessing and considering the risk of complications in diabetic patients (12). It can be performed at any time of the

day and does not require any special preparation such as fasting. These properties have made it the preferred test for assessing glycaemic control in people with diabetes. More recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes. HbA1c is formed when a ketoamine reaction occurs between glucose and the N-terminal amino acid valine of the β chain of hemoglobin. Initially, an unstable bond is formed between glucose and the hemoglobin molecule. With time, this bond rearranges to form a more stable compound in which glucose is covalently bound to the hemoglobin molecule. The amount of the unstable form may rise rapidly in the presence of a high blood glucose level, whereas the stable form changes slowly and provides a time-average integral of the blood glucose concentration through the 120-day lifespan of the red blood cell. Thus, glycohemoglobin levels provide an objective measurement of averaged diabetic control over time (13). According to the American Diabetes Association (ADA) (2022), the recommended target for appropriate diabetes mellitus (DM) control is maintaining an HbA1c value < 7 %, and the higher the HbA1c value, the higher the risk of DM complications (14).

Theoretically, there is a connection between HbA1c and lipid profile where reduced insulin function leads to increased lipase-sensitive hormones (15). This, in turn, triggers lipolysis, releasing fatty acids and glycerol into the bloodstream, ultimately leading to an increase in free fatty acids (16). Consequently, if an excessive amount of these fatty acids reaches the liver, they will undergo fat metabolism and be converted into phospholipids, cholesterol, and triglycerides. This process causes the level of cholesterol and triglyceride to increase, which then are transported into circulation via lipoproteins, namely LDL and HDL (17).

The measurement of HbA1c levels that can determine glucose control in patients with type 2 diabetes mellitus and estimate the risk of complications leads to develop an interest in investigating the correlation between HbA1c and lipid rations, as well as Apolipoprotein B/ Apolipoprotein A-1 ratios, in patients with type 2 DM.

METHODS

Study Design and Population

A cross-sectional study was employed as the study design. The current study population was type 2 DM patients who visited the Hasanuddin University Hospital (RSPTN-UH) for treatment. A total of 60 samples were involved, comprising 26 males and 34 females. This study was conducted at the Clinical Pathology Laboratory of Hasanuddin University Hospital (RSUH), the Clinical Pathology Laboratory of Labuang Baji Hospital, and the Health Service Unit (UPK) Laboratory of Makassar City Health Service Center. The study received ethical approval from the Health Research Ethics Committee (KEPK) of the Faculty of Medicine, Hasanuddin University, RSPTN-UH, with ethical number 164/UN4.6.4.5.31/ PP36/2023.

Measurement of HbA1c, Total Cholesterol, LDL, TG, HDL, Apo B, and Apo A-1 Levels

The participant's identities were recorded. Before blood sampling, the patients underwent a fasting period. Whole blood samples were collected for the HbA1c examination using the EDTA tubes. In contrast, the serum sample for the total cholesterol, LDL, TG, HDL, Apo B, and Apo A-1 was collected using tubes without an anti-coagulant. Then, the blood sample in the tube without an anti-coagulant was centrifuged at 3000 rpm for 10 - 15 minutes to separate the serum from the blood cell component. The serum obtained was then stored at -20ºC. The HbA1c assessment was done using the Alere Afinion AS100 instrument with the Boronette Affinity Assay method. Total cholesterol, LDL, TG, and HDL were analyzed using the Enzymatic Colorimetric method on the Cobas C111 instrument. On the other hand, Apo B and Apo A-1 were measured using the immunoturbidimetric method on the Cobas C311 device.

Data Analysis

The data obtained were then analyzed using SPSS software version 22. Data were analyzed by entering all variables, including age, gender, and laboratory examination results. The Kolmogorov-Smirnov test was conducted to determine the normality of the data distribution using a significant value (α = 0.05). A non-parametric Spearman correlation test was employed if the data is not normally distributed.

RESULTS

A total of 60 participants with type 2 diabetes mellitus were involved in this study, comprising 26 males and 34 females. The subjects were divided into age groups, including 6 participants aged 36-45 years, 14 participants aged 46-55 years, 32 participants aged 56-65, and 8 participants over 65 years (Table 1).

Table 1. Research Subjects' Characteristics

Characteristics	Category	Type 2 DM		
		n	%	Mean
Gender	Male	26	43.3	-
	Female	34	56.7	-
Age	36-45 years	6	10.0	-
	46-55 years	14	23.3	-
	56-65 years	32	53.3	-
	>65 years	8	13.3	-
HbA1c		60	100	8.98
Apo B		60	100	118.07
Apo A-1		60	100	128.70
Apo B/Apo A-1		60	100	1.09
CHOL		60	100	215.5
LDL		60	100	118.61
HDL		60	100	31.63
TG		60	100	168.15
CHOL/HDL		60	100	7.70
LDL/HDL		60	100	4.28
TG/HDL		60	100	6.14

Normality Test

As shown in Table 2**,** the Kolmogorov-Smirnov test results revealed that the p-value for HbA1c in individuals with type 2 DM was 0.055 ($p>0.05$), indicating that the data is normally distributed. On the other hand, the p-value of Apo B/Apo A-1 in type 2 DM subjects was 0.0001 ($p<0.05$), suggesting that the data does not exhibit a normal distribution. Similarly, the p-values for CHOL/HDL, LDL/HDL, and TG/HDL in type 2 diabetes mellitus subjects were all determined to be 0.0001 ($p<0.05$), indicating that the data for these variables were not normally distributed.

Table 2. Kolmogorov-Smirnov Normality Test

	Type 2 DM		
	Statistics	N	P
HbA1c	0.113	60	0.055
Apo B/Apo A-1	0.258	60	0.0001
CHOL/HDL	0.179	60	0.0001
LDL/HDL	0.194	60	0.0001
TG/HDL	0.171	60	0.0001

Comparison Test

Comparison of CHOL/HDL in Controlled and Uncontrolled Type 2 DM

According to a normality test conducted on the CHOL/HDL data in both controlled and uncontrolled type 2 DM groups, it was determined that there were non-normally distributed data. Consequently, the Mann-Whitney test was employed to assess the difference in CHOL/HDL levels between controlled

and uncontrolled type 2 DM (Table 3). By conducting the Mann-Whitney statistical test, a p-value = 0.037 was obtained. Since the p-value < α (alpha=0.05), it can be concluded that there is a significant difference in CHOL/HDL levels between controlled and uncontrolled type 2 DM subjects.

Comparison of LDL/HDL Levels in Controlled and Uncontrolled Type 2 DM

Based on the normality test performed on the LDL/HDL data in controlled and uncontrolled type 2 DM, it was concluded that non-normally distributed data were obtained. Thus, the Mann-Whitney test was carried out to determine the difference between LDL/HDL levels in controlled and uncontrolled type 2 DM (Table 3). The statistical test results revealed a p-value = 0.006. Since p-value < α (alpha=0.05), it can be concluded that there is a significant difference in LDL/HDL levels between the controlled and uncontrolled type 2 DM subjects.

Comparison of TG/HDL Levels in Controlled and Uncontrolled Type 2 DM

After a normality test was conducted on the LDL/HDL data in both controlled and uncontrolled type 2 DM groups, it was determined that the data was not normally distributed. Consequently, the Mann-Whitney test was carried out to assess the disparity in TG/HDL levels between both groups (Table 3). The results of the Mann-Whitney statistical test revealed a p-value = 0.244. Since p-value > α (alpha=0.05), it can be concluded that no significant difference was found in TG/HDL levels between controlled and uncontrolled type 2 DM subjects.

Comparison of Apo B/Apo A-1 Levels in Controlled and Uncontrolled Type 2 DM

Based on the normality test of Apo B/Apo A-1 data in controlled and uncontrolled type 2 DM, it can be concluded that the data obtained were not normally distributed. Therefore, the Mann-Whitney test was carried out to determine the difference between Apo B/Apo A-1 levels in controlled and uncontrolled type 2 DM (Table 3). The result of the Mann-Whitney statistical test obtained a p-value = 0.004. Since the p-value < α (alpha=0.05) indicates a significant difference between Apo B/Apo A-1 in controlled and uncontrolled type 2 DM subjects.

Table 3. Comparison Test of CHOL/HDL, LDL/HDL, TG/HDL, Apo B/Apo A-1 Levels in Controlled and Uncontrolled Type 2 Diabetes Mellitus

Group	n	Type 2 Diabetes Melitus			p
		CHOL/HDL			
		Range	Median	Mean±SD	
Controlled (HbA1c <7 %)	12	3.11-8.93	5.31	5.49±1.66	0.037
Uncontrolled (HbA1c ≥7 %)	48	3.38-28.26	6.87	8.25±4.60	
		LDL/HDL			
Controlled (HbA1c <7 %)	12	0.97-6.12	2.43	2.73±1.40	0.006
Uncontrolled (HbA1c ≥7 %)	48	1.12-27.50	3.80	4.67±3.91	
		TG/HDL			
Controlled (HbA1c <7 %)	12	2.47-8.93	4.14	4.62±1.80	0.244
Uncontrolled (HbA1c ≥7 %)	48	1.60-26.62	5.13	6.52±4.76	
		Apo B/Apo A-1			
Controlled (HbA1c <7 %)	12	0.24-1.00	0.67	0.65±0.17	0.004
Uncontrolled (HbA1c ≥7 %)	48	0.30-4.42	0.99	1.19±0.85	

Correlation Test

Correlation Test between HbA1c and CHOL/HDL in Type 2 DM

The results of the Spearman correlation test between HbA1c and CHOL/HDL levels in type 2 DM subjects showed a p-value = 0.021. Since p-value < α (alpha=0.05), it can be concluded that there is a significant correlation between HbA1c and CHOL/HDL levels in type 2 DM patients (Table 4).

As shown in Figure 1, the data distribution on the scatterplot forms a linear relationship pattern between the HbA1c variable and the CHOL/HDL variable. This indicates that there is a positive correlation between the HbA1c variable and the CHOL/HDL variable.

Table 4. Correlation Test between HbA1c and CHOL/HDL, LDL/HDL, TG/HDL, Apo B/Apo A-1 in Type 2 DM

Variable	CHOL/HDL		LDL/HDL		TG/HDL		Apo B/Apo A-1	
HbA1c	r =	0.298	r =	0.393	r = 0.181	r =	0.308	
	p =	0.021	p =	0.002	p = 0.165	p =	0.017	
	n =	60	n =	60	n = 60	n =	60	

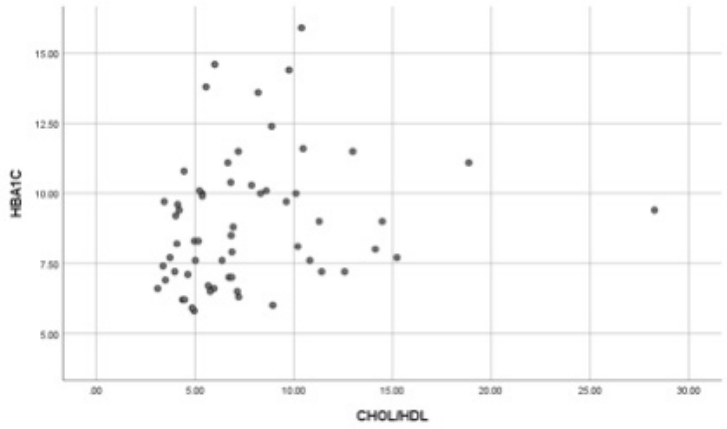

Figure 1. Scatterplot of HbA1c and CHOL/HDL

Correlation Test between HbA1c and LDL/HDL in Type 2 DM

The Spearman correlation test between HbA1c and LDL/HDL levels in type 2 DM subjects obtained a p-value = 0.002. Since p-value < α (alpha=0.05), it can be concluded that there is a significant correlation between HbA1c and LDL/HDL levels in type 2 DM patients (Table 4).

Figure 2 exhibits a linear relationship pattern between the HbA1c and LDL/HDL variables, as observed from the data distribution. This indicates that there is a positive correlation between the HbA1c variable and the LDL/HDL variable.

Correlation Test between HbA1c and TG/HDL Levels in Type 2 DM

The Spearman correlation test between HbA1c and TG/HDL levels in type 2 DM subjects obtained a p-value = 0.165. Because p value > α (alpha=0.05), it

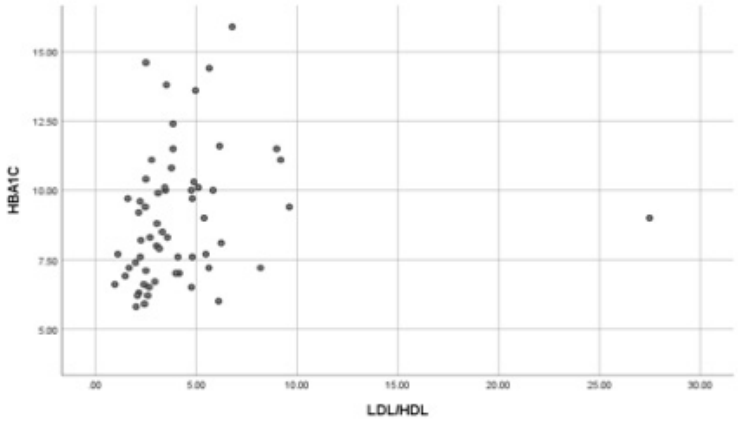

Figure 2. Scatterplot of HbA1c and LDL/HDL

can be concluded that there is no significant correlation between HbA1c and TG/HDL levels in patients with type 2 DM (Table 4).

The scatterplot in Figure 3 demonstrates a random relationship pattern between the data of the HbA1c variable and the TG/HDL variable, as evident from the data distribution. This indicates a positive but nut non-significant correlation between the HbA1c and TG/HDL variables.

Correlation Test between HbA1c and Apo B/Apo A-1 in Type 2 DM

The results of the Spearman correlation test between HbA1c and Apo B/Apo A-1 levels in type 2 DM subjects showed a p-value = 0.017. Since p-value < α (alpha=0.05), it can be concluded that there is a significant correlation between HbA1c and Apo B/ Apo A-1 levels in type 2 DM patients (Table 4).

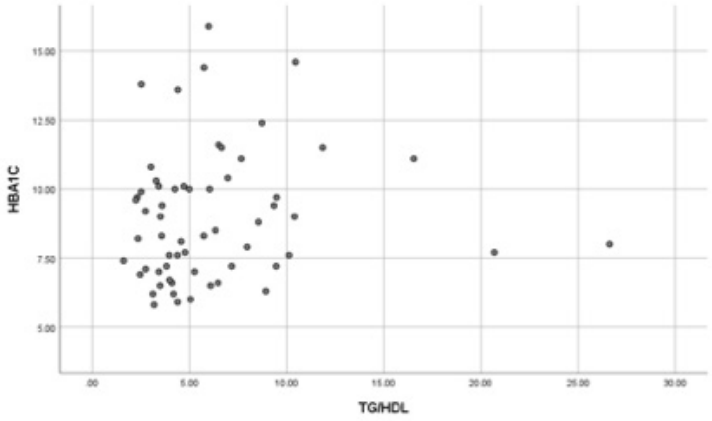

Figure 3. Scatterplot of HbA1c and TG/HDL

The scatterplot in Figure 4 above exhibits a linear relationship pattern between the HbA1c and Apo B/Apo A-1 variables, as evident from the data distribution. This indicates a positive correlation between the HbA1c and Apo B/Apo A-1 variables.

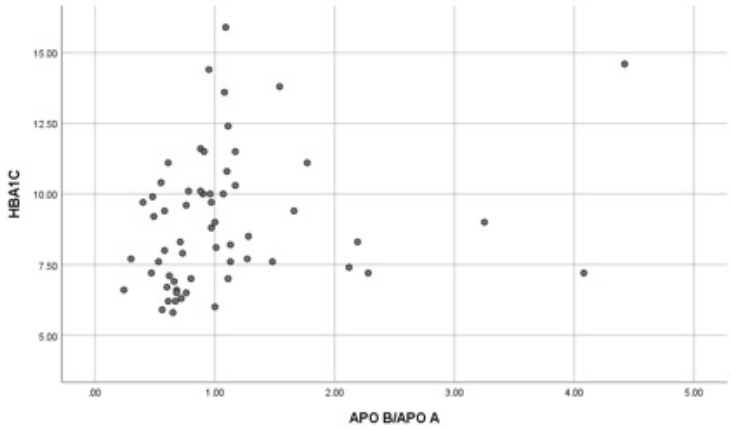

Figure 4. Scatterplot of HbA1c and Apo B/Apo A-1.

DISCUSSION

The current study determined the correlation of HbA1c with the ratio of total cholesterol/HDL, LDL, HDL, TG/HDL, and Apolipoprotein B/ Apolipoprotein A-1 in type 2 DM subjects that was conducted from April to May 2023. The findings of this study revealed that the mean values of total cholesterol/HDL, LDL/HDL, TG/HDL, and Apo B/ Apo A-1 ratios were higher in the uncontrolled type 2 DM group with HbA1c≥7. This is in line with the study of Pushparaj and Kirubakaran (2014), who indicated that the prevalence of inadequate glycemic control (HbA1C ≥ 7) in the study population was 66 %. The mean values of all the lipid parameters and atherogenic risk ratios were found to be higher in the HbA1C ≥ 7 groups and were statistically highly significant. Therefore, they concluded that HbA1C is not only a marker of chronic exposure to hyperglycemia but can also predict dyslipidemia (18). In addition, Zheng et al. investigated the associations between the ApoB/ApoA-I ratio and the risk of type 2 DM and pre-diabetes in a Chinese population and found that the increase in the Apo B/Apo A-1 ratio was associated with increased HbA1c levels. In addition, ApoB/ApoA-I ratios were significantly increased across the spectrum of normal glucose tolerance, pre-diabetes, and T2DM (19).

HbA1c provides a value that can be used for monitoring hyperglycemia and correlates well with the risk of long-term complications associated with diabetes. Diabetes mellitus often causes macrovascular and microvascular complications (20). Insulin resistance primarily contributes to macrovascular complications, whereas chronic hyperglycemia is responsible for the onset of microvascular complications. This vascular damage begins with endothelial dysfunction due to glycosylation and oxidative stress on endothelial cells. Endothelial dysfunction is key to maintaining vascular homeostasis (21).

The Spearman correlation test results showed no significant correlation between HbA1c and TG/ HDL levels. This is in correspondence with the results reported by Yan et al., who showed that when HbA1c increased, the TC/HDL and LDL/HDL ratios

also increased. Moreover, a significant correlation was observed between the HbA1c ratio and TC/HDL (P=0.039) and between the LDL/HDL and HbA1c (P=0.003). However, there was no significant correlation between HbA1c levels and TG/HDL ratio (P=0.301) (22). The study conducted in Indonesia to assess the correlation between the ratio of TG/HDL and HbA1c levels yielded a p-value = 0.250 (p>0.05), suggesting that there is no significant relationship between HbA1c levels with TG/HDL levels (23).

The absence of a significant correlation between the TG/HDL ratio and HbA1c levels could be attributed to various influencing factors, including the use of commonly prescribed metformin medication in treating diabetic patients. Considering the pathogenesis of type 2 DM, it is likely that it plays the dominant factor in increasing the TG/HDL ratio. As the HbA1c value increases, the TG/HDL ratio rises. This can be attributed to the excess glucose in the blood, which will be stored as fat, particularly triglycerides. Consequently, if glycemic control is poor (indicated by a high HbA1c value), there will be an increase in the levels of blood glucose. Furthermore, glucose will be converted into triglycerides, increasing triglyceride levels. A decrease will follow an increase in triglyceride levels in HDL levels in the blood.

Theory suggests that individuals with diabetes will experience significant increases in various lipid components, including total cholesterol, LDL, and triglycerides. As stated before, Hb1Ac serves as a valuable long-term indicator of blood sugar control and a reliable predictor of lipid profile. The utilization of HbA1c for monitoring glycemic control may offer an additional advantage by enabling the identification of diabetic patients who are at a greater risk of developing cardiovascular complications (23).

The relationship between HbA1c and Apo B/Apo A-1 levels in individuals with type 2 DM indicates a significant correlation between HbA1c and Apo B/Apo A-1 levels in patients with type 2 DM. In the same way, Zheng et al. revealed a positive association between the Apo B/Apo A-1 ratio and the risk of diabetes in patients (19). Furthermore, the study on Apolipoprotein-related mortality risk (AMORIS) which examined the Apo B/Apo A-1 ratio suggested that the concentration of apolipoprotein B (Apo B) and apolipoprotein A-1 (Apo A-1), as well as the Apo B/Apo A-1 ratio, can enhance the prediction of cardiovascular disease risk (11).

CONCLUSION

According to the results, it can be concluded that uncontrolled type 2 DM subjects exhibit higher ratios of CHOL/HDL, LDL/HDL, TG/HDL, and Apo B/Apo A-1 compared to controlled type 2 DM subjects. Significant correlations were observed between HbA1c levels and CHOL/HDL, LDL/HDL, and Apo B/Apo A-1 ratios in type 2 DM subjects. However, no significant correlation was found between HbA1c levels and TG/HDL ratio.

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Declaration of competing interest

All authors declare there is no conflict of interest in this study.

REFERENCES

1. Kharroubi AT. Diabetes mellitus: The epidemic of the century. World J Diabetes. 2015;6(6):850.
2. Reed J, Bain S, Kanamarlapudi V. A review of current trends with type 2 diabetes epidemiology, aetiology, pathogenesis, treatments and future perspectives. Diabetes, Metabolic Syndrome and Obesity. 2021;14:3567-3602.
3. Wulandari IAT, Herawati S, Wande IN. Description of Hba1c levels in type II diabetes mellitus patients at Sanglah Hospital. Udayana Medical J. 2020;9(1):71-75.
4. Pinakesty A, Azizah RN. Relationship of lipid profile with the progression of type 2 diabetes mellitus. 2020;8(2):66-72.

5. Yudha NSD, Arsana PM, Rosandi R. Comparison of Lipid Profile in Type 2 Diabetes Mellitus Patients with Controlled Glycemic Control and Uncontrolled Glycemic Control at Dr. Saiful Anwar Hospital Malang. Indonesian Journal of Internal Medicine. 2021;8(4).
6. Parveen K, Siddiqui WA, Kausara MA, Kuddusa M, Shahida SMA, Arif JM. Diabetic nephropathy - a major macrovascular complication. Int J Pharmaceuti Res Allied Sci. 2016;5:132-158.
7. Utomo AA, Aulia A, Rahmah S, Amalia R. Faktor Risiko Diabetes Mellitus Tipe 2. Jurnal Kajian dan Pengembangan Kesehatan Masyarakat. 2020;01:44-52.
8. Sanllorente A, Lassale C, Soria-Florido MT, Castañer O, Fitó M, Hernáez Á. Modification of High-Density Lipoprotein Functions by Diet and Other Lifestyle Changes: A Systematic Review of Randomized Controlled Trials. J Clin Med. 2021;10:1-43.
9. Kaneva AM, Potolitsyna NN, Bojko ER, Odland J. The Apolipoprotein B / Apolipoprotein A-I Ratio as a Potential Marker of Plasma Atherogenicity. Hindawi. 2015;2015:1-7.
10. Airaodion AI, Ogbuagu U, Ogbuagu EO, Paul A, Agunbiade AP, Airaodion EO, et al. Mechanisms for Controlling the Synthesis of Lipids – Review. Internat J Research. 2019;06(2):123-135.
11. Walldius G, Jungner I, Holme I, Aastveit AH, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): A prospective study. Lancet. 2001;358(9298):2026-2033.
12. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Libertas Academica. 2016:95-104.
13. Widyatmojo H, Suromo LB, Retnoningrum D. Relationship of Glycosylated Hemoglobin (Hba1c) with Cardiovascular Risk in Diabetes Mellitus Patients. Young Medical Media. 2018;3(2):1-6.
14. Association AD. Standards of Medical Care in Diabetes — 2022 Abridged for Primary Care Providers. 2022;40(01).
15. Juda TM, Zaidan HK, Issa AM. Polymorphism of Aldose Reductase Gene and Susceptibility for Developing Diabetic Retinopathy among Type 2 Diabetes Mellitus Patients. J Babylon University. 2016;24(5).
16. Wadhera RK, Steen DL, Khan I, Giugliano RP, Foody JM. A review of low-density lipoprotein cholesterol, treatment strategies, and its impact on cardiovascular disease morbidity and mortality. J Clin Lipidol. 2016;10(3):472-489.
17. Wahab Z, Novitasari A, W NF. Lipid profile as glycemic control in type II diabetes mellitus patients. Muhammadiyah J Med. 2015;4:1-10.
18. Pushparaj JL, Kirubakaran SS. HbA1C as a predictor of lipid profile in type 2 diabetic patients. J Evolution Med Dent. 2014;3(12):3157-3165.
19. Zheng S, Han T, Xu H, Zhou H, Ren X, Wu P. Associations of apolipoprotein B / apolipoprotein A-I ratio with pre-diabetes and diabetes risks: a cross-sectional study in Chinese adults. BMJ Open. 2017:1-8.
20. Hussain S, Shareef U, Giriraja, Mohan L. Correlation between Glycosylated Haemoglobin and Serum Lipid Profile in Patients with Type 2 Diabetes Mellitus in A Rural. IAR J Medical Sciences. 2020;1(6):290-295.
21. Decroli E. Diabetes Melitus Tipe 2. Internal Medicine Section Publishing Center: Padang; 2019. ISBN No.978-602-1332-25-2.
22. Yan Z, Liu Y, Huang H. Association of glycosylated hemoglobin level with lipid ratio and individual lipids in type 2 diabetic patients. Asian Pacific J Tropical Medicine. 2012;5(6):469-471.
23. Nainggolan OH, Wulanjani HA. Relationship of Triglyceride / HDL-C Ratio with HbA1c in Type 2 Diabetes Mellitus Patients. Medica Hospitalia. 2018;5(1):36-40.

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Effect of *Dangke* consumption on body weight, blood glucose, and total cholesterol in rats subjected to high-fat and fructose diet

Efecto del consumo de *Dangke* sobre el peso corporal, la glucosa en sangre y el colesterol total en ratas sometidas a dieta alta en grasa y fructosa

Ahmad[1a], Syahrijuita Kadir[2,a,b], Ratmawati Malaka[3c], Ilhamuddin[4,a,b], Gita Vita Soraya[5,a,b], Marhaen Hardjo[6,a,b*]

SUMMARY

Obesity occurs due to an imbalance in caloric intake, leading to excess fat accumulation in adipose tissue. This condition is associated with hyperglycemia and abnormal lipid levels. Dangke, a traditional Indonesian cheese, contains lactic acid bacteria and bioactive peptides known for their health benefits. This study aims to assess the effects of dangke consumption on body weight, glucose, and total cholesterol levels in rats subjected to a high-fat and fructose diet (HFFD). This research employed an experimental laboratory design. Twenty-four Sprague-Dawley rats, with weights ranging from 100 to 200 g, were divided into six groups, each consisting of four rats. Group 1 (ND) (received a normal diet. Group 2 (HFFD) was provided with a high-fat and fructose diet). Groups 3 and 4, were given the HFFD along with acarbose at a dosage of 0.9 mg/200 g and orlistat at a dosage of 1.08 mg/200 g, respectively. Finally, Groups 5 and 6 were fed the HFFD along with dangke at dosages of 1.8 g/200 g and 3.6 g/200 g, respectively. Results showed that dangke significantly inhibited weight gain and fasting glucose levels ($p<0.05$) compared to the normal diet and HFFD groups. Moreover, dangke consumption reduced total cholesterol levels compared to the HFFD group. In conclusion, dangke consumption demonstrated potential in preventing weight gain, high blood glucose levels, and elevated total cholesterol levels in rats subjected to HFFD.

Keywords: *Dangke, obesity, blood glucose, total cholesterol, functional food*

RESUMEN

La obesidad se produce debido a un desequilibrio en la ingesta calórica, lo que lleva a una acumulación

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ORCID: https://orcid.org/0000-0002-5149-2274[2]
ORCID: https://orcid.org/0000-0003-1934-4949[3]
ORCID: https://orcid.org/0000-0002-2656-4176[5]
ORCID: https://orcid.org/0009-0005-4945-4542[6]

[a]Master's Program in Biomedical Sciences, Hasanuddin University Graduate School, Makassar, Indonesia.

[b]Department of Biochemistry, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[c]Department of Animal Production, Faculty of Animal Science, Hasanuddin University, Makassar, Indonesia.

*Corresponding Author: Marhaen Hardjo
E-mail: marhaenhardjo@gmail.com

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excesiva de grasa en el tejido adiposo. Esta condición se asocia con hiperglucemia y niveles anormales de lípidos. Dangke, un queso tradicional de Indonesia, contiene bacterias del ácido láctico y péptidos bioactivos conocidos por sus beneficios para la salud. Este estudio tiene como objetivo evaluar los efectos del consumo de dangke sobre el peso corporal, la glucosa y los niveles de colesterol total en ratas sometidas a una dieta alta en grasas y fructosa (HFFD). Esta investigación empleó un diseño experimental de laboratorio. Veinticuatro ratas Sprague-Dawley, con pesos que oscilaban entre 100 y 200 g, se dividieron en seis grupos, cada uno compuesto por cuatro ratas. El Grupo 1 (ND) recibió una dieta normal. El grupo 2 (HFFD) recibió una dieta rica en grasas y fructosa. Los Grupos 3 y 4, recibieron HFFD junto con acarbosa a dosis de 0,9 mg/200 g y orlistat a dosis de 1,08 mg/200 g, respectivamente. Por último, los grupos 5 y 6 recibieron HFFD junto con dangke en dosis de 1,8 g/200 gy 3,6 g/200 g, respectivamente. Los resultados mostraron que dangke inhibió significativamente el aumento de peso y los niveles de glucosa en ayunas ($p<0,05$) en comparación con los grupos de dieta normal y HFFD. Además, el consumo de dangke redujo los niveles de colesterol total en comparación con el grupo HFFD. En conclusión, el consumo de dangke demostró potencial para prevenir el aumento de peso, los niveles altos de glucosa en sangre y los niveles elevados de colesterol total en ratas sometidas a HFFD.

Palabras clave: *Dangke, obesidad, glucosa en sangre, colesterol total, alimentos funcionales.*

INTRODUCTION

Obesity is a complex, multifactorial, and largely preventable disease, affecting, along with overweight, over a third of the world's population today. Obesity has become a major health issue, with far-reaching consequences for various life-threatening diseases, becoming a significant health problem worldwide over the last few decades reaching epidemic proportions (1). Physiologically, the condition arises from an imbalance in caloric intake, leading to the accumulation of excess fat in adipose tissue (2,3). Obesity greatly increases the risk of chronic disease morbidity — namely disability, depression, cardiovascular disease, certain cancers — and mortality, and type 2 diabetes mellitus due to decreased insulin sensitivity characterized by an increase in fasting serum glucose levels that exceed normal values (4-6). In addition to that, it can cause abnormalities in lipid fractions or dyslipidemia (7). One of the parameters marked in lipid fraction abnormalities is an increase in serum total cholesterol levels that exceed normal limits (8).

Currently, it is proposed that the safest method that can be used to reduce the risk of obesity and its comorbidities is to modify lifestyle, including diet and exercise programs (9). Consuming dairy products is included in a healthy diet associated with better diet quality because they contain high levels of calcium and vitamin D (10). Dairy products have been studied to provide possible beneficial physiological effects through the presence of bioactive peptide micro-organisms and macromolecules (11,12) that act as anti-cancer and anti-diabetic agents, reduce the risk of stroke, and may influence adipose tissue function, inflammation, and the gut microbiome (13-16).

Dangke is a traditional type of cheese originating from Indonesia that is made using fresh cow's milk as raw material. *Dangke* is classified as a soft cheese because of its high water content. The *dangke* coagulation process is carried out by heating the milk and adding the papain enzyme to the papaya sap (17). The evidence indicates several beneficial effects in the health sector, such as increasing phosphate and calcium, decreasing bacterial colonies in dental plaque (18), improving the nutritional status of children (19), and increasing the hemoglobin levels of pregnant women with anemia (17). In addition, whey dangke can reduce cholesterol levels (20). However, there is little information regarding the effect of *dangke* on obesity and the risk of complications. Therefore, this study aimed to evaluate the effect of administering *dangke* on body weight, glucose levels, and total cholesterol in rats fed with a high-fat and fructose diet (HFFD).

METHODS

Study design and sample size

This research employed an experimental laboratory design. The study involved twenty-

four healthy and active male Sprague-Dawley rats, aged 6-8 weeks and weighing 100-200 g. Animals were divided into six groups, group 1 was a negative control who received a normal diet (ND), and groups 2-6 were treatment groups. Group three received an Acarbose treatment dose of 0.9 mg/200 g body weight rats (21), and group four received an orlistat treatment dose of 1.08 mg/200 g body weight rats (22). Groups five and six received *dangke* interventions of 1.8 g and 3.6 g/200 g rat body weight (17,18). This research was conducted in the animal laboratory of the Faculty of Medicine, Hasanuddin University, Makassar. Indonesia.

Animal handling and ethical approval

Rats were acclimatized for one week before the beginning of the experiment. The animals received standard rat chow diet and drinking water *ad libitum*, and were housed under controlled conditions of a 12-h light-dark cycle and a temperature range of 26-28°C. The study was approved by the Animal Ethics Committee of the Ethics Commission in the Faculty of Medicine, Hasanuddin University, with letter Number: 125/ UN4.6.4.5.31/ PP36/ 2023.

Diet and medication

The diet employed in the study was a high-fat and fructose combination, comprising regular diet components (AD II Super), along with pork oil, duck egg yolk, and cholic acid in proportions of 70.5 %, 13.5 %, 15 %, and 1 %, respectively. The rats in all groups, except for group 1, received 40 mL of fructose solution (Rose Brand, Indonesia) mixed in drinking water with a ratio of 3:7 (final concentration: 0.2 g/mL). The *dangke* used in this study was obtained from the milk technology laboratory, Faculty of Animal Husbandry, Hasanuddin University, Makassar, Indonesia. The nutritional content of *dangke* consisted of 17.20 % protein, 32.81 % fat, 2.32 % minerals and 45.75 % water content. All rats were fed 10-20 g daily using a 10 % rat body weight formula for four weeks.

Treatment scheme

Sprague-Dawley rats were randomly divided into six groups, each comprising four rats. Group 1 (ND) received a normal diet, and Group 2 (HFFD) received a high-fat and fructose diet. Group 3 was acarbose (receiving HFFD + Acarbose diet of 0.9 mg/200 g of rat body weight). Group 4 was Orlistat (receiving HFFD + Orlistat 1.08 mg/200 g of rat body weight). Group 5 was *dangke* 1.8 (receiving HFFD + *dangke* 1.8 g/200 g of rat body weight). Group 6 was dangke 3.6 (receiving HFFD + *dangke* 3.6 g/200 g of rat body weight). Meanwhile, HFFD, orlistat, acarbose, and *dangke* were administered by oral gavage daily for four weeks.

Collection and analysis of specimens

Throughout the experiment, measures were taken to minimize any discomfort experienced by the rats. After four weeks of treatment, the rats were subjected to a 12-h fasting period before being euthanized using ketamine. Blood samples were collected through the sub-jugular vein as much as 1.5 mL in a non-anticoagulant tube (Tiger-top tube). The sample underwent centrifugation at 300 rpm for 20 min. The serum obtained was collected to analyse glucose and total cholesterol levels.

The rats' body weight was monitored every seven days throughout the experiment. Fasting blood glucose levels were examined according to the guidelines provided by Meril Diagnostic® (Gujarat, India) commercial kits. The total cholesterol levels were determined using enzymatic colorimetry principles with Glory Diagnostic® (Barcelona, Spain). Sample absorbance was measured using Ganesy 150 UV-VIS from Thermo Scientific (Madison, USA).

Statistical Analysis

The statistical analysis was conducted using IBM SPSS Statistics 26 (SPSS Inc, Chicago). The statistical differences among the means were determined using a one-way analysis of variance

(ANOVA), followed by Tukey's Post Hoc test to assess differences in group means. Results were considered statistically significant when the p-value was <0.05.

RESULT

The Effect of *Dangke* Consumption on Rat Body Weight after Four Weeks of Treatment

At the end of the experiment, each group displayed different body weights, with the HFFD group exhibiting the highest weight, followed by the HFFD+Acarbose, HFFD+*dangke* 3.6 g, HFFD+*dangke* 1.8 g, HFFD+Orlistat groups, and the lowest weight was observed in the normal diet treatment. p<0.05 (HFFD) vs. (Normal diet, HFFD+orlistat, HFFD+*Dangke* 1.8 g), #p<0.05 ND vs HFFD, HFFD+orlistat, HFFD+*dangke* 1.8g and 3.6g (Figure 1).

The Effect of *Dangke* Feeding on the Serum Glucose Levels in Rats

The HFFD group exhibited the highest mean glucose level, followed by the normal diet group. These two treatments demonstrated significant differences in their value compared to the HFFD+*dangke* 1.8 g, HFFD+*dangke* 3.6 g, and HFFD+acarbose groups. Meanwhile, the HFFD+*dangke* 1.8 g showed the lowest mean glucose level. *p<0.001 (Normal diet, HFFD) vs. HFFD+*dangke* 1.8g, HFFD+*dangke* 3.6 g, HFFD+acarbose: # p<0.001 Normal diet vs. HFFD (Figure 2).

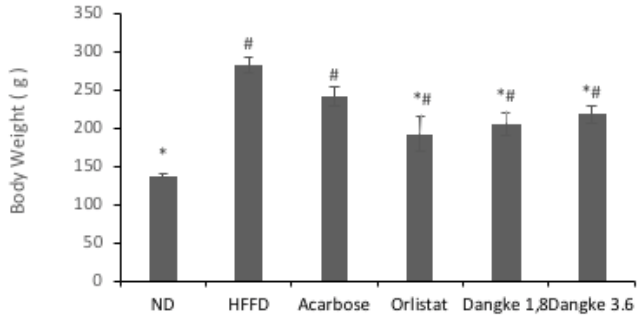

Figure 1. Total weight gain during treatment- Significance values were determined by using a One-Way Anova test, followed by Tukey's Post-Hoc. *p<0.05 (HFFD) vs (Normal diet, HFFD+orlistat, HFFD+*dangke* 1.8 g), #p<0.05 ND vs HFFD, HFFD+orlistat, HFFD+*dangke* 1.8 g and 3.6 g

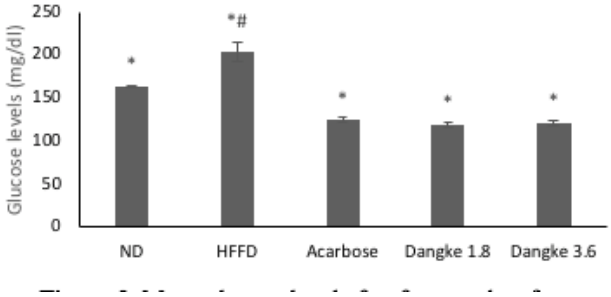

Figure 2. Mean glucose level after four weeks of treatment. The significance value was determined by utilising a One-Way Anova test, followed by Tukey's Post-Hoc. *p<0.001 (Normal diet, HFFD) vs HFFD+*dangke* 1.8 g, HFFD+*dangke* 3.6 g, HFFD+acarbose: # p<0.001 Normal diet vs HFFD.

The Effect of *Dangke* Feeding on the Total Cholesterol Level in Rats

The HFFD treatment group displayed the highest mean total cholesterol level, which differed significantly from the HFFD+*dangke* 1.8 g and HFFD+*dangke* 3.6 g groups. However, the groups receiving *dangke* and orlistat treatments showed no significant difference compared to the normal diet group. *p<0.05 HFFD vs. HFFD+dangke 1.8g, HFFD+*dangke* 3.6 g (Figure 3).

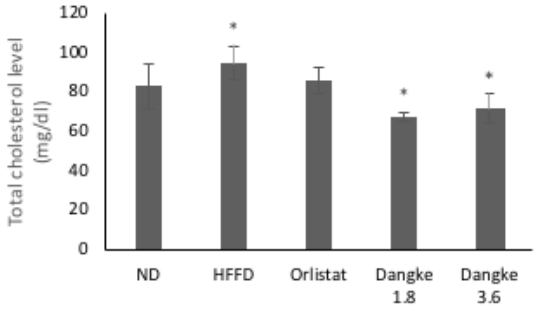

Figure 3. Mean total cholesterol levels four weeks after treatment. The significance level was determined by utilizing a One-Way Anova test, followed by Tukey's Post-Hoc *p<0.05 HFFD vs. HFFD+*dangke* 1.8 g, HFFD+*dangke* 3.6 g.

DISCUSSION

Preventive trials *dangke* in reducing the risk of metabolic syndrome are carried out to find a breakthrough in controlling this disease. *Dangke* is a dairy product rich in probiotic bacteria, essential amino acids, and other nutrients that have a positive impact on health. Probiotic bacteria have been widely associated with improvements in metabolic syndrome conditions through improvements in glucose and lipid profiles (23). The diet employed in the current study demonstrated a notable increase in the risk of metabolic syndrome based on the tested parameters. These results are in agreement with findings from prior research which demonstrated that HFFD induces insulin resistance and gut microbiota dysbiosis and accentuates dyslipidaemia in Watanabe rabbits; that when subjected to HFFD, might become a potential diet-induced MetS animal model with two main features, dyslipidaemia and insulin resistance (24); and in male C57BL/6 mice fed high-fat high-fructose diet (HFD) for 60 days, to induce Non-alcoholic fatty liver disease (NAFLD) and -steatohepatitis (NASH) that imply a state of excessive fat built-up in livers with/or without inflammation (25). Our present results indicated that 4-week treatment period, the group fed with HFFD showed a 70 % rise in body weight, leading to a notable decline in the movement performance of the rats. In fact, it has been reported that the decrease in metabolic ability among obese individuals displays an inverse relationship with weight loss, decreased contractile function, and movement (26). In contrast, rats treated with *dangke* 1.8 g and 3.6 g and orlistat experienced an increase in body weight of 14 %, 30 %, and 15 %, respectively. The lowest weight gain was observed in the normal diet group at 0.9 %. Orlistat is a medication used in the management of obesity. Orlistat acts by reversibly inhibiting gastric and pancreatic lipases. The inactivation of lipases prevents the hydrolysis of triglycerides, and thus free fatty acids are not absorbed (27). *Dangke* is believed to exert its effects on weight control by increasing energy metabolism and muscle contraction, thereby regulating weight gain through its lactic acid bacteria (LAB) and bioactive peptides. The findings are in line with a previous study (28), which suggests that milk

on daily consumption does not lead to weight gain and may even decrease the risk of type 2 diabetes mellitus.

Our data show that feeding rats with *dangke* could successfully inhibit the rise in glucose levels. Indeed, *dangke* consumption in the HFFD-fed group demonstrated an anti-hyperglycaemic effect when compared to both the normal diet and HFFD groups ($p<0.05$). According to Mozaffarian, the consumption of dairy products can reduce the risk of type 2 diabetes mellitus (28). Furthermore, previously it was shown that fermented *dangke* has the effect of anti-hyperglycemia, since reduced fasting blood glucose in rats treated with propylthiouracil and a high-fat diet after the administration of *dangke* cheese at 1.5 g/200 g body weight of rats for 14 days.

A prior study demonstrated that rat consumption of *dangke* at 1.5 g/200 g body weight was more effective in reducing fasting blood glucose levels comparable to that of rats treated with acarbose, a drug known to lower blood sugar by preventing the breakdown of starch into sugar (29). In line with the present findings, administration of *dangke* at 1.8 g/200 g body weight effectively inhibited the increase in glucose levels, even though it did not was a significant difference when compared to the acarbose group.

The HFFD treatment group displayed the highest mean total cholesterol level, which differed significantly from the groups administered with *dangke* (1.8 g and 3.6 g) ($p<0.05$). These findings are in accordance with the research of Fadhilah et al., which demonstrated that *dangke* contains lactic acid bacteria that are capable to ferment sugar or carbohydrates to produce large amounts of lactic acid and reduce cholesterol levels (30). Similarly, Sulmiyati et al., also stated that administering whey *dangke* can reduce total cholesterol levels in the research subjects, specifically broiler chicken (20). Among the doses tested, 1.8 g of *dangke* proved to be the most effective in preventing an increase in total cholesterol levels, outperforming the 3.6 g dose and the control drug Orlistat.

The hypoglycemia and anti-hypercholesterol activity of *dangke* is obtained from fermentation-derived bioactive peptides by enhancing insulin uptake and inhibiting key enzymes involved in glucose metabolism (31,32). Recent findings (32) have isolated several types of amino acids contained in *dangke* as potential bioactive peptides such as arginine 3.6 %, histidine 2.3 %, isoleucine 5.1 %, leucine 9.2 %, lysine 7.3 %, methionine 4.1 %, and tryptophan 1.3 %. Bioactive peptides play a role in improving dyslipidaemia by interfering with micelle solubility and absorption of dietary cholesterol, altering enterohepatic bile acid circulation, and promoting cholesterol catabolism, as well as regulating lipogenic proteins and genes. Typically, this peptide remains encrypted within its parent protein sequence and is released either during maturation or through processes like chemical, microbial, or enzymatic hydrolysis (31). Furthermore, it can bind bile acids, which then can inhibit the reabsorption of bile acids in the ileum, can attach to starch and prevent it from being digested, thereby lowering blood cholesterol levels (33,34).

Additionally, *dangke* contains probiotic bacteria (30,35-37). The highest count of lactic acid bacteria contained in *dangke* was observed after three days of fermentation, with a total colony of 0.912 x 108 CFU/mL (29). Probiotic bacteria are living microorganisms that can improve the nutritional status of their host if given in the right dose (38). Probiotic bacteria have a positive impact on weight loss (39) and also exhibit anti-hyperglycemic effects through their antioxidant activity, which helps prevent oxidative damage, inhibits lipid peroxidation, elevate the levels of antioxidants such as glutathione, superoxide dismutase, and glutathione peroxidase; additionally, probiotic bacteria can enhance the bioavailability of gliclazide, as well as inhibit and or delay intestinal glucose absorption (40). Based on a meta-analysis (41), probiotic bacteria demonstrated a significant reduction in serum total cholesterol levels. Probiotic bacteria intake can lead to elevated levels of short-chain fatty acids (SCFA), particularly propionate, which effectively inhibits hydroxymethylglutaryl coenzyme A reductase (HMG CoA reductase) in the liver. This is a rate-limiting step of the cholesterol synthesis pathway, leading to increased cholesterol metabolism (42).

A limitation of this study is that we did not measure all parameters associated with metabolic

syndrome conditions. In addition, the duration of the treatment seems to be still short enough for conditioning metabolic syndrome in experimental animals. However, our findings have revealed some of the advantages that *dangke* has in preventing or reducing the risk of metabolic syndrome.

CONCLUSION

Dangke consumption has been shown to effectively inhibit the increase in body weight, fasting blood glucose levels, and total cholesterol levels in rats subjected to high-fat and fructose diets. These findings serve as valuable reference points for future clinical research trials on the effects of *dangke* consumption on body weight, glucose levels, and total cholesterol levels using human subjects. However, carrying out similar studies with diverse parameters is necessary to uncover the potential influence that *dangke* may have on human metabolic processes.

REFERENCES

1. Marques C, Meireles M, Norberto S, Leite J, Freitas J, Pestana D, et al. High-fat diet-induced obesity Rat model: A comparison between Wistar and Sprague-Dawley Rat. Adipocyte. 2016;5(1):11-21.
2. Gadde KM, Martin CK, Berthoud HR, Heymsfield SB. Obesity: Pathophysiology and Management. J Am Coll Cardiol. 2018;71(1):69-84.
3. Catrysse L, van Loo G. Adipose tissue macrophages and their polarization in health and obesity. Cellular Immunology. 2018;330:114-119.
4. Benaicheta N, Labbaci FZ, Bouchenak M, Boukortt FO. Effect of sardine proteins on hyperglycaemia, hyperlipidaemia and lecithin: Cholesterol acyltransferase activity, in high-fat diet-induced type 2 diabetic rats. Br J Nutrit. 2016;115(1):6-13.
5. Burhans MS, Hagman DK, Kuzma JN, Schmidt KA, Kratz M. Contribution of Adipose Tissue Inflammation to the Development of Type 2 Diabetes Mellitus. Comprehensive Physiology. 2018;9(1):1-58.
6. Chait A, den Hartigh LJ. Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease. Frontiers in Cardiovascular Medicine. 2020;7.
7. Sustar U, Kordonouri O, Arens S, Kovac J, Sedej K, Battelino T, et al. Evaluation of Body Mass Index, Overweight and Obesity Status, and Cholesterol Levels in Younger Children. JAMA Network Open. 2023;6(4):e238141–e238141.
8. Hill MF, Bordoni B. Hyperlipidemia. In: StatPearls. StatPearls Publishing; 2022.
9. Grossman DC, Bibbins-Domingo K, Curry SJ, Barry MJ, Davidson KW, Doubeni CA, et al. Screening for obesity in children and adolescents: US Preventive Services Task Force recommendation statement. JAMA. 2017;317(23):2417-2426.
10. Fraschetti EC, Skelly LE, Ahmed M, Biancaniello EC, Klentrou P, Josse AR. The Influence of Increased Dairy Product Consumption, as Part of a Lifestyle Modification Intervention, on Diet Quality and Eating Patterns in Female Adolescents with Overweight/Obesity. Children. 2022;9.
11. Baruah R, Ray M, Halami PM. Preventive and therapeutic aspects of fermented foods. J Applied Microbiol. 2022;132(5):3476-3489.
12. Nampoothiri KM, Beena DJ, Vasanthakumari DS, Ismail B. Health benefits of exopolysaccharides in fermented foods. In: Fermented foods in health and disease prevention. Elsevier; 2017.p.49-62.
13. Marangoni F, Pellegrino L, Verduci E, Ghiselli A, Bernabei R, Calvani R, et al. Cow's milk consumption and health: A health professional's guide. J Am Coll Nutrit. 2019;38(3):197-208.
14. Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis of cohort studies. Am J Clin Nutrit. 2013;98(4):1066-1083.
15. Alexander DD, Bylsma LC, Vargas AJ, Cohen SS, Doucette A, Mohamed M, et al. Dairy consumption, and CVD: A systematic review and meta-analysis. Br J Nutrit. 2016;115(4):737-750.
16. Zhao D, Cao J, Jin H, Shan Y, Fang J, Liu F. Beneficial impacts of fermented celery (*Apium graveolens L.)* juice on obesity prevention and gut microbiota modulation in high-fat diet-fed mice. Food & Function. 2021;12(19):9151-9164.
17. Riyandani R, As'ad S, Hidayanty H, Ahmad M, Usman AN. Effectiveness of Giving Dangke Crackers on Improving Hemoglobin Levels in Trimester Pregnant Woman II with Anemia. Internat J Current Res Rev. 2020;12(22):158-161.
18. Samad R, Achmad H, Burhanuddin DP, Rieuwpassa I, Ardiansyah M, Nisrina, et al. Influence of *dangke* (Cheese Typical Enrekang, South Sulawesi) consumption to calcium and phosphate levels in saliva, remineralization of enamel, number and type of bacteria in dental plaque. J Internat Dental Med Res. 2018;11(3):960-966.

19. Wijaya IK. Improvement Of Nutritional Status of Children Aged 3-5 Years Through Giving Additional Food of Dangke Chips. Comprehensive Nursing J. 2021;7(2).
20. Sulmiyati RM. Pemberian Whey-Dangke dalam Air Minum Menekan Kadar Kolesterol, Trigliserida dan Lipoprotein Darah Ayam Broiler. J Veteriner Juni. 2017;18(2):257-262.
21. Zhao B, Wu F, Han X, Zhou W, Shi Q, Wang H. Protective effects of acarbose against insulitis in multiple low-dose streptozotocin-induced diabetic mice. Life Sciences. 2020;263:118490.
22. Othman ZA, Zakaria Z, Suleiman JB, Ghazali WSW, Mohamed M. Anti-Atherogenic Effects of Orlistat on Obesity-Induced Vascular Oxidative Stress Rat Model. Antioxidants (Basel, Switzerland). 2021;10(2).
23. Tenorio-Jiménez C, Martínez-Ramírez MJ, Gil Á, Gómez-Llorente C. Effects of Probiotics on Metabolic Syndrome: A Systematic Review of Randomized Clinical Trials. Nutrients. 2020;12(1):124.
24. Moughaizel M, Dagher E, Jablaoui A, Thorin C, Rhimi M, Desfontis JC, et al. Long-term high-fructose high-fat diet feeding elicits insulin resistance, exacerbates dyslipidemia and induces gut microbiota dysbiosis in WHHL rabbits. PLoS One. 2022;17(2):e0264215.
25. Chyau CC, Wang HF, Zhang WJ, Chen CC, Huang SH, Chang CC, et al. Antrodan alleviates high-fat and high-fructose diet-induced fatty liver disease in the C57BL/6 mice model via AMPK/Sirt1/SREBP-1c/PPARγ pathway. International J Molecular Sciences. 2020;21(1):360.
26. Seebacher F, Tallis J, McShea K, James RS. Obesity-induced decreases in muscle performance are not reversed by weight loss. International J Obesity. 2017;41(8):1271-1278.
27. Sjöström L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP, Krempf M. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regains in obese patients. European Multicentre Orlistat Study Group. Lancet. 1998;352(9123):167-172.
28. Mozaffarian D. Dairy Foods, Obesity, and Metabolic Health: The Role of the Food Matrix Compared with Single Nutrients. Advances in Nutrition. 2019;10(5):917S-923S.
29. Sasmita S, Djabir Y, Yustisia I, Malaka R, Kurniawan LB, Aminuddin A, et al. Potential use of fermented *dangke* cheese to improve glycemic control in rats fed with a high-fat glucose diet and propylthiouracil. Azerbaijan Medical J. 2023;63:7089-7096.
30. Fadhilah AN, Hafsan H, Nur F. Reduction of cholesterol levels by lactic acid bacteria from *dangke in vitro*. In: Proceedings of the National Seminar on Biology. 2015.
31. Udenigwe CC, Rouvinen-Watt K. The role of food peptides in lipid metabolism during dyslipidemia and associated health conditions. International J Molecular Sciences. 2015;16(5):9303-9313.
32. Antony P, Vijayan R. Bioactive Peptides as Potential Nutraceuticals for Diabetes Therapy: A Comprehensive Review. International J Molecular Sciences. 2021;22(16):9059.
33. Park YW, Nam MS. Bioactive peptides in milk and dairy products: a review. Korean J Food Science of Animal Resources. 2015;35(6):831.
34. Evaristus NA, Wan Abdullah WN, Gan CY. Extraction and identification of α-amylase inhibitor peptides from Nephelium lappacheum and Nephelium mutabile seed protein using gastro-digestive enzymes. Peptides. 2018;102:61-67.
35. Malaka R, Laga A, Ako A, Zakariah M, Mauliah FU. Quality and storage time of traditional dangke cheese inoculated with indigenous lactic acid bacteria isolated from Enrekang District, South Sulawesi, Indonesia. Biodiversitas J Biological Diversity. 2022;23(6).
36. Nur F, Hatta M, Natzir R, Djide MN. Isolation of lactic acid bacteria as a potential probiotic in dangke, a traditional food from Enrekang, Indonesia. International J Sciences: Basic and Applied Research. 2017;35(1):19-27.
37. Syah SP, Sumantri C, Arief II, Taufik E. Research article isolation and identification of indigenous lactic acid bacteria by sequencing the 16S rRNA from dangke, A traditional cheese from Enrekang, South Sulawesi. Pakistan J Nutr. 2017;16:384-392.
38. Mendonça AA, Pinto-Neto WD, da Paixão GA, Santos DD, De Morais MA, De Souza RB. Journey of the Probiotic Bacteria: Survival of the Fittest. Microorganisms. 2023;11.
39. León Aguilera XE, Manzano A, Pirela D, Bermúdez V. Probiotics and Gut Microbiota in Obesity: Myths and Realities of a New Health Revolution. J Personalized Medicine. 2022;12(8):1282.
40. Zhang Q, Wu Y, Fei X. Effect of probiotics on glucose metabolism in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. Medicina. 2016;52(1):28-34.
41. Wang L, Guo MJ, Gao Q, Yang JF, Yang L, Pang XL, et al. The effects of probiotics on total cholesterol: A meta-analysis of randomized controlled trials. Medicine. 2018;97(5):e9679.
42. Momin ES, Khan AA, Kashyap T, Pervaiz MA, Akram A, Mannan V, et al. The Effects of Probiotics on Cholesterol Levels in Patients with Metabolic Syndrome: A Systematic Review. Cureus. 2023;15(4).

ARTÍCULO ORIGINAL

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Relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital

Relación entre la ansiedad y la calidad del sueño en pacientes con cáncer en quimioterapia del Hospital Público Central Dr. M. Djamil

Weny Amelia[1a], Ria Desnita[2a], Fitria Alisa[3a], Lola Despitasari[4a]

SUMMARY

Introduction: *Cancer is a disease caused by abnormal division and growth of body tissue cells, so these cells turn into cancer cells which are harmful to the body. One of the treatments for cancer patients is chemotherapy. The impact of chemotherapy in cancer patients on the psychological aspects of experiencing anxiety and disrupting sleep quality. This study aimed to determine the relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital.*
Methods: *The type of research used is an analytic survey using a cross-sectional study design. The sample was 90 respondents with the sampling technique is accidental sampling. The stress instrument uses the DASS (Depression on Anxiety Stress Scale) 42 which consists of 14 questions about anxiety while the sleep quality instrument uses the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The results of this study were processed using the Chi-Square test.*
Results: *The results of this study for anxiety showed that 12.2% of respondents experienced mild anxiety, 45.6% of respondents experienced moderate anxiety, 36.7% of respondents experienced severe anxiety, and 5.5% of respondents experienced very severe anxiety. As for sleep quality, the results showed that 93.3% of respondents experienced poor sleep quality and 6.7% of respondents experienced good sleep quality. It can be concluded that there is a relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy (p = 0.0001).*
Conclusion: *The results of this study show a relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital. With this research, it can help nurses identify the anxiety of cancer patients undergoing chemotherapy.*

Keywords: *Anxiety, Cancer, Chemotherapy, Sleep Quality*

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ORCID: 0009-0006-6395-4495[1]
ORCID: 0000-0003-2667-5017[2]
ORCID: 0009-0008-8898-2091[3]
ORCID: 0009-0001-6846-6013[4]

[a]Bachelor of Nursing Program, STIKes Mercubaktijaya Padang, West Sumatera, Indonesia.

*Corresponding Author: Weny Amelia
E-mail: wenyamelia@mercubaktijaya.ac.id
Address: Jalan Jamal Jamil Pondok Kopi Siteba Padang, Sumatera Barat

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RESUMEN

Introducción: *El cáncer es una enfermedad causada por la división y crecimiento anormal de las células de los tejidos del cuerpo, de modo que estas células se convierten en células cancerosas que son dañinas para el cuerpo. Uno de los tratamientos para los*

pacientes con cáncer es la quimioterapia. El impacto de la quimioterapia en pacientes con cáncer en los aspectos psicológicos de experimentar ansiedad y alterar la calidad del sueño. El objetivo de este estudio fue determinar la relación entre la ansiedad y la calidad del sueño en pacientes con cáncer sometidos a quimioterapia en el Hospital Público Central Dr. M. Djamil.

Métodos: *El tipo de investigación utilizado es una encuesta analítica utilizando un diseño de estudio transversal. La muestra es de 90 encuestados con la técnica de muestreo que es el muestreo accidental. El instrumento de estrés utiliza el DASS (Depression on Anxiety Stress Scale) 42 que consta de 14 preguntas sobre ansiedad mientras que el instrumento de calidad del sueño utiliza el cuestionario Pitssburgh Sleep Quality Index (PSQI). Los resultados de este estudio se procesaron mediante la prueba Chi-Cuadrado.*

Resultados: *Los resultados de este estudio para la ansiedad mostraron que el 12,2 % de los encuestados experimentaron ansiedad leve, el 45,6 % de los encuestados experimentaron ansiedad moderada, el 36,7 % de los encuestados experimentaron ansiedad severa y el 5,5 % de los encuestados experimentaron ansiedad muy severa. En cuanto a la calidad del sueño, los resultados mostraron que el 93,3 % de los encuestados experimentó una mala calidad del sueño y el 6,7 % experimentó una buena calidad del sueño. Se puede concluir que existe una relación entre la ansiedad y la calidad del sueño en pacientes oncológicos en quimioterapia (p = 0,0001).*

Conclusión: *Los resultados de este estudio muestran una relación entre la ansiedad y la calidad del sueño en pacientes con cáncer que reciben quimioterapia en el Hospital Público Central Dr. M. Djamil. Con esta investigación, puede ayudar a las enfermeras a identificar la ansiedad de los pacientes con cáncer que se someten a quimioterapia.*

Palabras clave: *Ansiedad, cáncer, quimioterapia, calidad del sueño.*

INTRODUCTION

Cancer is a disease caused by abnormal growth of body tissue cells a result of which these cells turn into cancer cells which are harmful to the body. Cancer is still a major health problem in the world and one of the highest causes of death in the world (1). According to the World Health Organization (WHO), the number of cancer data in the world in 2020 was 19 292 789 cases with the death rate due to cancer in the world in 2020 as many as 9 958 133 (10.65 %). In Southeast Asia, the number of cancer cases in 2020 was 1 100 037 cases with a death rate due to cancer in 2020 of 689 093 (10.08 %). Based on basic health research data (2018), the prevalence of cancer in Indonesia shows an increase from 1.4 per 1 000 population in 2013 to 1.79 per 1 000 population in 2018. Data on the incidence of cancer in Indonesia in 2020 reached 946 088 cases (2). According to data from GLOBOCAN, the number of new cancer cases in Indonesia in 2020 was 396 914. According to data from the Ministry of Health (Ministry of Health, 2019) in West Sumatra, cancer patients in 2019 were 2.4779 per 1 000 population with a death rate due to cancer in Indonesia in 2020 of 234 511 (3).

Chemotherapy is a treatment using drugs or hormones to reduce cancer cells. Chemotherapy is the process of administering anticancer drugs or cytokines whose function is to kill cancer cells through a chemotactic mechanism, by interfering with their function and reproduction to heal, regulate, or relieve symptoms (4). The proportion of cancer treatment with chemotherapy based on the 2018 Riskesdas results illustrates that most of the population in Indonesia is undergoing cancer treatment with chemotherapy of 24.9 %. The incidence of cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital in 2017 there were 423 patients. This figure has increased in 2018 to as many as 540 patients (5). Hospital medical record data from Dr. M. Djamil Central Public Hospital in 2020 shows that visits to receive chemotherapy services for cancer from January - June were 2 045 visits (6). Chemotherapy's side effects can arise both physically and psychologically. Physical side effects of chemotherapy include nausea, vomiting, hair loss, dry mouth, mouth sores, sore throat, diarrhea, pancytopenia, allergies, hypersensitivity effects on sexual organs, affecting nerves and muscles, skin problems, fatigue, and constipation. The psychological side effects are anxiety, depression, shame, helplessness, and anger (7).

According to a study by Khairani et al. (2019), 100 % of patients undergoing chemotherapy have a side effect, namely fatigue (8). The fatigue felt by cancer patients is caused by pain, sleep disturbances, emotional disturbances, and the effects of the treatment being carried out (9). Another study showed that around 30 % to 80 %

of women with cancer will experience sleep disturbances. This sleep disorder can result in a decrease in the patient's sleep quality (10).

Sleep quality is a state of sleep experienced by an individual that results in freshness and well-being when awake. From several studies in Indonesia, poor sleep quality is a problem that occurs in many cancer patients undergoing chemotherapy. Amelia et al. (2021) demonstrated that most cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital experienced poor sleep quality at 93.3 % (11). Krisdhiyanti in 2016 evaluated the sleep quality in cancer patients undergoing chemotherapy at Dr. Hasan Sadikin Bandung and showed that 69 patients experienced poor sleep quality out of 83 patients undergoing chemotherapy (12). This proves that the sleep quality of patients undergoing chemotherapy is poor.

One of the factors that affect the quality of sleep is anxiety. Anxiety is a psychological state caused by constant worry. Anxiety is a negative emotional reaction to a real or imagined threat that is accompanied by changes in the autonomic nervous system and subjective tension, fear, and anxiety sensations. The impact of anxiety that arises in cancer patients is in the form of fear that their age will be short (related to inner conflict). In addition, anxiety can also increase the effects of chemotherapy (13). Anxiety in cancer patients is a psychological disorder caused by patients facing uncertainty, worrying about the effects of cancer treatment, and fear of cancer development which results in death, in some situations they feel angry, scared, sad, and depressed and often experience mood swings (14). According to Afifah and Padoli's (2018) in their study on breast cancer patients, the anxiety level of breast cancer patients undergoing chemotherapy in the Working Area of the Pucang Sewu Health Center, Surabaya, most (55 %) experienced mild anxiety, a small proportion (15 %) experienced moderate anxiety, and almost half experiencing severe anxiety (30 %) (15). A study conducted by Retnaningsih (2020) also stated that 73.3 % of breast cancer patients undergoing chemotherapy at Urip Sumoharjo Hospital Bandar Lampung in the chemotherapy room or 22 people experienced anxiety (16). Furthermore, Purwati and Maryati (2016), at Prof. Hospital. Dr. Margono Soekarjo Purwokerto revealed that there is a relationship between anxiety and the sleep quality of patients with breast cancer (17). On the contrary, Linawati (2014) revealed that in their research there was no relationship between anxiety and the sleep quality of breast cancer patients at Dharmais Hospital, Jakarta (18). Thus, the evidence about the relationship between anxiety and sleep quality is still a matter of debate. The present study aimed to assess the possible relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital.

METHODS

The type of research conducted was an analytic survey with a cross-sectional research design. The sampling technique used the consecutive sampling method. The sample was cancer patient respondents undergoing chemotherapy in the chemotherapy room of RSUP Dr. M. Djamil Central Public Hospital which is suitable as a source of data according to the inclusion and exclusion criteria. Inclusion criteria for samples that were eligible to be included or worthy of research were: willing to be respondents, able to communicate well (cooperative), and cancer patients undergoing chemotherapy were present at the time of the study. While the exclusion criteria in the study were respondents experiencing physical impairment (disability), respondents experiencing hearing loss, and respondents taking sleeping pills. The total sample in this study was 90 cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital.

The research instruments used in this study were the Pittsburgh Sleep Quality Index (PSQI) which was used to measure sleep quality in adults and the DASS (Depression Anxiety Stress Scale) which was used to measure anxiety. This research was carried out through an ethical test at Dr. M Djamil Central Public Hospital.

RESULTS

Characteristics of Respondents Undergoing Chemotherapy

As shown in Table 1, based on gender most of the cancer patient respondents were (90 %) women. Half of cancer patients based (58.9 %) were ≥ 47 years old. More than half were with breast cancer (53.3 %), with a frequency of chemotherapy mostly (87.8 %) <5 times.

Table 1

Characteristics of Respondents in Cancer Patients Undergoing Chemotherapy at the Dr. M. Djamil Central Public Hospital (n= 90)

Characteristic of respondents	f	%
Age		
<47	37	41.1
≥47	53	58.9
Total	90	100.0
Gender		
Man	9	10
Woman	81	90
Total	90	100
Type of cancer		
Acute myeloid leukemia	1	1.1
Breast cancer	48	53.3
Carsinoma cervix	11	12.2
Colorectal cancer	4	4.4
Endometrial Cancer	1	1.1
Tongue cancer	1	1.1
Ovary cancer	12	13.3
Lung cancer	1	1.1
Rectal cancer	3	3.3
Nasopharyngeal cancer	3	3.3
Hodgkin's lymphoma	2	2.2
Multiple myeloma	1	1.1
Uterine sarcoma	1	1.1
Squamous cell carcinoma	1	1.1
Total	90	100.0
Chemotherapy to		
<5	79	87.8
≥5	11	12.2
Total	90	100.0

The Anxiety of Cancer Patients Undergoing Chemotherapy

Most respondents who experienced cancer and underwent chemotherapy were found to have a moderate anxiety level of 45.6 %, while 33 % had heavy anxiety (Table 2).

Table 2

Distribution of anxiety frequency of cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital (n=90)

ANXIETY	f	%
Mild anxiety	11	12.2
Moderate anxiety	41	45.6
Heavy anxiety	33	36.7
Very serious anxiety	5	5.5
Total	90	100.0

Sleep Quality of Cancer Patients Undergoing Chemotherapy

Most of the respondents, as much as 93.3 % of the 90 respondents who underwent chemotherapy, stated that their sleep quality was bad (Table 3).

Table 3

Frequency distribution of sleep quality in cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital (n=90)

Sleep Quality	f	%
Good	6	6.7
Bad	84	93.3
Total	90	100.0

The Relationship between Anxiety and Sleep Quality in Cancer Patients Undergoing Chemotherapy

As shown in Table 4, respondents with moderate anxiety had poor sleep quality as much as 45.6 % of 90 respondents. Meanwhile, respondents with mild anxiety had good sleep quality as much as 6.7 % of 90 respondents (p-value = 0.0001, p ≤0.05).

Table 4

Distribution of anxiety frequency of cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital (n=90)

Anxiety	Sleep Quality						P values
	Good		Bad		Total		
	f	%	f	%	f	%	0.0001
Mild	6	6.7	5	5.5	11	12.2	
Moderate	0	0.0	41	45.6	42	45.6	
Heavy	0	0.0	33	36.7	33	36.7	
Very serious	0	0.0	5	5.5	5	5.5	
Total	6	6.7	90	93.3		100.0	

DISCUSSION

Chemotherapy is the process of administering anti-cancer drugs in the form of liquid pills or capsules or through infusions with the purpose to destroy cancer cells and prevent tumor growth (4,7). Patients with chemotherapy often experience anxiety which causes sleep pattern disturbances, usually, anxiety often occurs in breast cancer patients undergoing chemotherapy in the first, second, and third stages, the management that can be done by a nurse is to provide education about emotional support, assess needs patients, fears, and patient coping mechanisms (14).

Characteristics of Respondents Undergoing Chemotherapy

Our present results show that 91 % of cancer patients were women. According to Handayani and Udani (2016), judging from the gender factor, the risk of cancer in women and men is the same, but with the many incidences of cervical cancer and breast cancer in women, it seems that the incidence of cancer in women is higher (19). However, when analyzing the age factor, the incidence of cancer in women and men is not the same. In children under 15 years, the incidence of cancer in men is higher, at the age of 15-55 years the incidence of cancer is higher in women, especially in the age range of 35-50 years. After the age of 60 years, the incidence of cancer is higher in men. Our present study indicates that cancer patients based on age, more than half (58.9 %) were ≥ 47 years old, showing similarities with the theory which states that the incidence of cancer increases with age. According to the American Cancer Society, about 76 % of cancer incidence occurs over the age of 55. This makes age a risk factor for cancer (20). Based on the theory, the frequency of cancer has increased with increasing age, due to the accumulation of somatic mutations that cause the development of malignant neoplasms, and with increasing age, the higher the risk of developing breast cancer (21).

The most common type of disease was breast cancer (53.3 %). According to the 2018 Basic Health Research (Riskesdas), the highest incidence rate in Indonesia for men is lung cancer, which is 19.4 per 100 000 population, followed by liver cancer, which is 12.4 per 100 000 population. Meanwhile, the highest incidence rate for women was breast cancer, which was 42.1 per 100 000 population, followed by cervical cancer, which was 23.4 per 100 000 population (22).

Regarding the frequency of chemotherapy, our data show that most (87.8 %) were <5 times. In effect, Afifah and Sarwoko (2020) observed in their study that of the 32 respondents, the highest frequency of chemotherapy was second chemotherapy (23). Patients who undergo chemotherapy every cycle have a treatment process with chemotherapy interspersed with recovery periods.

Anxiety of Cancer Patients Undergoing Chemotherapy

Cancer patients undergoing chemotherapy have different levels of anxiety with various factors causing anxiety such as age and education, anxiety disorders can occur at all ages, more often in adulthood. As an adult, a person usually has a heavier mind load, lasts a long time, and is accompanied by many physiological components such as sleep disturbances, restlessness, imagining, fear, and anxiety. Indeed, the respondents who experienced cancer and underwent chemotherapy were found to have a moderate anxiety level of 45.6 %. The results of this study are supported by previous research conducted by Primal et al. (2020) concerning the level of anxiety and sleep patterns of breast cancer patients who are undergoing chemotherapy. Their results showed that 55 breast cancer respondents who underwent chemotherapy (60.0 %) experienced moderate anxiety (24).

An overview of the factors that affect the level of anxiety based on the age of women aged 45-50 years because of the knowledge factor and influence anxiety. Changes in hormone levels, life changes, and sleep disturbances during menopause can cause anxiety. In addition to generalized anxiety, people may also experience sudden, intense panic attacks. People can often manage these symptoms with lifestyle changes, medications, and psychotherapy (25). Arsittasari (2017) stated that the frequency of chemotherapy experienced by patients who are undergoing treatment for the first time is a valuable experience for subsequent treatment (26). Chemotherapy treatment which consists of several cycles is a long-term treatment, if the first experience of undergoing chemotherapy is not subject to the side effects of chemotherapy, it will affect the level of anxiety in the next chemotherapy treatment (27). Simanullang and Manullang (2020) found that most respondents who were going to undergo second chemotherapy experienced moderate anxiety because the respondent had undergone chemotherapy more than once so the respondent already had experience dealing with and experiencing the side effects (28).

The emergence of anxiety experienced by respondents while undergoing chemotherapy is caused by many things including changes in the physique that begin to experience a decline in health and can affect the quality of life which has an impact on many things, one of which is emotional. The anxiety felt by the respondent also had an impact on the patient's recovery because if the patient always experienced anxiety, it was possible that the respondent could stop the chemotherapy, the symptoms felt by the patient who was experiencing anxiety were anxiety, difficulty sleeping, and difficulty concentrating.

Sleep Quality of Cancer Patients Undergoing Chemotherapy

Sleep disorders are said to be the most common and annoying symptoms of cancer patients who have recently undergone treatment. In the present study most of the respondents, as much as 93.3 % of the 90 respondents who underwent chemotherapy, stated that their sleep quality was poor. The results are in line with the study of Amelia et al. (2021) concerning the relationship between stress and sleep quality in breast cancer patients undergoing chemotherapy during the COVID-19 pandemic at Dr. M. Djamil Central Public Hospital involving 45 respondents. The results of their study showed that 93.3 % of breast cancer respondents who underwent chemotherapy at Dr. M. Djamil Padang have poor sleep quality, and 6.7 % of respondents have good sleep quality (12).

Age is also a factor that affects the quality of sleep. Age is one of the determining factors for the length of sleep a person needs. The older a person is, the less sleep they need. Individuals who have become adults sleep about 8-10 h a day. Meanwhile, individuals who have become old adults sleep about 6-8 h a day (29).

Apart from the age factor, the frequency of chemotherapy also affects the sleep quality of breast cancer patients. In patients undergoing chemotherapy for the first time or afterward, they still experience sleep disturbances due to frequent awakenings in the middle of the night to go to the bathroom, restlessness, or being unable to get to sleep before or after waking up in the middle of the night (30).

Good quality sleep is needed by the patient's body, a sick body will have difficulty starting and maintaining sleep, if the body experiences sleep

deprivation, the body will experience decreased endurance, decreased daily activities, feel tired, and can have an impact on psychological health and have an impact on the recovery of the respondent's illness. The results of the study used the PSQI (Pittsburgh Sleep Quality Index) questionnaire involving 90 cancer respondents undergoing chemotherapy and it was found that almost all respondents experienced poor sleep quality, namely (93.3 %) with complaints of frequently using the bathroom, feeling hot, often waking up in the middle of the night or early in the morning and other complaints such as nightmares and feelings of anxiety. Quality sleep is needed by cancer patients who are undergoing chemotherapy to regenerate and repair body cells.

The Relationship between Anxiety and Sleep Quality in Cancer Patients Undergoing Chemotherapy

Anxiety in breast cancer patients can increase pain, interfere with sleep ability, increase nausea and vomiting after chemotherapy, as well as disrupt their quality of life (27). Our results support this concept since respondents with moderate anxiety had poor sleep quality as much as 45.6 % of 90 respondents. Meanwhile, respondents with mild anxiety had good sleep quality as much as 6.7 % of 90 respondents (p-value = 0.0001 ($p \leq 0.05$), suggesting a relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy. Similar results were reported by Afifah and Padoli (2018) regarding the relationship between anxiety and sleep quality in breast cancer patients in the working area of the Pucang Sewu Public Health Center, Surabaya (15), showing that nearly half of breast cancer patients experienced light (30 %) and poor (30 %) sleep quality and a small proportion experienced good sleep quality (25 %) and moderate sleep quality (15 %). Most (55 %) experienced mild anxiety, a small number experienced moderate anxiety (15 %), and almost half experienced severe anxiety (30 %). Severe anxiety with poor sleep quality at the second chemotherapy frequency was observed due to unpleasant side effects of chemotherapy to continue the next chemotherapy.

Anxiety is an unpleasant emotional reaction to real or imagined danger which is accompanied by changes in the autonomic nervous system and subjective experiences such as pressure, fear, and anxiety (28). The negative impact of anxiety can occur in cancer patients (27).

Cancer patients undergoing chemotherapy have different levels of anxiety with various factors that cause anxiety such as age. Anxiety disorders can occur at any age, more often in adulthood. The more mature a person usually the heavier burden of the mind, lasts a long time, and is accompanied by many physiological components such as sleep disturbances, anxiety, fear, and anxiety. In addition, anxiety also occurs in new patients undergoing chemotherapy for the first time.

Cancer patients who do chemotherapy have moderate levels of anxiety and poor sleep quality disturbances, and so do respondents who experience very severe anxiety have poor sleep quality. This is because many cancer patients undergoing chemotherapy are worried about the effects of the chemotherapy and anxiety that occurs in respondents was also influenced by age being ≥47 years old. A person's sleep quality is said to be good because he does not show signs of sleep deprivation and does not experience sleep problems. The lower the anxiety experienced, the better the quality of sleep, and the higher the level of anxiety, the worse the quality of sleep.

CONCLUSIONS

It was found that there is a relationship between anxiety and sleep quality in cancer patients undergoing chemotherapy at Dr. M. Djamil Central Public Hospital.

REFERENCES

1. National Cancer Institute at the National Institutes of Health. What is Cancer? Jakarta: NCINIH, 2019.
2. World Health Organization. All Cancers - Global Cancer Observatory. USA: WHO, 2019.
3. Ministry of Health. Indonesian Basic Health Research 2018. In the Ministry of Health of the Republic of Indonesia. Jakarta: KEMENKES, 2019.
4. Seprian S, Dwin D, Puspitosari P, Warih A. Emotion Regulation in the Management of Cancer Patients: A Literature Review. J Nursing Respati Yogyakarta. 2019;6(2):597-605.

5. Hospital Medical Records. Cancer patient data. Padang: RS Dr. M. Djamil Padang, 2019.
6. Hospital Medical Records. Cancer patient data. Padang: RS Dr. M. Djamil Padang, 2020.
7. Firmana D. Chemotherapy Nursing. Jakarta:Salemba Medika, 2019.
8. Khairani S, Keban SA, Afrianty M. Evaluation of the side effects of chemotherapy drugs on the quality of life (QoL) of breast cancer patients at X Hospital. Jakarta. J Ilmu Kefarmasian Indonesia. 2019;17(1):9-13.
9. Rossa G, Della D. Correlation between physical activity and quality of life of cancer patients undergoing chemotherapy in the chemotherapy room of RSUP. Jakarta, 2018.
10. Palesh O, Ulusakarya A, Tudela EO, Gerry AA. Sleep Disruption in Breast Cancer Pain Patients And Survivors. J National Comprehensive Cancer Network. 2013;11:1523-1530.
11. Alifiyanti D, Hermayanti Y, Setyorini D. Sleep quality of breast cancer patients based on therapy given at RSUO Dr. Hasan Sadikin Bandung. J Indonesian Nursing Education. 2017;3(2):115-125.
12. Amelia W, Despitasari L, Alisa F, Sari E, Lidya, Lativa N, et al. The Relationship between Stress and Sleep Quality in Cancer Patients Undergoing Chemotherapy During the COVID-19 Pandemic at RSUP. Dr. M. Djamil Padang. Muhammadiyah Nursing J. 2021;6(2):122-130.
13. Vichaya EG, Chiu GS, Krukowski K, Lacourt TE, Kavelaars A, Dantzer R, et al. Mechanisms of chemotherapy-induced behavioral toxicities. Frontiers in Neuroscience. 2015; 9(1):131-37.
14. Baqutayan S. How Can Anxiety Be Better Managed? Depression, Anxiety, And Coping Mechanisms Among Cancer Patients. Word Cancer Research J. 2019;6(1):1-10.
15. Afifah M, Padoli P. The Relationship between Anxiety and Sleep Quality in Breast Cancer Clients in the Working Area of the Puncang Sewu Health Center, Surabaya. J Chemical Information and Modeling. 2018;2953(9):1689-1699.
16. Retnaningsih D. Palliative Nursing (10th Ed). Jakarta, 2021
17. Purwati RA, Maryati S. The relationship between anxiety level and sleep quality of breast cancer patients in the Bougenvil Ward of RSUD. Prof. Dr. Margono Soekarjo Purwokerto. J Health Sci Technol. 2016;7(1):23-29.
18. Linawati L. Sleep disorders in breast cancer patients at Dharmais Hospital, Jakarta. Darmianus J Medicine. Jakarta: Faculty of Medicine, 2019.
19. Handayani H, Udani G. Sleep quality and distress in cancer patients undergoing chemotherapy. J Nursing. 2016;XII(1):66-72.
20. Amelia W, Andika M, Yulanda D. Effect of walking exercise on sleep quality in breast cancer patients undergoing chemotherapy at RSUP. Dr. M. Djamil Padang. Lighthouse Health J. 2020;3(1):16-27.
21. Solehati. Concept and application of relaxation in community nursing. Bandung: PT Refika Aditama, 2015.
22. Basic Health Research. Center for Data and Information 2018. Jakarta: Ministry of Health of the Republic of Indonesia, 2018.
23. Afifah VA, Sarwoko S. Factors that influence the Quality of Life of Breast Cancer Patients Undergoing Chemotherapy. J Health Communication. 2020;XI(1):106-119.
24. Primal D, Arif M, Dewi S. Anxiety levels and sleep patterns of breast cancer patients undergoing chemotherapy. Procedure of Perintis Health Seminar. 2020;3(1):143-149.
25. Situmorang S. Description of the Factors Affecting the Anxiety Level of Women Aged 45-50 Years in Facing the Menopausal Period in the Waterfall Village, Medan Marelan District. IMELDA J Nursing Science. 2016;1(2):32-39.
26. Arsittasari T. Factors that influence the incidence of breast cancer in the Yogyakarta city hospital in 2016". Yogyakarta; Ministry of Health Health Polytechnic, 2017.
27. Yudono D. Analysis of Factors Affecting Patient Ca Mamae's Anxiety with Chemotherapy Actions. J Health. 2019;1(2):53-63.
28. Simanullang S, Manullang M. Anxiety Level of Patients Undergoing Chemotherapy Actions of Chemotherapy at Martha Pulo Brayan Hospital Medan. J Darma Agung Husada. 2022;7(2):1-79.
29. Yulnefia Y. Relationship between Age and Sleep Quality in Abdurrab University Employees in 2016. 2016;3(2):60-65.
30. Putri DS, Makiyah N, Puspita D. The Application of the Prophet's Sunnah Before Sleep Improves Sleep Quality in Breast Cancer Patients. J Med Health. 2018;18(2):61-66.

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Relationship between self-efficacy with self-management and quality of life among Type 2 Diabetes Mellitus: A systematic review

Relación entre la autoeficacia con el automanejo y la calidad de vida en diabetes mellitus tipo 2: una revisión sistemática

Emilia Erningwati Akoit[1a], Ferry Efendi[2b]*, Yulis Setiya Dewi[3b], Santo Imanuel Tonapa[4c]

SUMMARY

Objective: *Self-efficacy is one aspect predicted to influence the self-management of type 2 Diabetes Mellitus (DM) patients. Low self-efficacy will impact DM patients' motivation to carry out self-care, causing uncontrolled blood glucose levels and decreasing the quality of life. This study aimed to determine the relationship between self-efficacy, self-management, and quality of life in type 2 DM patients using a systematic review.*
Materials and Methods: *The study design used was a systematic review. A literature search was conducted on databases such as Scopus, Web of Science, PubMed, and EBSCOhost (CINAHL) with the keywords "self-efficacy," "type 2 diabetes," "self-management," and "quality of life." Nine texts meet the inclusion criteria, including population, namely, type 2 DM patients; exposure: self-efficacy; the output was diabetes self-management, and the quality of life of type 2 DM patients, and the study type was cross-sectional.*
Results: *The results showed that there was a relationship between self-efficacy and diabetes self-management, with patients who have high self-efficacy showing greater adherence to diabetes self-management. Furthermore, there was a relationship between self-efficacy and quality of life: where self-efficacy increases, the quality of life for type 2 DM patients also increases.*
Conclusions: *Self-efficacy is needed in diabetes self-management to improve the quality of life of type 2 DM patients. Health professionals need to continue implementing several strategies to increase patient confidence and confidence in diabetes management to increase the quality of life of type 2 DM patients.*

Keywords: *Self-efficacy, self-management, quality of life, type 2 diabetes.*

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ORCID ID: 0000-0002-1230-5691[1]
ORCID ID: 0000-0001-7988-9196[2]
ORCID ID: 0000-0003-4407-0433[3]
ORCID ID: 0000-0002-9730-1939[4]

[a]Doctoral Program Student, Faculty of Nursing, Universitas Airlangga, Surabaya, Indonesia.
[b]Faculty of Nursing, Universitas Airlangga, Surabaya, Indonesia
[d]College of Nursing, Kaohsiung Medical University, Kaohsiung, Taiwan.

*Corresponding Author: Ferry Efendi
E-mail: ferry-e@fkp.unair.ac.id

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RESUMEN

Objetivo: *La autoeficacia es un aspecto que se prevé influirá en el automanejo de los pacientes con Diabetes Mellitus (DM) tipo 2. La baja autoeficacia impactará en la motivación de los pacientes con DM para llevar a cabo el autocuidado, causando niveles de glucosa en sangre descontrolados y disminuyendo la calidad de vida. Este estudio tuvo como objetivo determinar la relación entre la autoeficacia, el automanejo y la*

calidad de vida en pacientes con DM tipo 2.
Materiales y Métodos: *El diseño del estudio utilizado fue una revisión sistemática. Se realizó una búsqueda bibliográfica en bases de datos como Scopus, Web of Science, PubMed y EBSCOhost (CINAHL) con las palabras clave "autoeficacia", "diabetes tipo 2", "autogestión" y "calidad de vida". Nueve textos cumplen con los criterios de inclusión, entre ellos: población, es decir, pacientes con DM tipo 2; exposición: autoeficacia; el resultado es el autocontrol de la diabetes y la calidad de vida de los pacientes con DM tipo 2 y el tipo de estudio es un estudio transversal.*
Resultados: *Los resultados mostraron que existe una relación entre la autoeficacia y el automanejo de la diabetes, siendo los pacientes que tienen autoeficacia alta los que muestran mayor adherencia al automanejo de la diabetes. Además, existe una relación entre la autoeficacia y la calidad de vida, donde aumenta la autoeficacia, también aumenta la calidad de vida de los pacientes con DM tipo 2.*
Conclusiones: *Es necesaria la autoeficacia en el autocontrol de la diabetes para que pueda mejorar la calidad de vida de los pacientes con DM tipo 2. Los profesionales de la salud deben continuar implementando varias estrategias para aumentar la confianza del paciente y la confianza en el control de la diabetes para aumentar la calidad de vida de los pacientes con DM tipo 2.*

Palabras clave: *Autoeficacia, automanejo, calidad de vida, diabetes tipo 2.*

INTRODUCTION

Diabetes Mellitus (DM) is one of the most common chronic diseases and the most significant health problem in many countries (1). If the blood glucose levels rise out of control, it can lead to several problems that can affect the patient's comfort and quality of life (2). In 2016, the World Health Organization (WHO) mentioned that DM is a long-term metabolic disease marked by high blood glucose levels that damage the heart, blood vessels, eyes, kidneys, nerves, and nerve endings. DM is one of the leading causes of death worldwide, with around 1.5 million yearly deaths. The number of DM patients worldwide for 2021 is 537 million and is predicted to increase to 643 million in 2030 and 783 million in 2045 (3). One of the study's findings was that people with DM have a life expectancy of 4-8 years shorter than those without the disease (4). Therefore, DM patients need adequate management by maximizing self-efficacy and abilities that exist themselves.

Self-efficacy is an individual's belief in his ability to display activities that affect his life, which is related to his ability to do self-care (5). A study reported that 63.9 % of type 2 DM patients showed less self-efficacy in DM management (6), while another study showed that the majority of type 2 DM patients have an adequate (64.9 %), low (10.4 %), and high (24.7 %) quality of life (7). Some of these problems show how important it is for type 2 DM patients to improve their self-management and quality of life by building their self-efficacy.

Type 2 DM patients need good adherence to self-management of diabetes, but sometimes patients are unsure of their ability to carry out self-care. This fits with a previous study which indicates that a person's self-efficacy is insufficient after being diagnosed with DM and having complications (8). Another point of view explains that everyday DM patients have to perform self-care tasks that are difficult for them and burden patients, thus affecting their self-efficacy (9). Also, it was shown that type 2 DM patients often don't stick to their diets because they don't understand, and they use things like self-efficacy, motivation, knowledge, practical goals, and social support, which help people take care of themselves (10). Furthermore, self-efficacy is indirectly related to self-management through efforts to overcome obstacles, commitment to a therapeutic regimen, and persistence in following a self-management plan (11).

Evidence indicated that self-efficacy influences self-management and quality of life in type 2 diabetes patients, helping people with type 2 diabetes to take better care of themselves (12). Self-efficacy also positively affects self-management and the quality of life of people with type 2 diabetes (6,13). However, low self-efficacy makes people with type 2 diabetes less likely to take care of themselves, having a lower quality of life if they didn't think they could do things well (14).

Previous research shows a relationship between self-efficacy and DM self-management (12,15-17). Self-efficacy affects self-management, especially when giving insulin injections, taking medications as prescribed, and checking blood

glucose levels independently (18). Another point of view indicates that when people with type 2 diabetes have low self-efficacy, they don't feel confident in their ability to care for themselves, leading to complications (19). Furthermore, several studies show a relationship between self-efficacy and quality of life in type 2 DM patients (14,20). This can be explained by a study on self-efficacy in type 2 DM patients, which shows that type 2 DM patients with poor self-efficacy will have a decreased quality of life (13).

Based on a literature review related to self-efficacy, most studies show the effectiveness of self-efficacy on diabetes self-management and improving the quality of life of type 2 DM patients, especially regarding drug regulation or diabetes medication (21). Other studies have also found no significant relationship between self-efficacy and the quality of life of type 2 DM patients, especially in the physical health component (22).

Several systematic studies are being conducted to analyze the relationship between self-efficacy and diabetes self-management and the quality of life of type 2 DM patients in developing countries. But most studies haven't gone into detail about how strong self-efficacy is for the self-management of diabetes and the quality of life of people with type 2 DM. This is shown by the fact that health professionals aren't told how to improve self-efficacy as a separate intervention. When taking a patient's medical history, health professionals can start by figuring out how good the patient is at taking care of themselves. Next, they can teach the patient about self-management of diabetes as an intervention that can be built into health services. Health workers can teach people about the importance of self-efficacy in diabetes self-management and improving the quality of life for people with type 2 diabetes if they know its importance. Thus, we conducted a systematic review to determine the relationship between self-efficacy, diabetes self-management, and the quality of life of people with type 2 DM in developing countries.

METHODS

This study's design was a systematic review using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (23).

Inclusion and exclusion criteria

This study examined the relationship between self-efficacy and self-management of diabetes and the quality of life of individuals with type 2 DM. The inclusion criteria in this systematic review: population (P) in patients diagnosed with type 2 DM. Exposure (E) is self-efficacy. The main outcome (O) expected in this paper is diabetes self-management and quality of life of type 2 DM patients. The study design (S) used in the research is a cross-sectional study. Exclusion criteria for this systematic review: type 1 diabetes, and all other types of diabetes. Other outcomes, including social support, are excluded. This research employs a cross-sectional design for its analysis and PEO (S) framework in Table 1.

Table 1. PEO(S) Framework

PEO (S)	Description of detail
Population	Type 2 Diabetes Mellitus patients
Exposure	Self-efficacy
Outcome	Self-management and quality of life
Study Design	Cross-sectional study

Literature search strategy

From 2018 to 2022, a literature search was conducted using the databases Scopus, Web of Science, PubMed, and EBSCOhost (CINAHL). The search strategy consisted of multiple steps, including entering keywords to view articles pertinent to the research. Combining the terms "self-efficacy", "type 2 diabetes", "self-management", and "quality of life" led to this result. The following step was to check for duplicates between databases and remove duplicate articles, followed by reading the title and abstract. Adjusting to the established inclusion and exclusion criteria is the next step. In the

end, we obtained the full text of the articles and identified nine that met the criteria for a systematic review. In addition, a manual study selection process was conducted for articles that met the research objectives. Articles that did not align with the objectives of the study were excluded. If articles were duplicated, then the duplicated articles were removed. In addition, relevant titles and abstracts were screened for relevance to the research objectives.

Data extraction

The authors reviewed all of the abstracts returned by the initial search and eliminated any studies that did not meet the inclusion criteria. During the data extraction process, the author, publication year, study design, baseline sample, final sample size, and duration of exposure were collected. After the data extraction process, all authors reevaluated the extracted data to ensure its accuracy. Inconsistent data was discussed in face-to-face meetings.

Critical assessment of the methodological quality of the study

Utilizing a checklist recommended by the Joanna Briggs Institute, this guide evaluates the quality of the study methodology (24). This cross-sectional research checklist contains eleven items. Each response item is rated as "yes," "no," "clear," or "not applicable" based on the information provided by the relevant article. Calculated by dividing the number of items rated "yes" by the total number of items, the score indicates the quality of the study as a whole. Studies with a score of 75 % were categorized as high quality, those between 50 % and 74 % as medium quality, and those with a score of 50 % as low quality. The evaluation of the study's quality yielded a score of 88.9 percent, or high quality (Table 2).

Data synthesis

Each selected article's full text was reviewed to extract essential information for a table summary. This section included the study's design, the sampled population, the instruments used, the variables and measurements, and the main conclusions. The key findings from the included studies were analyzed in narrative form (Table 3).

RESULTS

Study selection

A search of 4 databases, Scopus, Web of Science, PubMed, and EBSCOhost (CINAHL) yielded 1519 articles and two articles from other methods (citations) that may be pertinent to the research objectives (Figure 1). There were up to 270 duplicate records issued, leaving a total of 1 249 articles. In addition, up to 1 177 records were issued despite not meeting the inclusion criteria. The remaining 72 articles are being considered for review. In addition, 72 articles were evaluated for eligibility, and 65 were excluded because they did not meet the inclusion criteria, which included populations with type 1 DM patients or other types, the articles were not about self-efficacy, the results were inappropriate, and the articles were literature reviews and qualitative studies. Seven articles from database searches (12-15,17,25,26); and two articles from citation searches with full-text readings (16,20), where nine articles were included in this systematic review. Figure 1 details the study selection procedure.

Study and subject characteristics

Table 3 shows the characteristics of study participants among nine studies, of which seven studies were conducted in Asian countries, including two studies conducted in Indonesia (13,15), one study conducted in Malaysia (20), Saudi Arabia (16); Iraq (17); Turkey (14); and China (26). Furthermore, two studies were conducted in African countries, Sudan (12) and Ethiopia (25). 4 337 patients with type 2 diabetes, aged 20 to 80, participated in the study. Two studies were conducted in primary health care (13,20); five studies were conducted at the hospital (12,14,15,17,25); and two studies

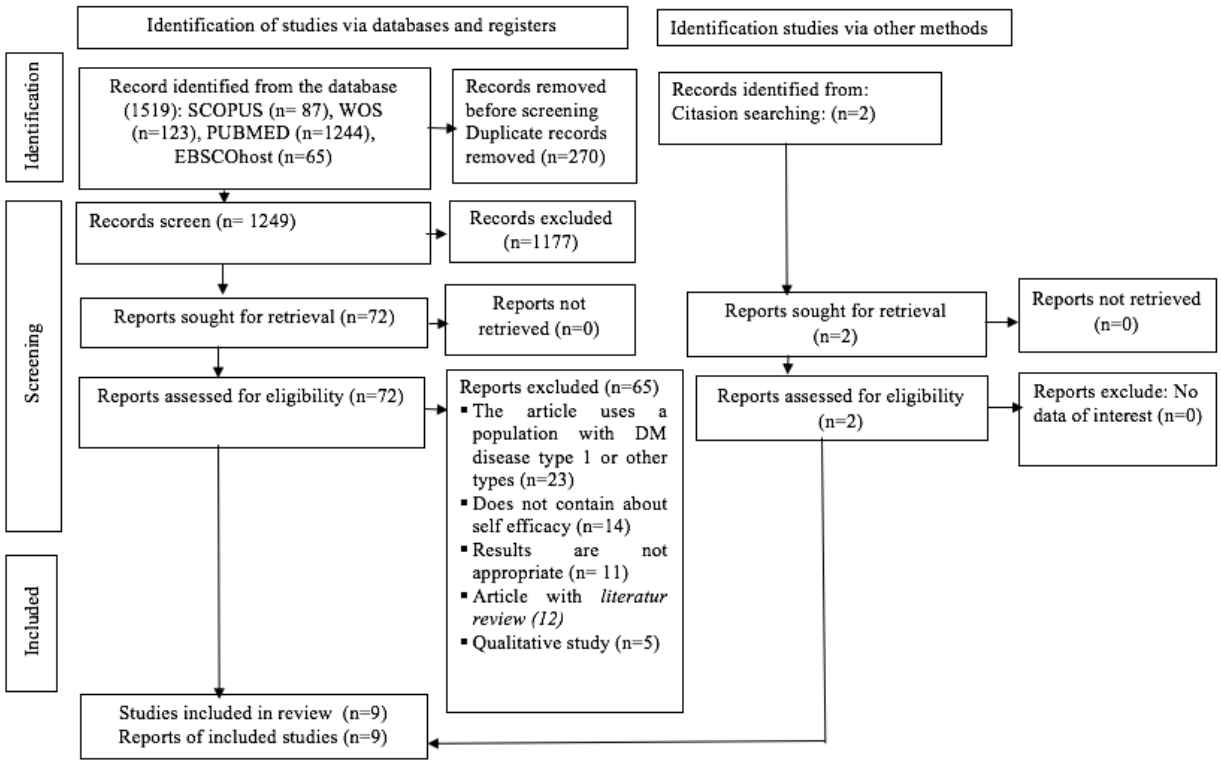

Figure 1. Flow chart of study selection.

were conducted in the community (16,26). Every study utilized a cross-sectional design. This study included patients with type 2 diabetes, including 1 974 men (45.5 %) and 2 363 women (54.5 %). The average age of type 2 DM patients in the studies included in this review ranges from 45 to 66.7 years (13,20). The duration of diabetes mellitus was categorized as five years for as many as 1360 people (31.4 %), >5–10 years for as many as 1516 people (35.5 %), and >0 years for as many as 1 461 people (33.6 %).

Measures

The majority of studies use the Diabetes Management Self-Efficacy Scale (DMSES) as a measurement tool or instrument to assess the self-efficacy of type 2 diabetes patients, according to a review of the literature (12–16,25). The Diabetes Empowerment Scale Short Form (DES-SF) measures a person's level of empowerment with diabetes. Malay version of the MU in Self-efficacy Questionnaire/MUSE (20), Diabetes Self Efficacy/DSE (17,26). The Health Survey Medical Outcomes Study Short Form/SF-36 (13), the WHO Quality of Life Scale (14), and the Revised Diabetes Quality of Life-13 are used to assess the quality of life (RVDQOL-13). The Revised Summary of Diabetes Self-Care Activity (12); the Summary of Diabetes Self-Care Activity (15,16); and the Diabetes Self-Management Questionnaire are used to assess diabetes self-care or management (25).

Methodological appraisal of included studies

The methodological quality of the nine cross-sectional studies revealed that the vast majority of studies (n = 9) were of high quality (Table 2).

Table 2. Study quality assessment for cross-sectional study

First Authors	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	%
Amelia et al., 2018	Yes	Yes	Yes	Yes	No	No	Yes	Yes	75.0
Amer, 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	87.5
Cagan, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	87.5
Clara et al., 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	87.5
Saad et al., 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100.0
Madram, 2022	Yes	Yes	Yes	Yes	No	No	Yes	Yes	75.0
Oluma et al., 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100.0
Yao et al., 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	87.5
Rosly et al., 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	87.5

Question description:

Un = Unclear

1) Were the criteria for inclusion clearly defined?; 2) Were the subjects and settings of the study described in detail?; 3) Are exposure measurements valid and reliable?; 4) What objectives and standard criteria were used to measure the conditions?; 5) Were confounding factors identified?; 6) Were strategies to prevent confounding variables explained?; 7) Are the results measured accurately and reliably?; 8) Was the statistical analysis employed suitable? (24).

As shown in Table 1, all studies were of high quality. Two studies lack the identification of confounding factors (13,17). Seven studies do not explain strategies for preventing confounding factors, according to the findings of the literature review (12-15,19,20,26);

The relationship between self-efficacy and self-management

From a total of nine studies, six explain the relationship between self-efficacy and diabetes self-management in type 2 DM patients, as indicated by the literature review results. According to the findings of the six studies in Table 3, type 2 DM patients with high self-efficacy have superior self-management skills (12). Another study found that for every 1-point increase in self-efficacy, self-management behaviour increases by 0.060 days after knowledge and duration of diabetes control (15). One study elaborated that type 2 DM patients with high self-efficacy could self-manage their condition effectively, including better diet arrangements, exercise, blood glucose monitoring, and foot care (16). According to additional studies, higher self-efficacy correlates with increased self-management behaviour (17). It was further explained that type 2 DM patients with high self-efficacy were 17.3 times more likely to improve good self-management behaviour than those with low self-efficacy (25). According to the findings of the most recent study, a one-point increase in self-efficacy increases self-management behaviour by 1.25 times (26).

The relationship between self-efficacy and quality of life

Three studies explain the relationship between type 2 DM patients' self-efficacy and quality of life. Table 3 demonstrates that type 2 DM patients with high self-efficacy enjoy a high quality of life. It was further explained that type 2 DM patients with high self-efficacy are 8.9 times more likely to enjoy a high quality of life than those with low self-efficacy (13). Other studies have found that self-efficacy has a weak positive relationship with life quality (14). It was elaborated that patients with high self-efficacy regarding treatment comprehension have a higher quality of life (20).

Table 3. Characteristics of the included studies

No	Title, Author, year, country	Research purposes	Design and Settings	Sample and age (age range)	Measuring instrument	Results and Conclusions
1.	Self-efficacy in type 2 diabetes mellitus patients and the relationship with the quality of life in Medan City (13), 2018, Indonesia	Analyzing the relationship between self-efficacy and quality of life among patients with type 2 diabetes at the Tuntungan Health Center in Medan	A cross-sectional study, Tuntungan Primary Health Care in Medan	83 patients with type 2 diabetes who met the inclusion criteria	Diabetes Management Self-Efficacy Scale (DMSES) for assessing self-efficacy and medical outcomes Examine the SF-36 to evaluate quality of life.	There is a relationship between self-efficacy and quality of life among type 2 DM patients at the Tuntungan Medan Health Center, with a p-value of 0.012 (p 0.05) and a 95% confidence interval for the odds ratio (OR) of 1.227-9.950. To increase the self-efficacy of type 2 DM patients, there is an immediate need for relevant and enduring health education.
2.	Influence of self-efficacy management on adherence to self-care activities and treatment outcome among diabetes mellitus type 2 Sudanese patients (12), 2018, Sudan	Determine the relationship between self-efficacy management and self-care behaviour adherence and treatment outcomes among type 2 diabetes patients in Sudan.	A cross-sectional analysis of two nursing care facilities (Zabir Abu Elitz Diabetes Center and The Outpatient Clinic in Soba Teaching Hospital)	392 patients with type 2 DM	Diabetes Management Self-Efficacy Scale (DMSES) to measure self-efficacy and Diabetes Self-Management Activity Scale (SDSCA) to measure diabetes self-management.	The relationship between self-efficacy and self-management of type 2 DM patients has a p-value of 0.002 (p 0.05) OR 2.1 with CI 1.3-3.5. Patients with a high level of self-efficacy are compliant with nutrition management, physical exercise, and medication management. Diabetes self-efficacy management is the only predictor of diabetes control.
3.	Examination of self-efficacy and quality of life of patients with type 2 diabetes regarding diabetes management (14), 2021, Turkey	Understanding the level of self-efficacy of type 2 DM patients in relation to their self-care and the factors that influence them, as well as analyzing the relation-	Cross-sectional study, State hospital	342 patients with type 2 DM 2166 patients with type 2 DM 321 patients with type 2 DM	WHO Diabetes Management Self-Efficacy Scale (SES) to measure self-efficacy, and the Diabetes Manage-	Patients with type 2 diabetes have a relationship between self-efficacy and quality of life with a p-value of 0.000 0.05 and a correlation coefficient (r-value) of

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…continuation Table 3. Characteristics of the included studies.

No	Title, Author, year, country	Research purposes	Design and Settings	Sample and age (age range)	Measuring instrument	Results and Conclusions
		ship between self-efficacy and quality of life in type 2 DM patients.			ment Self-Efficacy Scale (SES). To measure the quality of life, the Quality of Life Scale-Brief Form-Turkish Version (WHOQOL-BREF-TR) is administered	0.461 (weak strength of positive relationship). Higher diabetes self-efficacy exists among patients who are married, college-educated, have received disease-related training/information, have no other chronic diseases, and lack complications. Patients who received oral antidiabetic medications and exhibited no complications had a higher quality of life (p 0.05).
4.	Self-Efficacy as a Predictor of Self-Management Behavior Practice Among People with Type 2 Diabetes Mellitus (15), 2021, Indonesia	Identifying the association between self-efficacy and self-management behaviour in patients with type 2 Diabetes Mellitus	Cross-sectional study, Bekasi hospital	112 DM type 2 patients	Diabetes Management Self-Efficacy Scale (DMSES) to measure self-efficacy and Diabetes Self-Management Activity Scale (SDSCA) to measure diabetes self-management.	With a p-value of 0.000 0.05, there is a significant relationship between self-efficacy and self-management behaviour. Multivariate analysis reveals a relationship between self-efficacy and self-care behaviour after controlling for knowledge and duration of diabetes (B = 0.060 and R Square = 0.248, respectively).
5.	Self-efficacy, self-care, and glycemic control in Saudi Arabian patients with type 2 diabetes mellitus: Across-sectional survey(16), 2017, Saudi Arabia	Understanding the association between self-efficacy and self-management behaviour in patients with type 2 diabetes	Cross-sectional study, The Sultan bin Abdulaziz Humanitarian City in Riyadh	123 patients with type 2 DM	Diabetes Management Self-Efficacy Scale (DMSES) to measure self-efficacy and Diabetes Self-Management Activity Scale	There is a correlation between self-efficacy and self-management behaviour (good diet level (p = 0.000, OR = 0.115), exercise (p = 0.003, OR = 0.275), blood

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…continuation Table 3. Characteristics of the included studies.

No	Title, Author, year, country	Research purposes	Design and Settings	Sample and age (age range)	Measuring instrument	Results and Conclusions
					(SDSCA) to measure diabetes self-management.	sugar test (p = 0.000, OR = 0.219), and foot care (p = 0.000, OR = 0.843).
6	Self-efficacy and its relationship to self-care among type II diabetic patients (17), 2022, Iraq	Evaluating the relationship between self-efficacy and self-care in patients with type II diabetes	A correlational study, AL-Zahraa Teaching Hospital in Wasit Province/ Iraq	400 patients with type 2 DM	The Morisky Medication Adherence Scale consists of 34 items to measure self-efficacy and 30 items to measure diabetes self-management adherence.	The correlation between self-efficacy and self-care is significant (positive) (r=0.126; p=0.012). The results of the simple linear regression test indicated that self-efficacy had a significant effect on the self-care of type 2 DM patients (p=0.012, B=0.156, and beta=0.126).
7.	Perceived Self-Efficacy and Associated Factors Among Adult Patients with Type 2 Diabetes Mellitus at Public Hospitals of Western Ethiopia, (25), 2020, Ethiopia	Assessing the impact of perceived self-efficacy and related factors on type 2 diabetes patients at the Ethiopian West General Hospital.	A cross-sectional study, Public hospitals in Western Ethiopia	398 type 2 DM patients	Diabetes mellitus self-efficacy Scale (DMSES) to measure self-efficacy and the Diabetes Self Management Questionnaire (DSMQ) to measure self-management of diabetes.	Self-efficacy and self-care behaviour are related (p value 0.001; OR = 17.262) (CI9.516,31.312). Perceived self-efficacy is at a high level. Self-testing blood glucose at home, self-care behaviours, physical activity, and a special diet were significantly associated with a high perception of self-efficacy. Policymakers must pay attention to changes in patient behaviour in developing self-efficacy so that they can confidently administer diabetes care.

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…continuation Table 3. Characteristics of the included studies.

No	Title, Author, year, country	Research purposes	Design and Settings	Sample and age (age range)	Measuring instrument	Results and Conclusions
8	The association between self-efficacy and self-management behaviors among Chinese patients with type 2 diabetes (26), 2019, China	Determine how patients with type 2 diabetes in China feel about themselves and how they manage on their own.	A cross-sectional survey, of Essential Public Health Service (EPHS) in Shandong Province, China	2 166 patients with type 2 DM	Assessing self-efficacy in diabetes management with the Diabetes Empowerment Scale-Short Form (DES-SF).	There is a correlation between self-efficacy and self-management behaviour in patients with type 2 diabetes (p = 0.001 and OR = 1.25 (1.16–1.35)). Self-efficacy in managing diabetes is related to self-management behaviour among Chinese patients with type 2 DM. Some strategies are required to improve the patient's self-efficacy in self-management.
9	Relationship of Self-Efficacy in Medication Understanding with Quality of Life among Elderly with Type 2 Diabetes Mellitus on Polypharmacy in Malaysia (20), 2022, Malaysia	Understanding the relationship between self-efficacy in medication understanding and quality of life and factors related to quality of life in older adults with type 2 diabetes at the pharmacy.	A cross-sectional study, Institutional Primary Care Specialist Clinic (PCSC) in Selangor	321 patients with type 2 DM	The Self Efficacy in Medication Understanding (MUSE) Malay version and the Revised Version of Diabetic Quality of Life (RVDQOL-13) Malay version were used to measure self-efficacy and quality of life, respectively.	There is a correlation between self-efficacy in treatment comprehension and quality of life in patients with type 2 diabetes (p = 0.012, r = -0.140, Standardized Coefficients Beta () = 0.193). (0.852, 0.270). In elderly patients with type 2 DM on polypharmacy, a negative correlation was found between MUSE and DQOL, particularly between the domains of medication taking and satisfaction and medication taking and impact, where those with greater SE in taking medication had greater satisfaction and impact. To improve the quality of life of type 2 DM patients, self-efficacy in understanding treatment is required.

DISCUSSION

The relationship between self-efficacy and diabetes self-management

The results of the study showed that there is a relationship between self-efficacy and diabetes self-management in type 2 DM patients. Self-efficacy in managing diabetes in people with type 2 diabetes can have a positive effect on patient knowledge about diabetes and understanding of diabetes as a protective factor, making management more effective (27). It was further explained that self-efficacy correlates with diabetes self-management by reducing the risk of complications, improving foot care, and developing eating patterns or diet plans (28). Some of these explanations are reinforced by the statement that self-efficacy contributes to a better understanding of changing health behaviours by increasing knowledge, behaviour, and skills (29). Furthermore, self-efficacy plays an essential role in improving self-care behaviour and is influenced by knowledge and the duration of DM (30).

Self-efficacy can be a predictor of success in diabetes self-management. Type 2 DM patients with good self-efficacy can carry out diabetes self-management to achieve adequate glycemic control (31). One of the studies showed a negative correlation between self-efficacy and HbA1c levels, with the understanding that the more self-efficacy increases, the lower the HbA1c levels (32). Other studies explain that self-efficacy is a strong predictor of glycemic control. Furthermore, self-efficacy is related to self-management behaviours such as higher levels of diet and exercise, monitoring of blood sugar levels, and medication adherence (16). The statement reinforces that self-efficacy contributes to better diabetes outcomes and is significantly correlated with diet and physical activity (33).

Health professionals must emphasize patient self-efficacy's importance in carrying out their roles and functions in serving patients. Indeed, self-efficacy is crucial in diabetes self-management, especially in performing recommended activities and maintaining psychosocial functioning (34). In response to this point of view, healthcare professionals must help patients feel more confident in their ability to self-manage their diabetes. If the patient has good self-management, this can reduce complications due to diabetes (35). Also, patients who do an excellent job of self-managing their diabetes could help the healthcare system save money (36) social and environmental. In this case, this would be in the form of lower medical costs. Efforts to improve self-efficacy will affect how well patients follow their self-management plans to get their blood sugar under control. Health professionals can take measures, including teaching patients how to gauge the difficulty level they believe they can overcome. Furthermore, the patient needs to know the strength of his belief and how far the belief in this ability is applied, whether the patient can carry out all aspects of self-management or is it limited to certain aspects. Thus, aspects of patient self-efficacy that contribute to improving diabetes self-management will be identified.

The relationship between self-efficacy and quality of life in type 2 DM patients

The results showed that self-efficacy has a solid link to the quality of life of people with type 2 diabetes. This is made clear by the fact that people with type 2 diabetes who have a good sense of self-efficacy also have a good quality of life. DM is a metabolic disease that lasts long and can't be cured. It can affect many parts of life. Type 2 DM has been shown to reduce health-related quality of life (37). It was also shown that people with diabetes who take care of themselves well have better outcomes, live longer, have a higher quality of life, have fewer symptoms, and have fewer complications (38). In support of this study it was shown that better self-care, especially exercise, is associated with better HbA1c levels, better Body Mass Index (BMI), fewer diabetes complications, and higher quality of life (39). In effect, Rosli et al., 2022 showed a relationship between self-efficacy and the quality of life of type 2 DM patients, and these patients can have a better quality of life if they understand their treatment. One of the results also explains that type 2 DM patients who have high self-efficacy will have an impact on increasing quality of life (26).

DM patients who are managing their disease need self-efficacy. Type 2 DM patients with good self-efficacy show a good quality of life. Health

professionals must emphasize the importance of self-efficacy to type 2 diabetes patients. Type 2 DM patients urgently need the self-efficacy factor to increase individual confidence in their ability to self-care, which will impact the quality of their lives (9). This statement is reinforced by the study that showed that type 2 DM patients have a lower quality of life if they have lower self-efficacy or self-confidence in managing the disease (40). Therefore, nurses are essential in increasing the self-efficacy of type 2 DM patients through health education so that patients can perform self-care and thereby improve their quality of life. There is also a reciprocal relationship such that type 2 DM patients with a high quality of life can carry out good self-management (41).

Strengths and limitations

Our study employed a stringent search strategy to cover a large number of eligible studies, a stringent review procedure, and appropriate data analysis, thereby increasing the reliability of the results. Self-efficacy plays a significant role in diabetes self-management and in enhancing the quality of life of type 2 DM patients, according to most of the literature review results; however, the amount of literature utilized is minimal (9 publications). It is necessary to explain the limitations of this literature review, and the results should be interpreted with caution. The first factor is that several terms may be omitted from the initial keyword search to conceal related studies. Due to time constraints and limited resources, this systematic review did not register and publish a predetermined protocol before beginning the review. The third factor is that the review only contains English-language articles, so there is the possibility of using other languages that meet the inclusion criteria but were omitted.

CONCLUSION

The practical implication of this study is that nurses must evaluate the confidence and ability of type 2 DM patients to engage in self-care behaviours to achieve normal blood glucose levels, which will positively impact the quality of life. For patients to effectively manage their disease, nurses must continue to encourage them by boosting their self-esteem. Self-confident patients with type 2 DM can self-manage their diabetes, which includes regulating diet, engaging in physical activity or exercise, managing medications, monitoring blood glucose levels, foot care, and stress management. Proper diabetes self-management will result in adequate glycemic control, enhancing the quality of life. Additional research can be conducted, particularly on the role of self-efficacy in alleviating psychological stress in type 2 DM patients.

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Conflict of interest

The author affirms that no conflicts of interest exist.

REFERENCES

1. Zamanzadeh V, Zirak M, Hemmati Maslakpak M, Parizad N. Distance education and diabetes empowerment: A single-blind randomized control trial. Diabetes Metab Syndr Clin Res Rev. 2017;11:S247-51.
2. Lin HC, Tseng CW, Hsieh PJ, Liang HL, Sue SP, Huang CY, et al. Efficacy of Self-Management on Glucose Control in Type 2 Diabetes Mellitus Patients Treated with Insulin. Healthc. 2022;10(10):1-9.
3. International Diabetes Federation. Diabetes Atlas. Sixth edition. Africa; 2021.
4. Wander GS, Bansal M, Kasliwal RR. Prediction and early detection of cardiovascular disease in South Asians with diabetes mellitus. Diabetes Metab Syndr Clin Res Rev. 2020;14(4):385-393.
5. Sousa MC de, Malaquias BSS, Chavaglia SRR, Ohl RIB, Paula FFS de, Silva KS da, et al. Self-efficacy in elderly with type 2 Diabetes Mellitus. Rev Bras Enferm. 2020;73(Suppl 3):e20180980.
6. Gedik S, Kocoglu D. Self-efficacy level among patients with type 2 diabetes living in rural areas. Rural Remote Health. 2018;18(1).

7. Nooseisai M, Viwattanakulvanid P, Kumar R, Viriyautsahakul N, Muhammad Baloch G, Somrongthong R. Effects of diabetes self-management education program on lowering blood glucose level, stress, and quality of life among females with type 2 diabetes mellitus in Thailand. Prim Heal Care Res Dev. 2021;22.
8. Toygar İ, Hançerlioğlu S, Utku T, Şimşir IY, Çetinkalp Ş. Effect of an Educational Intervention Based on Bandura's Theory on Foot Care Self-Efficacy in Diabetes: A Prospective Quasi-Experimental Study. Int J Low Extrem Wounds. 2022;21(4):414-419.
9. Tan CCL, Cheng KKF, Hwang SW, Zhang N, Holroyd E, Wang W. Effect of a Diabetes Self-Efficacy Enhancing Program on Older Adults With Type 2 Diabetes: A Randomized Controlled Trial. Clin Nurs Res. 2020;29(5):293-303.
10. Al-Salmi N, Cook P, D'souza MS. Diet Adherence among Adults with Type 2 Diabetes Mellitus: A Concept Analysis. Oman Med J. 2022;37(2).
11. Al-Dwaikat TN, Rababah JA, Al-Hammouri MM, Chlebowy DO. Social Support, Self-Efficacy, and Psychological Wellbeing of Adults with Type 2 Diabetes. West J Nurs Res. 2021;43(4):288-297.
12. Amer FAM, Mohamed MS, Elbur AI, Abdelaziz SI, Elrayah ZAB. Influence of self-efficacy management on adherence to self-care activities and treatment outcome among diabetes mellitus type 2 Sudanese patients. Pharm Pract (Granada). 2018;16(4):1-7.
13. Amelia R, Ariga RA, Rusdiana, Sari MI, Savira M. Self-efficacy in type 2 diabetes mellitus patients and the relationship with the quality of life in Medan city. In: Journal of Physics: Conference Series. 2018.
14. Çağan Ö, Yeşilaydin G, Koca B. Examination of Self-Efficacy and Quality of Life of Patients with Type 2 Diabetes Regarding Diabetes Management. J Basic Clin Heal Sci. 2021;(2):43-50.
15. Clara H, Irawaty D, Dahlia D. Self-Efficacy as a Predictor of Self-Management Behavior Practice Among People with Type 2 Diabetes Mellitus (T2DM). KnE Life Sci. 2021;2021:440-453.
16. Saad AMJ, Younes ZMH, Ahmed H, Brown JA, Al Owesie RM, Hassoun AAK. Self-efficacy, self-care and glycemic control in Saudi Arabian patients with type 2 diabetes mellitus: A cross-sectional survey. Diabetes Res Clin Pract. 2018;137:28-36.
17. Madran DM, Jassim AH. Self-efficacy and its relationship to self-care among type II diabetic patients. Int J Health Sci (Qassim). 2022;6(May):15199-15208.
18. Bolaños-Medina A, Núñez JL. A preliminary scale for assessing translators' self-efficacy. Across Lang Cult. 2018;19(1):53-78.
19. Juarez LD, Presley CA, Howell CR, Agne AA, Cherrington AL. The Mediating Role of Self-Efficacy in the Association Between Diabetes Education and Support and Self-Care Management. Heal Educ Behav. 2022;49(4):689-696.
20. Rosli NA, Mazapuspavina MY, Ismail Z, Ismail NE. Relationship of Self-Efficacy in Medication Understanding with Quality of Life among Elderly with Type 2 Diabetes Mellitus on Polypharmacy in Malaysia. Int J Environ Res Public Health. 2022;19(5):1-17.
21. Kav S, Yilmaz AA, Bulut Y, Dogan N. Self-efficacy, depression and self-care activities of people with type 2 diabetes in Turkey. Collegian. 2017;24(1):27-35.
22. Walker et al. Effect of diabetes self-efficacy on glycemic control, medication adherence, self-care behaviors, and quality of life in a predominantly low-income, minority population. HHS Public Access. 2020;24(3):349-355.
23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. The BMJ. 2021;(372).
24. The Joanna Briggs Institute. Checklist for systematic reviews and research syntheses. Joanna Briggs Inst. 2016;13(3):1-7.
25. Oluma A, Abadiga M, Mosisa G, Fekadu G, Turi E. Perceived self-efficacy and associated factors among adult patients with type 2 diabetes mellitus at public hospitals of western Ethiopia, 2020. Patient Prefer Adherence. 2020;14:1689-1698.
26. Yao J, Wang H, Yin X, Yin J, Guo X, Sun Q. The association between self-efficacy and self-management behaviors among Chinese patients with type 2 diabetes. PLoS One. 2019;14(11):1-12.
27. Huda N, Sukartini T, Pratiwi NW. The Impact of Self Efficacy on the Foot Care Behavior of Type 2 Diabetes Mellitus Patients in Indonesia. J Ners [Internet]. 2019;14(2):181-186.
28. Qiu T, Huang J, Wang W. Association between Diabetes Knowledge and Self-Efficacy in Patients with Type 2 Diabetes Mellitus in China: A Cross-Sectional Study. Int J Endocrinol. 2020;2020.
29. Amelia R, Lelo A, Lindarto D, Mutiara E. Analysis of factors affecting the self-care behaviors of diabetes mellitus type 2 patients in Binjai, North Sumatera-Indonesia. Asian J Microbiol Biotechnol Environ Sci. 2018;20(2):361-367.
30. D'Souza MS, Karkada SN, Parahoo K, Venkatesaperumal R, Achora S, Cayaban ARR. Self-efficacy and self-care behaviours among adults with type 2 diabetes. Appl Nurs Res. 2017;36:25-32.
31. Has EMM, Aulia A, Kusumaningrum T, Efendi F. Ethnic Foods Diet Program Improve Self-efficacy and Diet Compliance Among Type 2 Diabetic Patients. J Ners [Internet]. 2019;14(2):155-160.

32. Lin PY, Lee TY, Liu CY, Lee YJ. The effect of self-efficacy in self-management on diabetes distress in young people with type 2 diabetes. Healthc. 2021;9(12):1-11.

33. Gao Y, Xiao J, Han Y, Ji J, Jin H, Mawen DG, et al. Self-efficacy mediates the associations of diabetes distress and depressive symptoms with type 2 diabetes management and glycemic control. Gen Hosp Psychiatry. 2022;78(June):87-95.

34. Qin W, Blanchette JE, Yoon M. Self-Efficacy and Diabetes Self-Management in Middle-Aged and Older Adults in the United States: A Systematic Review. Diabetes Spectr. 2020;33(4):315-323.

35. Becker J, Emmert-Fees KMF, Greiner GG, Rathmann W, Thorand B, Peters A, et al. Associations between self-management behavior and sociodemographic and disease-related characteristics in elderly people with type 2 diabetes — New results from the population-based KORA studies in Germany. Prim Care Diabetes. 2020;14(5):508-514.

36. World Health Organization. World Health Statistics - Monitoring Health For The Sdgs. World Heal Organ. 2016:1-121.

37. Amin MF, Bhowmik B, Rouf R, Khan MI, Tasnim SA, Afsana F, et al. Assessment of quality of life and its determinants in type-2 diabetes patients using the WHOQOL-BREF instrument in Bangladesh. BMC Endocr Disord. 2022;22(1):1-14.

38. Gemeda ST, Woldemariam ZB. Assessment of self-care practice amongst patients with type II diabetes attending Adama Hospital Medical College, Ethiopia. BMC Endocr Disord. 2022;22(1):1-10.

39. Ausili D, Bulgheroni M, Ballatore P, Specchia C, Ajdini A, Bezze S, et al. Self-care, quality of life and clinical outcomes of type 2 diabetes patients: An observational cross-sectional study. Acta Diabetol. 2017;54(11):1001-1008.

40. Peters M, Potter CM, Kelly L, Fitzpatrick R. Self-efficacy and health-related quality of life: A cross-sectional study of primary care patients with multi-morbidity. Health Qual Life Outcomes. 2019;17(1):1-11.

41. Alaofè H, Amoussa Hounkpatin W, Djrolo F, Ehiri J, Rosales C. Factors Associated with Quality of Life in Patients with Type 2 Diabetes of South Benin: A Cross-Sectional Study. Int J Environ Res Public Health. 2022;19(4).

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Isolated fungal sinusitis of the sphenoid sinus - A case report

Sinusitis fúngica aislada del seno esfenoidal - reporte de un caso

Muhammad Fadjar Perkasa

SUMMARY

Introduction: *Isolated sphenoidal fungal sinusitis is a rare disease, representing 3% of all sinusitis cases. The disease usually occurs together with other paranasal sinus infections. Viral, bacterial, parasitic, and fungal infections can cause sinusitis. Fungal infection of the sphenoidal sinuses is rarely diagnosed, as it has no characteristic symptoms and is not much different from bacterial or other sinusitis infections. The diagnosis of fungal sphenoid sinusitis is based on history taking, physical examination, and supporting examination. The therapy aims to reduce sinus cavity inflammation, improve drainage, and overcome the pressure on the sinuses that cause painful symptoms. Endoscopic Sinus Surgery (ESS) is a surgical technique on the paranasal sinuses using an endoscope that aims to improve ventilation and mucociliary clearance of the sinuses.*
Case report: *A 67-year-old man came for treatment with symptoms of headache that was felt especially in the forehead for the last 2 years. Both limbs felt weakened 4 months ago. A non-contrast skull CT-Scan showed solid lesions with calcifications in the left sphenoid and temporal regions. The patient then performed ESS surgery with a sphenoidectomy approach.*
Conclusion: *Fungal sinusitis infection of the sphenoid is uncommon but is increasing in incidence. Patients usually complain of non-specific symptoms such as headache, facial pain, visual disturbances, and decreased consciousness. ESS with a sphenoidectomy approach is the best option for managing fungal sinusitis.*

Keywords: *Fungal sinusitis, isolated sphenoid sinusitis, endoscopic sinus surgery.*

RESUMEN

Introducción: *La sinusitis fúngica esfenoidal aislada es una enfermedad rara, que representa el 3 % de todos los casos de sinusitis. La enfermedad generalmente ocurre junto con otras infecciones de los senos paranasales. La sinusitis puede ser causada por infecciones virales, bacterianas, parasitarias y fúngicas. La infección fúngica de los senos esfenoidales rara vez se diagnostica, ya que no tiene síntomas característicos y no es muy diferente de las infecciones bacterianas u otras sinusitis. El diagnóstico de la sinusitis esfenoidal fúngica se basa en la anamnesis, la exploración física y la exploración complementaria. La terapia tiene como objetivo reducir la inflamación de la cavidad sinusal, mejorar el drenaje y superar la presión en los senos paranasales que causa los síntomas de dolor. La Cirugía Endoscópica de Senos*

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ORCID: https://orcid.org/0000-0002-8861-1476

Department of Otorhinolaryngology-Head and Neck Surgery Medical Faculty Hasanuddin University, Makassar, Indonesia.

Corresponding author: Muhammad Fadjar Perkasa
E-mail: perkasa715@gmail.com
Address: Jl. Perintis Kemerdekaan Km. 10, Makassar 90245, South Sulawesi, Indonesia

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paranasales (CES) es una técnica quirúrgica sobre los senos paranasales mediante endoscopio que tiene como objetivo mejorar la ventilación y el aclaramiento mucociliar de los senos paranasales.
Presentación de caso: *Un hombre de 67 años acudió a tratamiento con síntomas de dolor de cabeza que se sentía especialmente en la frente durante los últimos 2 años. Ambas extremidades se sentían debilitadas desde hace 4 meses. Una tomografía computarizada de cráneo, sin contraste, mostró lesiones sólidas con calcificaciones en el esfenoides izquierdo y las regiones temporales. Posteriormente, se le realizó al paciente una cirugía de CES con un abordaje de esfenoidectomía.*
Conclusión: *La sinusitis fúngica esfenoidal aislada es una condición poco común pero que actualmente está teniendo una incidencia incrementada. Los pacientes suelen quejarse de síntomas inespecíficos como dolor de cabeza, dolor facial, alteraciones visuales y disminución de la conciencia. La CES con abordaje de esfenoidectomía es la mejor opción para el manejo de la sinusitis fúngica en este momento.*

Palabras clave: *Sinusitis fúngica, sinusitis esfenoidal aislada, cirugía endoscópica de senos paranasales.*

INTRODUCTION

The sphenoid sinus is contained within the sphenoid bone. It separates the pituitary gland from the nasal cavity. The sphenoid sinus is located posteriorly at the apex of the nasal cavity. The walls of this sinus are attached to the optic canal, dura mater, pituitary gland, and cavernous sinus, which consists of the internal carotid artery and the third, fourth, and sixth cranial nerves (1,2). This sinus comprises pseudo-ciliated epithelium with fewer mucus-secreting cells than the other paranasal sinuses. This leads to less drainage, resulting in isolated sphenoiditis (1). The most common etiology of the disease is caused by *Staphylococcus aureus* and *Streptococcus*. Gram-negative bacteria and anaerobic organisms are sometimes found in culture. Noninvasive fungal sinusitis is usually found in one sinus and the most frequently caused by *Aspergillus* (1,3).

Sphenoid sinus infection by fungi is rarely diagnosed, as it has no characteristic symptoms and resembles the symptoms of sinusitis by other microbes. According to sphenoid sinus anatomy and depending on its contiguous structures, it is frequently difficult to diagnose, as patients present with various nonspecific symptoms and complications such as headache, visual disturbance, facial and retro-orbital pain, cranial nerve palsies and decreased consciousness (3-5). Endoscopic examination of the nose sometimes reveals purulent secretions in the sphenoethmoidal sinus and thinning of the anterior sphenoidal wall (4).

Radiologic examination plays an important role in diagnosing isolated fungal sphenoidal sinusitis. For more accurate results, culture tests are needed to determine the cause of infection in the sinuses (6).

Surgical intervention is the main option in managing cases of fungal sinusitis. Sphenoidectomy with nasal endoscopy is recognized as the gold standard surgical management of isolated sphenoidal sinusitis. Compared to the external approach, endoscopic surgery provides better visualization and thus allows faster healing, and better aesthetic results (1,7).

CASE REPORT

A 67-year-old Asian male presented with a main complaint of headache, especially in the forehead, which had been experienced in the last 2 years ago (Figure 1). The headache was previously mild and improved with analgesics. The headache has become more severe and difficult to handle in the last three months. Headache accompanied by nausea and dizziness. The patient has a history of active pulmonary tuberculosis and has been undergoing treatment for 2 months.

Figure 1. The clinical picture of the patient.

The results of the anterior rhinoscopy examination showed no secretions in the left and right rice cavities, both inferior conchas were within normal limits, and no masses were seen. Nasoendoscopy showed purulent secretion coming from the sphenoid sinus. Non-contrast head CT scan showed hyperdense lesions with calcification in the left sphenoidal and temporal sinus regions (Figure 2). Laboratory results were within normal limits. ESS was planned after the patient completed tuberculosis treatment.

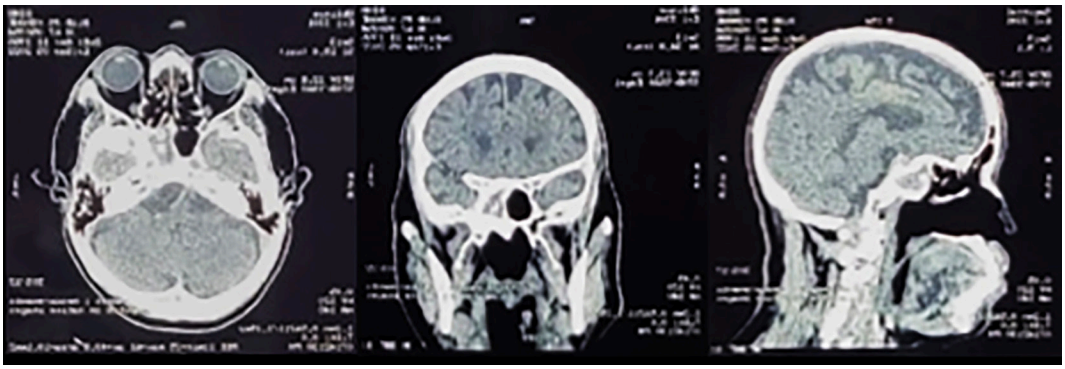

Figure 2. Non-contrast CT scan of the head. A solid lesion with calcification within the sphenoid and temporal sinus region of sinistra.

The surgical procedure was to perform ESS using a sphenoidectomy approach. The left superior conchal conchotomy was performed before performing the sphenoidectomy. A brown-black mass was seen in the sphenoid sinus. The sphenoid sinus was cleared of pathologic tissue and taken for histologic examination (Figure 3).

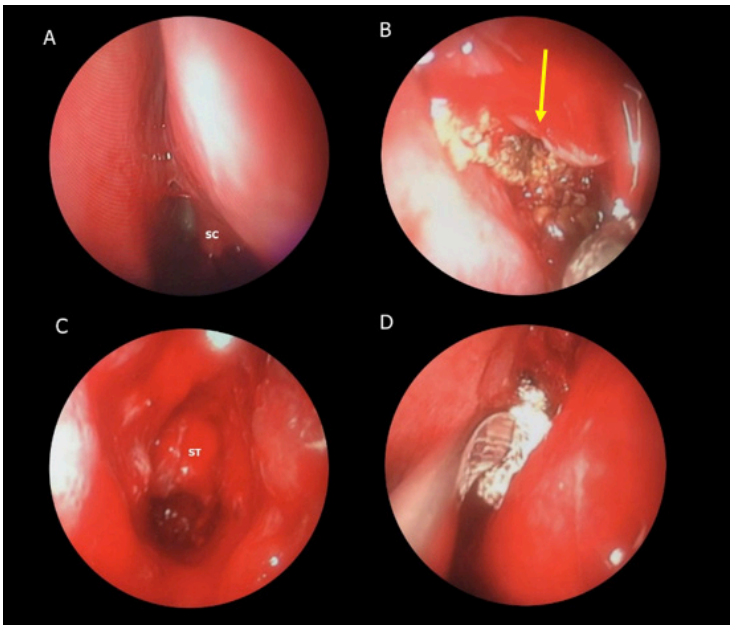

Figure 3. (A) Cut the left superior concha (SC), exposing the ostium naturalis of the sphenoid sinus. (B) Perform sphenoidectomy and a brown-black mass is seen in the sphenoid sinus and sinus mucosa (yellow arrow). (C) The Sella turcica floor (ST) appears intact. (D) Close the surgical wound using an absorbable hemostat (surgical).

In the postoperative care, no significant complaints were reported, the patient was conscious, and there was no active bleeding from the nose. The patient received broad-spectrum antibiotics and analgesics. The patient was discharged 2 days after surgery.

The patient was controlled in the outpatient department, complaining of slight pain at the surgical site. Endoscopy results showed no secretions and visualized sphenoid sinus ostium. The results of the anatomical pathology examination showed a picture of fungal spores and hyphae. Patients are given nasal irrigation therapy with sodium chloride.

DISCUSSION

Isolated sphenoid sinusitis is an inflammation of the sphenoid sinus caused by infection. Fungus is a microorganism that can cause infection in the paranasal sinuses (8). Fungal infections in the paranasal sinuses are usually caused by the irrational use of drugs, such as long-term use of antibiotics and steroids, impaired sinus ventilation, and a humid environment (6,9). The type of fungus that most commonly causes fungal sinusitis is *Aspergillus* (10).

The sphenoidal sinus is known to be the second most common sinus involved in fungal balls (11). Generally, patients have normal immunologic status. High-risk groups include patients with blood dyscrasias, diabetes, systemic steroids, or other conditions associated with immunodeficiency (12). These patients have a history of tuberculosis, leading to a state of immunosuppression.

The classification of fungal sinusitis is divided into invasive and non-invasive. Fungus balls and allergic fungal sinusitis belong to non-invasive fungal sinusitis (11,12). Invasive sinusitis includes chronic invasive fungal sinusitis and fulminant invasive disease in immunosuppressed patients. Chronic invasive fungal sinusitis is divided into granulomatous and non-granulomatous (13). This case report found a patient with non-invasive fungal sphenoid sinusitis.

The most common symptom suffered by patients with fungal sphenoid sinusitis is headache (4). This is because the sinus is innervated through the fifth cranial nerve and afferent fibers through the sphenopalatine ganglion (4,14). Another symptom that patients usually complain about is a visual disturbance or diplopia caused by optic nerve function disorders (15).

Table 1. Fungal sinusitis clas

Invasive
Acute Invasive Fungal Sinusitis
Chronic Invasive Fungal Sinusitis
Chronic Granulomatous Invasive Fungal Sinusitis
Non-invasive
Allergic fungal sinusitis
Fungus ball (fungus mycetoma)

Radiologic examination plays an essential role in diagnosing this disease. CT scan of the paranasal sinuses shows abnormalities in the paranasal sinuses, orbit, and intracranial areas (6). In addition, CT scans can show different pathological abnormalities and help rule out inflammatory diseases, neoplasms, and bacterial and fungal infections. Magnetic Resonance Imaging (MRI) is used if there is suspicion of central nervous system or eye complications (16). Culture test results can provide information on the type of germ-causing sphenoidal sinusitis (17).

Only a few cases of chronic sphenoidal rhinosinusitis reported in the literature are responsive to medicamentous therapy, and the rest require surgical intervention (1). Sphenoidal sinus surgery is indicated when bacterial sinusitis does not respond to appropriate medical therapy for 6-8 weeks and when the diagnosis of rhinosinusitis or fungal mucocele has been established (1,18). Cases with cranial nerve involvement may require more immediate surgical treatment to restore or optimize all nerve functions in time (19).

Sphenoidal sinus surgery consists of an ESS approach and external sphenoidectomy. Compared to the external approach, endoscopic surgery provides better visualization and thus allows for faster healing, better aesthetic results, lower morbidity, and higher success rates (1,7).

The concept of the ESS technique is based on reversible changes in mucociliary function and mucosal pathology by correcting the disease pathology of chronic sinusitis in the sphenoid sinus region and restoring the physiology of ventilation and drainage of the paranasal sinuses in the sphenoidal region because although abnormalities in the sphenoidal sinus area are minimal, they can interfere with sinus ventilation and mucociliary clearance (7).

Several techniques can open the sphenoid sinus. Unlike tumor surgery, resection of the middle

meatus's inferior part is usually unnecessary (1). The sphenoid ostium is then widely opened and enlarged so that any infectious or inflammatory reaction within the sphenoid sinus cavity can be completely eliminated (18).

CONCLUSIONS

Sphenoid sinus infection by fungi is rarely diagnosed, as it does not have typical symptoms that distinguish it from sinus infection by bacteria or others. Headache and blurred vision are the most common symptoms. The diagnosis can usually be made through a radiologic examination. Endoscopic sinus surgery with a sphenoidectomy approach is the primary option in these cases, with low morbidity compared to other surgical techniques.

REFERENCES

1. Charakorn N, Snidvongs K. Chronic Sphenoid Rhinosinusitis: Management challenge. J Asthma and Allergy. 2016;9:199-201.
2. Baskin J, Kuriakose A, Lebowitz R. The anatomy and physiology of the sphenoid sinus. Operative techniques in otolaryngology – head and neck surgery. 2003;14(3):168-172.
3. Gondim J, Quidute AR, Maciel M, Carneiro A, Tavares C, Fontenele E, et al. Cushing's disease and sphenoidal aspergilloma. Acta Radiologica. 2003;44:685-687.
4. Yiotakis, Psarommatis, Seggas, Ferekidis, Adamopoulos. Isolated sphenoid sinus aspergillomas. Rhinology. 1997;35(3):136-139.
5. Zanchin G, Rossi P, Licandro AM, Fortunato M, Maggioni F. Clusterlike headache. A Case of Sphenoidal Aspergilloma. Headache. 1995;35(8):494-497.
6. Trtz A, Dagli M, Akmansu H, Han O, Arslan B, Eryilmaz A. Isolated fungal sinusitis of the sphenoid sinus. Turk J Med Sci. 2009;39(3):453-456.
7. Hun Jung Dhong, Donald C. Fungal Rhinosinusitis. In: David W, William E, Zinreich J, editors. Diseases of the sinuses diagnosis and management. London: B. C. Decker; 2001.p.184-199.
8. Yap HJ, Ramli RR, Yeoh ZX, Sachlin IS. Series of isolated sphenoid disease: Often neglected but perilous. SAGE Open Medical Case Reports. 2022;10:2050313X221097757.
9. Dhong HJ, Lanza DC. Fungal rhinosinusitis. In: Kennedy DW, Bolger WE, Zinreich SJ, editors. Diseases of the sinuses diagnosis and management. London: BC Decker; 2001.p. 84-99.
10. Han DH, An SY, Kim SW, Kim DY, Rhee CS, Lee CH, et al. Primary and secondary fungal infections of the paranasal sinuses: Clinical features and treatment outcomes. Acta Otolaryngol. 2007;558(Suppl):78-82.
11. Karkas A, Rtail R, Reyt E, Timi N, Righini CA. Sphenoid sinus fungus ball. Eur Arch Otorhinolaryngol. 2013;270(3):893-898.
12. Deutsch PG, Whittaker J, Prasad S. Invasive and Non-Invasive Fungal Rhinosinusitis-A Review and Update of the Evidence. Medicina (Kaunas). 2019;55(7):319.
13. Alotaibi NH, Omar OA, Altahan M, Alsheikh H, Al Mana F, Mahasin Z, et al. Chronic Invasive Fungal Rhinosinusitis in Immunocompetent Patients: A Retrospective Chart Review. Front Surg. 2020;7:608342.
14. Ishak NL, Subha ST, Abu Bakar S. Isolated sphenoid sinusitis: A big headache. Malays Fam Physician. 2019;14(1):29-30.
15. Hu L, Wang D, Yu H. Isolated sphenoid fungal sinusitis and vision loss: The case for early intervention. J Laryngol Otol. 2009;123(2):e8.
16. Alali M, Khatib AA, Azzeh GA. Isolated sphenoid inflammatory diseases. Int J Otorhinolaryngol Head Neck Surg. 2018;4(5):1130-1134.
17. Tan H, Ong Y. Acute Isolated Sphenoid Sinusitis. Ann Acad Med Singapore. 2004;33(5):656-659.
18. Villemure-Poliquin N, Nadeau S. Surgical treatment of isolated sphenoid sinusitis - A case series and review of the literature. Int J Surg Case Rep. 2021;79:18-23.
19. El Mograbi A, Soudry E. Ocular cranial nerve palsies secondary to sphenoid sinusitis. World J Otorhinolaryngol Head Neck Surg. 2017;3(1):49-53.