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Clinical characteristics of exotic fruit anaphylaxis and the causative allergens

Características clínicas de la anafilaxia de frutas exóticas y los alérgenos causantes

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SUMMARY

Food allergies affect all ages and cause various clinical symptoms like hives, edema, respiratory distress, gastrointestinal problems, and anaphylaxis. Diagnosis is challenging due to self-reported allergies overstating prevalence and objective testing like skin prick tests and oral food challenges. Plant allergens are widespread factors in food allergy, and accurate identification of the provoking product is necessary for targeted treatment. Clinical allergy to exotic fruits, manifested by an allergic syndrome, is quite common. Due to the wide distribution of the problem, this work is devoted to an empirical study of the prevalence of food allergy to exotic fruits, as well as an analysis of their combinations and characteristic clinical manifestations. **Objective:** *The research aimed to empirically analyze whether patients had a predisposition in the past to acquire a food allergy after consuming exotic fruits.* **Method:** *An analysis of clinical cases of patients with impaired immunological status (211 patients) and a pre-test for the most common allergens of exotic fruits were carried out.* **Results:** *In the studied sample of patients, 43 % had episodes of transferred food allergy to fruits in the anamnesis, which in most cases were manifested by oral allergic syndrome, dermatitis, and itching. The skin prick test results showed that the fruits of cherimoya and lychee showed the most significant number of positive and highly positive samples of various degrees of severity. The fewest positive samples were found on avocado, pineapple, and jackfruit. Sensitization to fruit allergens was found in most patients with allergic multimorbidity and bronchial asthma.*

Keywords: *Cross-immunological reactions, food allergy, lychee, jackfruit, cherimoya.*

RESUMEN

Las alergias alimentarias afectan a todas las edades y provocan diversos síntomas clínicos como urticaria, edema, dificultad respiratoria, problemas gastrointestinales y anafilaxia. El diagnóstico es difícil debido a que las alergias autodeclaradas exageran la prevalencia y a las pruebas objetivas, como las pruebas de punción cutánea y las pruebas orales con alimentos. Los alérgenos vegetales son factores muy extendidos en la alergia alimentaria, y la identificación precisa del producto provocador es necesaria para un tratamiento específico. La alergia clínica a frutas exóticas, manifestada por un síndrome alérgico, es bastante común. Debido a la amplia distribución del problema, este trabajo está dedicado a un estudio empírico de la prevalencia de la alergia alimentaria a frutas exóticas, así como a un análisis de sus combinaciones y manifestaciones clínicas características. **Objetivo:** *El objetivo de*

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la investigación fue analizar empíricamente si los pacientes tenían predisposición en el pasado a adquirir alergia alimentaria tras consumir frutas exóticas. **Método:** *Se realizó un análisis de casos clínicos de pacientes con estado inmunológico alterado (211 pacientes) y una prueba previa para los alérgenos más comunes de frutas exóticas*. **Resultados:** *En la muestra de pacientes estudiada, el 43 % de los individuos presentaron en la anamnesis episodios de alergia alimentaria transferida a frutas, que en la mayoría de los casos se manifestaron por síndrome alérgico oral, dermatitis y picazón. Los resultados de la prueba cutánea realizada mostraron que el mayor número de muestras positivas y altamente positivas de diversos grados de gravedad se presentaron en los frutos de chirimoya y lichi. La menor cantidad de muestras positivas se encontraron en aguacate, piña y yaca. Se encontró sensibilización a los alérgenos de las frutas en la gran mayoría de los pacientes con multimorbilidad alérgica y asma bronquial.*

Palabras clave*: Reacciones inmunológicas cruzadas, alergia alimentaria, lichi, yaca, chirimoya.*

INTRODUCTION

During the past years, there has been a global outbreak of allergic diseases, presenting a considerable medical and socioeconomic burden, acquiring the scale of a global medical and social problem (1,2). Food allergy (FA) is defined as an immune reaction to proteins in the food and can be immunoglobulin (Ig)E-mediated or non-IgE-mediated. IgE-mediated food allergy is a worldwide health problem that affects millions of persons and numerous aspects of a person's life. Allergic reactions secondary to food ingestion are responsible for various symptoms involving the skin, gastrointestinal tract, and respiratory tract (1,2). Jensen-Jarolim et al. (3) food allergy described as a side effect of food components, which is characterized by a comprehensive polymorphism of clinical manifestations on the part of different organ systems and is found in almost 20 % of patients in European countries. In Poland, a study conducted by Wawrzeńczyk et al. (4) involving 120 adult patients with pollen allergies found that 58.3 % were sensitized to the lipid transfer proteins (LTPs), which are a large protein family found in multiple plants (representing a pan allergen) with an important role in the plant's defense against stressors. They are described as one of the most prevalent and cross-reactive allergen families in the general population. LTPs are small proteins of 6 to 9 kilodaltons resistant to heat and digestion and are distributed among the plant kingdom and in different plant organs ranging from pollen to fruits. Thus, they can initiate allergic reactions with very different outcomes, such as asthma and food allergy. LTPs are present in fruits, vegetables, nuts, seeds, legumes, cereals, and various pollens. Fruits like peaches, apples, and nuts were the most commonly reported by Wawrzeńczyk et al. (4), as they contain high levels of LTPs. Eiwegger et al. (5) stated that a third of the world's population has suffered or is being treated for allergic pathologies. According to the organization's forecasts, allergic pathologies tend to lead to the structure of general morbidity in connection with the expansion of the spectrum of allergens. The body's cells receive the heaviest antigenic load from daily food products, which are not always from local food industries and act as aggressive allergens. Recent extensive surveys of American and Canadian adults and children provide considerable insight into allergy prevalence for the major allergens. These data indicate that there is a significant variation in prevalence among eight allergens that are thought to account for 90 % of food allergy reactions, with FA being one of the most common primary causes of allergic diseases of both acute and chronic types. The eight major food allergens are milk, eggs, fish, crustacean shellfish, tree nuts, peanuts, wheat, and soybeans, commonly called the "Big 8." (6). The increase in cases of food allergy diagnosis and its pathophysiological influence on the formation of immunological sensitization to other groups of antigens emphasizes the need for scientific research on the clinical manifestations of various types of food anaphylactic reactions (4,7,8).

Allergists are increasingly registering allergic reactions to exotic fruits, which are becoming increasingly common in the diets of consumers of all ages, and growing numbers of patients report symptoms of hypersensitivity after ingestion of exotic fruits (9). Among the clinical responses, a wide range of manifestations is distinguished, from moderate dermatological symptoms to extensive anaphylactic reactions (10,11). The variety of clinical manifestations of allergic reactions after eating exotic fruits and the presence

of combined and cross forms of anaphylaxis create certain difficulties in diagnosing FA and the main provoking allergen. The evidence indicates that the most prone group of patients to develop FA to exotic fruits are people with already existing allergic pathologies and cross-anaphylactic conditions (12). Ignoring this problem by patients is relevant from the point of view of the marketing presentation of tropical fruits as "superfoods," products that significantly improve well-being and contain high nutritional value (13). Following the social trend, patients with a history of atopic and sensitization syndromes often do not consult their family doctor about the advisability of introducing exotic fruits into their daily diet. As a result, such a group of patients may develop cross-allergic reactions, the differential diagnosis and treatment of which is often complicated by detecting an allergen from a wide range of possible ones. Therefore, understanding allergens in the form of exotic and tropical fruits is a relevant issue in allergology and the general practice of family doctors and therapists.

Studies of the last decade in the field of evidence-based allergology have demonstrated that more than 200 foods have been shown to be allergenic, and ten regulatory agencies have recognized the need to focus allergen labeling regulations on a limited set of priority allergens. In 2004, the US Congress passed the Food Allergen Labeling and Consumer Protection Act (FALCPA), which mandates that the label of a food that contains an ingredient that is or is derived protein from a "major food allergen" must declare the presence of the allergen in the manner described by the law (6). However, the emergence of new exotic fruits that often do not have special warning labels, despite their potential sensitizing properties, underscores the need for improved allergen labeling regulations. Therefore, studying their connection with the possible development of FA is an urgent problem for both the medical, industrial, and marketing spheres.

The research aimed to analyze current scientific data on the diagnosis and prevalence of FA to exotic fruits, understand the clinical picture and variations of anaphylactic reactions associated with these allergies and assess the predisposition to FA in patients with pre-existing allergic conditions. Based on the data obtained, an empirical study was conducted on the presence of a background predisposition to the development of FA to exotic fruits in patients with background allergic diseases to assess the likelihood of developing an allergic reaction. Jackfruit (*Artocarpus integrifolia*), mango (*Mangifera indica*), cherimoya (*Annona cherimola*), lychee (*Litchi sinensis*), annatto (*Bixa orellana*), avocado (*Persea americana*), and pineapple (*Ananas comosus*) were among the particular exotic fruits that were tested. By achieving these objectives, the study sought to provide insights that could enhance diagnostic accuracy, inform clinical practice, and guide patient management regarding allergies to exotic fruits.

The prevalence of immunological reactions to allergens of plant origin depends on the patient's age and geographical location, which determines the limitation of his sustainable standard diet (15). Proteins of plant origin are heterogeneous in concentration in different parts of exotic fruit, so the amount of allergen that enters the body with food also depends on the maturity of the fruit, the volume used, the country of origin, and external factors during its cultivation and transportation to the place of commercial sale (16). However, during the development of allergic manifestations to exotic products of plant origin, they are united by common clinical manifestations in the form of skin, gastrointestinal, and general inflammatory symptoms, as shown by a review of literary sources (17). Among the skin manifestations of FA on exotic fruits, urticaria, itching, edema of the mucous membranes, and Quincke's edema of varying degrees of severity are distinguished (18). Hours after the initial response, a late-phase reaction can occur. This involves recruiting and activating other inflammatory cells like eosinophils, neutrophils, and T lymphocytes. According to the analyzed data, anaphylactic reactions with asphyxia and neurological changes are infrequent (7). Differential diagnosis of FA on exotic fruits is also aimed at identifying groups of patients with cross-immunological reactions (CIR). IgE-associated CIR in certain types of pollen in the patient, such as plants or products common in his region, increases the likelihood of developing an allergy to exotic fruits (19). IgE enhances antigen presentation to T cells, promoting further TH2

responses and increased IgE production, creating a positive feedback loop. Activated mast cells and basophils undergo degranulation, releasing preformed inflammatory mediators such as histamine, tryptase, and various cytokines. This causes immediate allergic symptoms. Activation also induces the synthesis of lipid mediators like prostaglandins and leukotrienes, which contribute to inflammation and smooth muscle contraction.

IgE antibodies bind to high-affinity Fc epsilon receptors (FcεRI) on the surface of mast cells and basophils. IgE can be produced locally in inflamed tissues, not just lymphoid organs, contributing to persistent inflammation. Long-lived memory B cells specific for allergens can rapidly produce IgE upon re-exposure, contributing to the chronicity of allergic conditions. A common allergen among exotic products is lychee fruit (*Litchi sinensis*), which belongs to the *Sapindaceae* family. The seeds contain a high amount of profilin, the oral intake of which can cause the development of extensive anaphylactic reactions in patients, especially in those with a history of sensitizing to the plant pan-allergen profilin or latex (13).

Allergic reaction to oral consumption of jackfruit (*Artocarpus integrifolia)* is usually accompanied by a typical specific IgE response of the immediate type in patients of adult and pediatric profiles (20). The cases of FA to jackfruit fruits described in the literature developed against the background of existing multiple sensitizations, which were confirmed by prick tests (19). Jackfruit, a popular tropical fruit, has been linked to allergic reactions in sensitive individuals, causing mild to severe symptoms, highlighting its potential as a food allergen. Oral Allergy Syndrome (OAS) is a mild allergic reaction to jackfruit characterized by itching or tingling sensations. Severe reactions include urticaria and angioedema. Gastrointestinal symptoms, such as nausea, vomiting, and diarrhea, indicate a systemic allergic response. Respiratory symptoms include wheezing, shortness of breath, and, in extreme cases, anaphylaxis (21,22). Jackfruit allergic reactions are primarily mediated by IgE antibodies, which bind to jackfruit proteins and interact with FcεRI receptors. This triggers inflammatory mediators, including histamine, which causes acute symptoms and prolongs the response. Plant defense proteins can cross-react with other allergens.

Mango fruits are grown in tropical and subtropical climate regions, some countries in Europe and South America (23). The mango fruit is available throughout the year in fresh or processed form and is quite common in the market. Clinical manifestations of sensitization to mango fruits are determined by type I hypersensitivity reactions with the development of erythematous skin lesions, urticaria, angioedema, and Oral Allergy Syndrome (OAS). Erythematous lesions are red, itchy, and warm, while urticaria is raised, itchy welts. Angioedema is swelling in the skin and mucous membranes, often affecting the face, tongue, and throat. OAS is a mild food allergy causing immediate symptoms in the mouth and throat. Treatment for these skin disorders involves a combination of topical and systemic medications. While systemic corticosteroids are indicated for severe instances, topical corticosteroids are used to relieve inflammation and irritation. Moisturizers and emollients are also advised. Antihistamines are used to reduce pain and itching (24). Epinephrine is used to treat angioedema to lessen swelling and stop it from getting worse. Treating oral allergy syndrome involves keeping an epinephrine auto-injector on hand, avoiding foods that provoke symptoms, and using antihistamines for moderate cases. It is essential to educate people about recognizing and preventing cross-reactive foods.

Severe allergic manifestations can manifest in the form of widespread anaphylactic responses of the type of hypersensitivity reactions of type IV, including variants of contact dermatitis, which is the most common variant (25). IgE-mediated reactions can have different effects depending on the tissue involved. For example, it can lead to bronchial hyperresponsiveness and airway remodeling in the lungs. IgE-mediated mast cell activation can stimulate nearby nerve endings, leading to the release of neuropeptides that further contribute to inflammation.

Cherimoya fruits (*Annona cherimola)* contain a large amount of carbohydrates but few acids. They are saturated with lutein, vitamins C and B6, riboflavin, and folate. They have become popular among consumers due to their antioxidant and antihyperlipidemic effects. In contrast to the health benefits, cases of allergic symptoms to the IgE-binding proteins of cherimoya have been described, including OAS and CIR "latex-fruit

syndrome," i.e., immediate-type sensitization reactions in response to the consumption of the fruit (5).

MATERIALS AND METHODS

A literature analysis and a systematic review of publications on diagnosed and verified data of FA on exotic fruits (avocado, pineapple, lychee, jackfruit, cherimoya, and others) in patients of different age categories and ethnicities were carried out. For data selection, the Latin names of exotic fruits were used, which appeared in statistical conclusions and reports on FA or anaphylactic reactions, published in peer-reviewed and verified scientific medical publications no later than 2019. Open databases from Scopus and Web platforms were used to search Science and PubMed, identify the search author, and use appropriate search filters. Duplicate works of the same group of scientists were not included in the analysis; clinical cases of FA on common fruits (banana, orange, various types of berries, kiwi); clinical cases in which the diagnosis was not confirmed by clinical analyses or samples but was based solely on the patient's subjective symptoms and clinical examination. The study includes information on isolated allergic reactions to exotic fruits, cross-allergic reactions, and multimorbid conditions.

Two hundred eleven patients who were under dispensary observation in a polyclinic for allergic syndromes were selected for conducting an empirical study. The criteria for inclusion in the empirical study were age from 18 to 60 years, voluntary consent to participate, absence of exacerbations of other background diseases, and absence of acute inflammatory skin diseases for skin tests. Exclusion criteria from the study were the presence of symptoms of exacerbation of allergic diseases and diabetes. All patients gave informed consent to use their medical data. To analyze the clinical status of the selected cohort of patients, their outpatient records (previous history, clinical examinations, and anaphylaxis episodes) were analyzed.

To identify the tendency to develop immediate-type allergic Immunoglobulin E-associated (IgE-associated) reactions to exotic fruits, all patients underwent an allergic skin test in the form of a prick test. Skin tests are sensitive and specific, detecting sensitizations that blood tests cannot. In cases where test extracts were unavailable, the prick-to-prick method was used (14). Accurate fruit allergy diagnosis requires a comprehensive medical history assessment and objective confirmation of sensitization through skin tests or *in vitro* tests. Skin tests are simple, safe, and reliable, especially for IgE-mediated allergies to exotic fruits. Patients were previously informed about the degree of invasiveness of the test, its adverse reactions, the spectrum of skin changes at the test site, and the duration of symptoms.

The test procedure included treatment of the skin of the forearm with ethanol, application of a control sample with histamine (positive sample), and physiological solution (control negative sample). The allergen concentration utilized in the skin prick testing was precisely calibrated. For every exotic fruit, standardized allergen extracts were made to guarantee that the solutions included consistent and clinically meaningful amounts of the allergenic proteins. Jackfruit (*Artocarpus integrifolia*), mango (*Mangifera indica*), cherimoya (*Annona cherimola*), lychee (*Litchi sinensis*), annatto (*Bixa orellana*), avocado (*Persea americana*), and pineapple (*Ananas comosus*) were among the exotic fruits that were tested. On the designated forearm regions, a little drop of each allergen extract was placed, making sure the spots were far enough apart to avoid cross-contamination. In the center of each drop, marked and located at a sufficient distance from each other, a superficial skin puncture was performed with a disposable sterile needle lancet. The assessment of the pre-test result was carried out for 15 minutes at maximum. To evaluate the reaction to the prick test (allergy skin test), the standard classification of dermatological reaction was used: the absence of changes on the skin was considered an adverse reaction, a hyperemia area of 1 to 2 mm was considered doubtful, 3 to 7 as positive, 8 to 12 as high positive, and 13 mm or more as hyperallergic. The obtained data were processed in the Statistica (version 10.0) and Microsoft Excel programs. The participants were informed about anonymous and voluntary participation and provided their consent.

RESULTS

A literature analysis of scientific publications was conducted to select allergens to detect susceptibility to the development of allergic symptoms of FA due to exposure to exotic fruits. These publications testified in favor of evidence on the development of FA due to consumption or contact with tropical fruits. In this way, several publications were analyzed, which were exclusively related to fruits and their primary influence on the development of allergic manifestations of any degree of severity (26).

Patients under observation for allergic diseases at the time of the study had no symptoms or episodes of exacerbation of the underlying disease. The total number of examined patients during the established observation and data collection period was 211 adults. Patients aged 26 to 40 years who dominated the selected cohort were mainly female. 41.7 % of patients were younger (18 to 25 years), while only 10 % were older (42 to 60 years). Almost all patients had a history of atopic dermatitis (89 %) or allergic rhinitis (74 %). A third of patients suffered from bronchial asthma (33 %). An important factor for the experiment was the presence of laboratory-confirmed allergic multimorbidity in most subjects (90 %). Almost half of the patients (43 %) had a history of FA episodes, confirmed at the time of application by appropriate allergy, antibody, and skin tests. Considering the purpose of the study, only provoking anamnestic allergens from the class of fruits previously detected in patients were selected (Table 1).

Table 1. Protein allergens in fruits that caused previously diagnosed episodes of food allergy in the examined cohort of patients

Sequence number	The name of the food product	Type of identified allergen
1	Apricot	Pru ar-3
2	Peach	Pru p-3
3	Kiwi	Act d-10
4	Banana	Mus a-3
5	Lemon	Cit l-3
6	Tangerine	Cit r-3

Source: compiled by the author based on the data of outpatient charts of patients.

The allergens in apricot and peach stone fruits are Pru p-3 and Pru ar-3. These are members of the lipid transfer protein (LTP) family, recognized for being a powerful allergen that can react severely in those sensitive to it. Additionally, Citrus l-3 and Citrus r-3, the two citrus fruits listed, are linked to comparable allergies. This implies that those allergic to these particular proteins may be cross-reactively sensitive to diverse citrus fruits. It is important to identify these specific allergies for a number of reasons. It makes it possible to diagnose food allergies more accurately, create immunotherapies or targeted treatments, and provide patients with detailed instructions on which foods to avoid. Furthermore, knowing these allergies might help anticipate cross-reactivities across other fruits with comparable protein structures.

The clinical picture of FA episodes, according to the objective data of the medical examination and clinical tests, included common symptoms in most diagnosed cases and included OAS in 86 % of patients, skin manifestations in the form of atopic dermatitis (71 %), allergic rhinitis (32 %), gastrointestinal disorders (90 %) and hyperthermia (42 %) (Figure 1). The FA episodes in the examined patients lasted no more than 7-9 days and were treated according to the protocol. Anaphylactic reactions (anaphylactic shock, severe Quincke's edema) were not detected during FA.

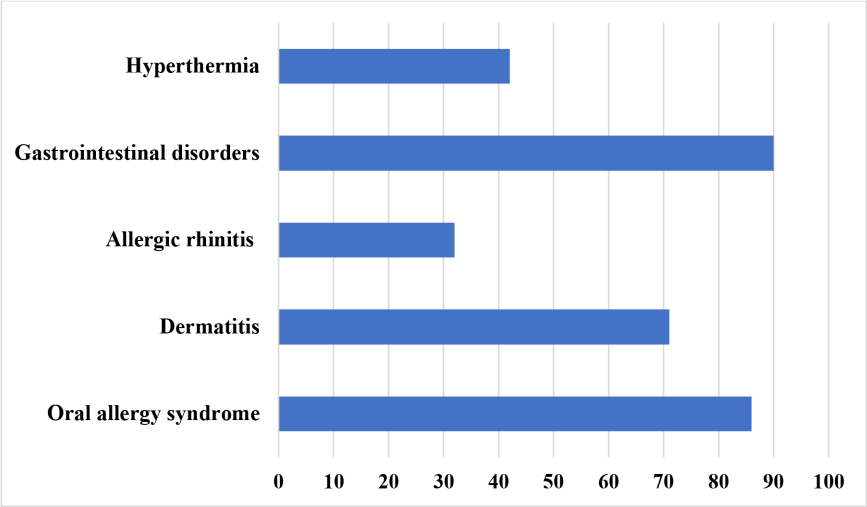

Figure 1. Clinical characteristics of past episodes of food allergy in the examined patients
Source: compiled by the author based on the data of outpatient charts of patients.

The high prevalence of gastrointestinal disorders in Figure 1 underscores the significant impact food allergies can have on the digestive system, potentially causing issues such as nausea, vomiting, diarrhea, or abdominal pain. Oral allergy syndrome is the second most prevalent characteristic, observed in about 86 % of the patients. This condition typically involves itching or swelling of the mouth, lips, and throat and is often associated with cross-reactivity between pollen and certain foods. Dermatitis, or skin inflammation, is reported in around 71 % of the cases. This highlights the common cutaneous manifestations of food allergies, including hives, eczema, or general skin irritation. The lower percentage of allergic rhinitis suggests respiratory symptoms are less common than gastrointestinal or skin reactions in food allergy episodes. The prevalence of hyperthermia indicates that food allergies can affect the body's temperature regulation in a significant portion of patients.

It emphasizes the need for comprehensive evaluation and management of food allergy patients, as symptoms can manifest in various ways across different body systems. The high prevalence of gastrointestinal and oral symptoms particularly highlights the direct impact of food allergens on the digestive tract and oral mucosa.

Figure 2 shows the distribution of patients with episodes of FA (total number—91 patients out of 211 studied in the total cohort) on fruits depending on the main allergic diagnosis. According to the obtained data, FA mainly occurred in patients with allergic multimorbidity, which does not exclude the presence of cross-allergic reactions. In second place regarding the number of detected FAs are patients with bronchial asthma, followed by atopic dermatitis and atopic rhinitis.

To identify the tendency to develop an allergic syndrome to tropical fruits, the next step was to conduct skin prick tests with allergens for jackfruit, mango, cherimoya, lychee, annatto, avocado, and pineapple. The test complied with the research protocol requirements during the remission of the main allergic disease. The skin reaction was assessed according to the scale mentioned above under the conditions of control. The results of the skin prick test with allergens for exotic fruits are shown in Table 2.

According to the results of the spot test, the most significant number of positive samples was found for the cherimoya allergen 48 (22.7 %) positive and 70 (33 %) highly positive skin samples). It is also an allergen that showed the smallest negative pre-tests and the most significant hyperergic reactions 12 (5.7 %). Cherimoya, a considerable allergen, is often associated with mild to severe systemic reactions in patients, indicating its importance, especially for those with pre-existing allergies, due to its

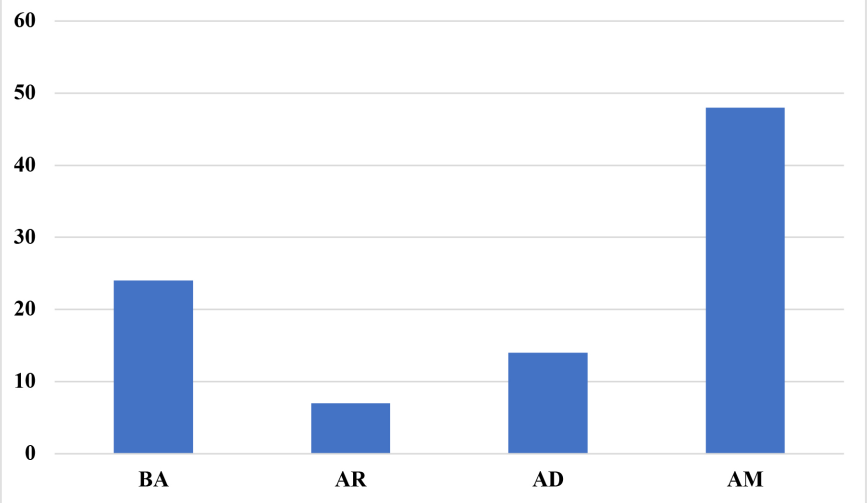

Figure 2. The distribution of patients with FA episodes on fruits depends on the primary allergic diagnosis. *BA stands for bronchial asthma; AR stands for allergic rhinitis; AD stands for atopic dermatitis; and AM stands for allergic multimorbidity. The source was compiled by the author based on the data of patients' outpatient charts.*

Table 2. Results of the skin prick test with allergens of exotic fruits in the examined patients

Sequence number	Allergen	Type of skin reaction according to the prick test				
		Negative	Questionable	Positive	Highly positive	Hyperergic
1	Jackfruit	112	43	33	18	5
2	Mango	92	18	56	43	2
3	Cherimoya	51	30	48	70	12
4	Lychee	70	27	65	43	5
5	Annato	98	4	54	54	1
6	Avocado	157	11	22	21	0
7	Pineapple	184	13	14	0	0

Source: compiled by the author.

high prevalence. Lychee fruit allergen was second in terms of the degree of detection of sensitization in the examined persons: a total of 65 positive samples (30.8 %) and 43 highly positive samples (20.4 %). The lowest number of positive and highly positive samples were found when testing with the pineapple allergen (14 positive samples). Lychee, like cherimoya, contains profilins and plant proteins that can cause IgE-mediated hypersensitivity reactions, indicating their potency in eliciting significant immune responses in sensitized individuals. Lychee allergy symptoms include oral allergy syndrome, skin reactions, and gastrointestinal symptoms. Severe reactions can occur, requiring careful management and avoidance strategies for sensitive individuals. In comparison, the highest number of questionable samples was found with the jackfruit allergen (43 samples, 20 %). The mango allergy test revealed 92 adverse skin reactions (43 %), 56 positives, and 43 highly positive reactions (26 % and 20 %).

The most significant number of negative samples was detected during tests with jackfruit, pineapple, and avocado allergens: 112 (53 %), 184 (87 %), and 157 (74.4 %) negative samples,

respectively. Based on the data, each patient showed at least two positive tests for exotic fruit allergens (from positive to hyperergic).

DISCUSSION

The study found mild IgE-associated reactions were the most common, with oral allergy syndrome (OAS) being the most common. Other common reactions included skin manifestations like urticaria and mild eczema, which were resolved with standard antihistamine treatment. Moderate IgE-associated reactions were more frequent, with atopic dermatitis and angioedema being more extensive. Gastrointestinal symptoms were reported by 90 % of patients. Severe IgE-associated reactions, less frequent but posing significant clinical challenges, included anaphylactic reactions, hyperergic reactions, and hypersensitivity to fruit allergens like cherimoya and lychee. The frequency of these reactions varied among the different fruits tested, with cherimoya and lychee being the most common triggers for severe and hyperergic reactions. Fruits like pineapple and avocado elicited fewer severe reactions, highlighting the differential allergenic potential of various exotic fruits.

Food allergy prevalence varies by age, with infants and young children having a higher prevalence due to the immaturity in their immune and digestive systems (27). Some outgrow their allergies as children grow, particularly to milk and eggs. Adolescence is also critical for changes in food allergy prevalence, with hormonal changes during puberty potentially influencing immune responses. Gender differences in food allergy prevalence increase in adulthood, with women having a higher prevalence due to hormonal influences, particularly estrogen, which can enhance immune responses and increase susceptibility to allergic reactions. Age-related immune responses, known as immunosenescence, significantly influence food allergy patterns, affecting the likelihood of developing new and existing allergy severity.

Genetic predispositions, environmental variables, and regional dietary practices all majorly impact the incidence of allergies in various demographic groups. Individual and population-level sensitivity to allergy diseases, including food allergies, is shaped by the interaction of several variables. For instance, allergies to peanuts are more frequent in Western countries, whereas allergies to rice are more common in East Asia. Evidence indicates that Israeli infants who were introduced to peanuts at a younger age had lower rates of peanut allergy than Jewish children in the UK. This finding emphasizes the influence of cultural dietary habits on allergy patterns (28).

Environmental variables greatly influence the development of allergies. The "hygiene hypothesis" postulates that an increased incidence of allergies may result from early-life microbial exposure that is minimized. Research indicates that Amish kids who spend more time on farms are less likely to develop allergies or asthma (29). Children who live in places with high traffic-related air pollution are more allergy-sensitive (30). Environmental variables could modify the expression of genetic predispositions, affecting allergy risk. Twin studies indicate that 50 %-80 % of the risk of allergic diseases is inherited, but the sharp rise in allergy prevalence points to a significant environmental component. The interaction between environmental variables and specific genetic variations linked to food allergies determines the risk of allergies (31).

Different groups have allergies to varying rates for various reasons. For example, genetic adaptations and seafood consumption make seafood allergies more common in coastal areas. Still, allergies to birch pollen are more common in Northern Europe because of the high concentration of birch trees in that region. Comprehending these geographical disparities is vital in devising focused preventive tactics and customized allergy handling, considering an individual's genetic heritage, environmental exposures, and dietary practices.

Among the exotic fruits studied, lychee and cherimoya allergens caused the most significant positive reactions, according to skin prick testing. Cherimoya mainly had the most important number of favorable and hyperergic responses. This implies that certain fruits could be more likely to cause allergic reactions in those sensitive to them, which calls for more study into the particular allergens. Interestingly, each patient

had at least two positive tests for exotic fruit allergies, even though some fruits, including avocado and pineapple, had lower rates of adverse responses. This highlights the intricacy of FA in individuals with allergic multimorbidity and suggests that there may be cross-reactivity among allergens found in exotic fruits.

Optimizing Management of Food Allergies with a Focus on Exotic Fruits

According to published clinical recommendations by Muraro et al. (32), the lack of adequate etiotropic and pathogenetic therapy for FA leads to the transition of the disease to a variant with a chronic course. It leads to a resistant recurrent course of pathology with possible involvement in exacerbations of other organs and systems and an expansion of the scope of sensitization to allergens of different types (pollen, animal). Thus, the data obtained during the empirical research are important for improving the management protocols of patients with frequent relapses of FA, bronchial asthma, or multimorbidity to prevent FA development on exotic fruits. The current research adds to the comprehensive treatment techniques provided by the recommendation of Muraro et al. by offering particular information on allergies to exotic fruits that might help guide these tactics. The comprehensive prevalence statistics on various fruit allergies can aid in developing more specialized management strategies. In contrast to the lack of adequate diagnosis and targeted treatment, the timely appointment of etiotropic therapy for FA caused by the consumption of exotic fruits allows for limiting the burden on the body by using only elimination diet therapy (18,33). This approach of timeliness and purposefulness in the treatment of food allergy allows for avoiding polypharmacy and in a short time (depending on the patient's condition) to achieve stabilization of inflammatory processes against the background of the immune response, to limit the frequency of relapses and, in the future, to prevent the progression of anaphylactic reactions on food products (16). The warning about the development of FA is the result of pre-tests in the examined cohort of patients who currently have clinically confirmed information about sensitization to such fruits.

According to Privitera-Torres et al. (34), there is an increased tendency to out-of-season exacerbations of the main allergic diseases in such groups of patients. CIRs between food and pollen allergens are explained by common antigenic determinants that form the basis of these factors. In the study, the patients had multimorbidity in their background. Still, the presence of sensitization to exotic fruits was not evaluated from the point of view of the impact on the seasonal dependence of the manifestations of the main disease. While the latter research offers information on the frequency of avocado allergy among a broader cohort of individuals with varied fruit allergies, Privietera-Torres et al. revealed a novel allergen exclusive to avocados. Avocado skin prick test results (out of 211 individuals, 22 had positive and 21 had extremely positive responses) in the current study provide important epidemiological information that supports the molecular findings of Privitera-Torres et al. This combination of detailed allergen identification and broad prevalence data improves our understanding of avocado allergy from a molecular and clinical standpoint.

An important aspect of the differential diagnosis of FA for exotic fruits is identifying groups of patients with CIR (16,35). The presence of cross-reactive IgE to certain types of pollen in the patient to plants or products common in his region increases the likelihood of developing an allergy to exotic fruits, as shown by an empirical study: patients with allergic multimorbidity showed more than two positive pre-tests to allergens with exotic fruits, and in the vast majority, they had previous episodes of FA in the history of more common types of fetuses.

Cross-Reactivity and Sensitization Patterns

One of the common allergens from the group of exotic fruits is lychee: in patients with a hypersensitivity reaction to lychee fruits, increased secretion of sulfidoleukotrienes, production of CD63 basophils, and a positive skin allergy test on lychee are clinically detected (6). In the empirical study, the lychee allergen was second in the number of detected positive and highly positive samples in the examined group of patients. According to Poncet et al. (12),

detecting circulating IgE antibodies is not always a specific sign of sensitization by the lychee fruit antigen, as in some cases, they may be within the physiological norm. In the current study, IgE was not determined, but it should be included in the following stages of work. The research provides a more comprehensive understanding of fruit allergies than the pollen-food allergy syndrome study by Poncet et al., which focused solely on pollen cross-reactivity. Poncet focuses on a single mechanism, while our analysis offers a more comprehensive clinical picture that includes several fruit allergies. Clinical cases of anaphylactic reactions to lychee with cross-reactivity to wormwood and antigens of the umbrella family have also been published (10). Also described are clinical cases of an anaphylactic reaction to lychee fruits in combination with a cross-reaction to wormwood (8). The work revealed only positive reactions to lychee and other exotic fruits (avocado, mango, annatto).

Several scientific publications testify in favor of the fact that some tropical fruits (mango, banana, jackfruit, kiwi, avocado) are primary factors in the development of cross-immunoreactivity with latex antigen in persons diagnosed with latex sensitization: a case of anaphylactic reactions to jackfruit in an elderly patient with previously diagnosed cases of moderate skin manifestations of latex allergy; analysis of cases of acute FA on kiwi against the background of sensitization to latex (20,21,36-39). Modern allergology describes this phenomenon as "latex-fruit syndrome" (40,41). In the examined cohort of patients, a combined pathology was revealed in the presence of previously diagnosed bronchial asthma, atopic dermatitis, or allergic rhinitis, together with sensitization to the allergens of exotic fruits. Still, the definition of the "latex fruit" syndrome is an urgent issue that needs to be included in the further stages of the work.

Allergic reaction to eating jackfruit (*Artocarpus integrifolia)* is usually accompanied by a typical specific IgE response. The described cases of FA developed against the background of already existing multiple sensitizations, which were confirmed by prick tests. However, in contrast, Chunduri and Prabhu (42) and Goodman and Feuille (43) state that jackfruit extract can treat some inflammatory and allergic symptoms in the respiratory system. During the conducted empirical research, a positive reaction to jackfruit of varying severity was found in 24 % of patients, usually together with a positive reaction to mango or pineapple, confirming this exotic fruit's allergic potential. The current study offers a more thorough picture of various fruit allergies than specialized studies such as the ones by Chunduri and Prabhu on jackfruit proteins or Goodman and Feuille on avocado in FPIES. This more comprehensive method enables cross-fruit comparisons and can reveal trends that may be missed in research with a more restricted scope.

Mango fruits (*Mangifera)* are widespread on the industrial market, and anaphylactic reactions to their use are rare and critical FA manifestations. In the examined cohort of 211 patients, 46 % of patients showed positive pre-test reactions of varying severity, which shows the prevalence of sensitization to this fruit in this group. However, no anaphylactic manifestations or delayed-type reactions were detected. However, such clinical cases are described by Forkel et al. (44) in a case study on mango allergy, which highlights severe manifestations. The latter research expands on this by providing a more comprehensive view of mango allergy prevalence and clinical presentations. The skin prick test results provide valuable data on sensitization frequency in a larger population, complementing detailed case analysis by Forkel et al.

Consuming cherimoya fruits (*Annona cherimola)* is a provoking factor in developing allergic symptoms to IgE-binding proteins of cherimoya, including OAS and CIR "latex-fruit syndrome." In contrast to sensitizing properties, there are studies regarding the perspective of using *Annona* fruits *cherimoya* as part of antidiabetic drugs (31,45). The study did not determine CIR or levels of IgE-binding proteins of cherimoya. However, a prick test with cherimoya allergens showed that less than half of the examined patients tended to sensitize, and five patients showed a hyperergic reaction.

Molecular allergy diagnostics allows for determining the protein to which sensitization develops in a specific patient (46). This stage of diagnosis is important for understanding the characteristics of the body's sensitization. It excludes allergens containing this component or its homologous variants from their structure. This

method is appropriate for further studies of the chosen topic for the pathogenetic understanding of allergic reactions to exotic fruits because the determination of the type of allergen helps provide the patient with more detailed recommendations regarding the diet to avoid and prevent the development of FA (47).

The present investigation offers significant perspectives on the frequency and clinical presentations of food allergies to exotic fruits. Nevertheless, its conclusions are limited by the small sample size, regional restrictions, absence of confounding factor control, and the narrow emphasis on certain fruits. These drawbacks emphasize the necessity of further studies using bigger, more varied sample sizes and stricter methodology to fully comprehend the intricacies of food allergies.

The study suggests that improving treatment recommendations, promoting better food labeling, enhancing patient education, improving diagnostic procedures, and influencing medical professional education can significantly improve food allergy management. This may result in improved patient outcomes, more effective therapy, and a deeper comprehension of the allergens that cause allergic diseases. A greater variety of allergens may be included in diagnostic tests, patients can be educated about the dangers of eating exotic fruits, personalized dietary plans can be created, emergency plans can be made, clinical guidelines can be updated, and research can be encouraged to offer patients with specialized care. This strategy can lower risks and improve the quality of life for those who suffer from food allergies.

CONCLUSIONS

The study's main emphasis, food allergies to exotic fruits, has produced substantial data about these allergies' prevalence and clinical presentation. The empirical inquiry and literature analysis demonstrate that allergies to exotic fruits, which are now a staple of many diets, are becoming more often reported by allergists. A broad range of clinical signs was seen in the individuals under study, from mild urticaria and edema to severe anaphylactic responses, but the latter were less common. Food allergies (FA) to exotic fruits can be difficult to diagnose because of their wide range of clinical symptoms and cross-reactivity with other allergens, which makes it difficult to pinpoint the allergen that is causing the allergy in the first place.

In the examined patients under medical observation, the tendency to develop food allergies to exotic fruits was mainly detected against the background of allergic multimorbidity, which does not exclude the presence of cross-allergic reactions in such patients. Each patient examined showed at least two positive, highly positive, or hyperergic tests for allergens of exotic fruits such as jackfruit, mango, avocado, pineapple, lychee, cherimoya, or annatto. The allergen also showed the lowest number of negative pre-tests and the highest number of hyperergic reactions in the examined group of patients. The lychee fruit allergen was second in terms of the degree of sensitization detected in the examined persons. The smallest number of positive and highly positive samples were detected during the test with the pineapple allergen, and the most significant number of questionable samples was detected with the jackfruit allergen. Patients previously diagnosed with atopic skin manifestations to other allergens and a history of anaphylactic reactions have a higher tendency to develop hypersensitivity reactions to tropical fruits.

The obtained data can be implemented in the protocols of the primary examination of patients with allergic diseases to prevent the development of cross-immune reactions. Moreover, it can be utilized in the industrial sphere to label exotic fruits as potentially causative factors in the development of hypersensitizing symptoms.

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