Healthcare in Low-resource Settings

eISSN: 2281-7824

https://www.pagepressjournals.org/index.php/hls/index

Healthc Low-resour S 2024 [Online ahead of print]

To cite this Article:

Lisiecka MZ. **Impact of gibberellin-regulated protein allergy on quality of life.** *Healthc Low-resour S* doi: 10.4081/hls.2024.12412

Impact of gibberellin-regulated protein allergy on quality of life

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Key words: immune response, cross-reaction, hypersensitivity, food, pollen.

Conflict of interest: the author declares no potential conflict of interest.

Funding: none.

Ethics approval and consent to participate: the study was conducted without human/animal participation. Ethical approval is not required.

Availability of data and materials: the data supporting the findings of this study are available on request from the corresponding author.

Abstract

The purpose of this study was to investigate possible allergens that cause gibberellin-regulated protein allergy. For this purpose, a thorough search of relevant information in the databases Embase, PubMed, Scopus, and Web of Science, presented for 2018-2023, was carried out. The study showed that about 4% of the world's population suffers from food allergies. The main manifestations of allergic reactions and the degree of resistance to allergens depend on the age group of patients. The study identified the following food allergens in gibberellin-regulated protein allergy: Pru p7 (peach), Pru m7 (Japanese apricot), Cit s7 (orange), Pun g7 (pomegranate), Pru av7 (sweet cherry), Cap a7 (bell pepper), Fra a3 (strawberry), Cup s7 (cypress pollen). Gibberellin-regulated protein allergy is characterised by a predominantly adolescent and young adult population. The symptoms of this allergy usually manifest themselves in the form of oral syndrome, facial swelling (including eyelids), anaphylactic reactions and are aggravated by the action of cofactors. Such manifestations substantially impair the quality of life of patients, causing a social, psychological, and economic burden.

Introduction

Epidemiological studies indicate a considerable increase in the prevalence of food allergies worldwide, namely, about 220 million cases. Severe symptoms are often reported in newborns and the elderly. About 4% of the world's population suffers from food allergies. Among them, about 2-12% of children aged 0-6 years and 0.5-7% of the adult population have a food allergy to fruit.[1] The significant prevalence of this pathology is conditioned by changes in the environment, the widespread use of chemicals in agricultural activities, the use of household chemicals, feeding newborns with

artificial formulas, and the uncontrolled use of antibacterial drugs (which leads to a disruption of the intestinal microbiome and a decrease in immune defense).

At the beginning of the 21st century, researchers discovered that a family of proteins contains representatives with allergenic properties. The main one is a gibberellin-regulated peptide. It is found in peaches, apricots, oranges, pomegranates, cherries, bell peppers, strawberries, and cypress pollen. An allergic reaction to gibberellin-regulated peptide usually manifests itself in the form of itching, redness, and swelling of the mucous membranes of the eyelids and mouth, watery eyes, sneezing, nasal congestion, dry cough, and mild skin rashes.[2] At the same time, anaphylactic shock often occurs, which, in the absence of emergency care, leads to immediate death. A characteristic feature of this type of allergy is dependence on the presence of a cofactor (medication and alcohol intake, active physical training, and menstruation). The disease affects mainly young people and adults.

An important problem is the understudied mechanism of gibberellin-regulated protein allergy and, accordingly, the lack of adequate pathogenetic treatment. That is why, when suffering from this type of allergy, patients' daily activities are substantially limited; they are forced to carefully select food and avoid contact with allergenic tree pollen, constantly monitor their diet, and carry allergy emergency equipment. All of this results in a heavy economic, social, and psychological burden for patients with gibberellin-induced protein allergy. Muraro *et al.* studied and assessed the impact of food allergies on the quality of life and proposed new recommendations for lifestyle, diet, prevention, and treatment of the most common types of food allergies.[3] Kuźmiński *et al*. investigated the prevalence, main characteristics, methods of prevention, and treatment of food allergy to nuts.[4] The topic of cross-reactivity between allergens from nuts and other plant sources, such as pollen, is covered. Unlike many other childhood food allergies, tree nut allergies typically start in childhood and are likely to last into adulthood. There is a wide variety of clinical symptoms, from mild oral allergy syndrome to severe, potentially lethal anaphylaxis. The sole management method that is currently approved is the strict avoidance of tree nuts.

Niewiem and Grzybowska-Chlebowczyk assessed the role of intestinal permeability markers on the course of allergic reactions.[5] Increased intestinal permeability in food allergies makes it possible for allergens and other dangerous chemicals to pass through the barrier and for the intestinal mucosa to react immunologically. The study emphasises how a weakened intestinal barrier is a major pathogenic component in allergic disorders and how managing and preventing these conditions may be aided by promoting intestinal barrier integrity from a young age through dietary modifications and the reduction of disrupting elements. Asero *et al*. highlighted new relevant information on lipid protein allergy.[6] The authors address debates over the therapeutic applicability of lipid protein sensitization because certain investigations reveal a high number of sensitised yet asymptomatic subjects. There are also questions about the most accurate diagnostic tests for lipid protein allergy. J. Morozińska-Gogol presented the problem of the prevalence of nematodes of the genus *Anisakis* and their role in the development of food allergies.[7] *Anisakis* are parasitic worms that can infect humans who consume raw or undercooked fish or cephalopods contaminated with the worm's larvae. A key point is that the allergens in *Anisakis* show high heat stability and resistance to digestive enzymes, making them difficult to remove through cooking.

Thus, many Polish and foreign scientists have conducted many meaningful studies on the types and characteristics of food allergies. Given the availability of a wide range of diverse information on food allergies and, at the same time, a small amount of data on gibberellin-regulated protein allergy, the purpose of this study was to investigate and describe the diagnosis and prevention of gibberellin-regulated protein allergy. The main objectives of the research are: i) to investigate the causes and risk factors associated with gibberellin-regulated protein allergy; ii) to characterize the main symptoms and clinical manifestations of gibberellin-regulated protein allergy; iii) to examine the methods and criteria for accurately diagnosing gibberellin-regulated protein allergy; iv) to determine the prevalence of gibberellin-regulated protein allergy across different populations and age groups.

Materials and Methods

Before conducting this review study, a thorough, structured, and systematic search for relevant information on food allergies and their types was performed in PubMed, Embase, Scopus, and Web of Science databases. During the study, all submitted papers with the necessary information (clinical trials, randomised controlled trials, reviews, systematic reviews, and meta-analyses) published from 2018 to 2023 in peer-reviewed journals in English, French, Polish, and German were found and reviewed. The search for the necessary data was carried out using a combined set of keywords: “allergic reaction”, “immune response”, “type of immune response”, “types of allergens”, “gibberellin-regulated peptide”, “immunoglobulins”, “food allergens”, “pollen”, “hypersensitivity”, “cross-reaction”, “anaphylactic shock”, “symptoms of food allergy”, “diagnosis of food allergy”, “prick test”, “treatment of allergic reactions”, “diet therapy”, “lifestyle”, “prevention of allergy”, “complications of allergic reactions”, “emergency care”.

The received papers were carefully studied, processed, and analysed, selected by titles and abstracts, and considering the relevance, time of publication, and suitable level of evidence for the case studies. To obtain more information sources, the lists of references for the relevant articles were examined, and the relevance of their content was assessed. Next, the duplicate studies were removed, along with those that did not correspond to the selected period since publication. The available articles were then assessed against the inclusion and exclusion criteria. Papers that did not meet the inclusion criteria in part or in full were immediately removed. Articles that contained outdated, unconfirmed, and irrelevant information; unreliable, poorly conducted studies and their findings; and descriptions of the study conducted only on animal models were not included in this study.

This study included papers from the last 6 years (2018-2023) with new data on the prevalence, causes, risk factors, mechanisms of development, symptoms, diagnosis, treatment, prevention, and emergency treatment of food allergies. The studies describing types of allergic reactions, types of allergens, innovative approaches, and methods of investigating allergic reactions without restrictions on gender, age, race, territory of residence, social status, details of medical and life history, or specific features of the course or severity of diseases were used. The papers describing the pathogenesis of

various types of allergic reactions and emergency protocols for anaphylactic reactions were selected and included; the allergens contained in food were identified. Attention was focused on the papers describing the best methods of nutrition for gibberellin-regulated protein allergy and the list of safe foods allowed, considering the possibility of cross-allergy.

A thorough, systematic selection process resulted in relevant articles that fully met the necessary selection requirements. To avoid errors, the selected sources of information were re-evaluated, processed, and verified. The results of the selected studies were cited in this paper in compliance with all necessary technical requirements and copyrights.

Results

Food allergies are harmful effects on the body's health that occur as a result of a specific immune response to repeated exposure to a particular food.[8-10] The characteristics of allergic reactions differ substantially depending on the age group of patients. Fruit allergies are classified into two types, depending on their ability to cross-react with pollen. The first type is an allergy associated with a cross-reaction to pollen, called food pollen allergy syndrome. It is an Immunoglobulin E (IgE)-mediated immediate allergic reaction caused by a cross-reaction between pollen and food antigens (Table 1).[11-15] It accounts for about 60% of allergy cases in adults and adolescents. Target organs: skin, oral mucosa, epithelium of the gastrointestinal tract, respiratory tract, and cardiovascular system. This type of allergy manifests itself in the form of an oral allergic syndrome. It occurs 10-15 minutes after allergen exposure and causes redness, tingling, and itching in the mucous membrane of the tongue, lips, and palate, as well as swelling of the oropharynx. Most of these manifestations disappear in 1-3 hours, but 1-8% of patients develop severe systemic complications in the form of anaphylactic reactions.[9,10]

Allergies in which the allergen is a nonspecific lipid carrier protein are called non-pollen fruit allergies. It is characterised by a significant degree of cross-reactivity between lipid carrier proteins

of different plant species. Nonspecific lipid carrier proteins form a large family of peptides found in many land plants. They are small, non-glycosylated proteins with a mass of about 7-8 kDa. Based on their molecular weight, these proteins were divided into two groups: LTP1 (9-10 kDa) and LTP2 (6-7 kDa). The main biological role of lipid carrier proteins is to transport and accumulate lipids to build important protective polymers on the surface of plant tissues (*e.g.*, wax on leaves, suberin in seeds and roots, sporopollenin in pollen grains).[16]

The following main allergens have been described in food allergies caused by lipid carrier proteins: Pru p3 (peach), Mal d3 (apple), Cit r3 (orange), Bra o3 (cabbage), Sin a3 (mustard), Jur r3 (nut), Cas s8 (chestnut). Sensitization occurs through the mouth, inhalation, or skin contact. At the same time, Pru p3 (peach) may be the main sensitizer of this food allergy. In a study in Spain, sensitization to Pru p3 was detected in 12% of 2,000 patients. In a group of 87 subjects susceptible to Pru p3, 44% had anaphylactic reactions; 43% had skin and oropharyngeal manifestations; and 13% were asymptomatic.[17] Disulphide bonds ensure that lipid carrier proteins fold into a compact structure with significant thermal and proteolytic stability, which explains their high allergenicity and severe symptoms. At the same time, at neutral pH and hot temperatures, the stability of proteins decreases due to the destruction of disulphide bonds. It is important to consider this when choosing a method of culinary processing food for people with this type of allergy.

Researchers have described a new allergen that has the same features as the above-mentioned allergic reactions to fruit: a gibberellin-regulated peptide.[1] It belongs to the family of plant antimicrobial peptides rich in cysteine. The first peptide of this family was isolated from potatoes in 1999. At the same time, the first representative of these peptides that could potentially cause allergies was found in peaches (Pru p7).[1] Gibberellin-regulated peptides are involved in plant growth and protection against pathogenic factors. They also control germination, cell division, dormancy, flowering, and fruit development. The expression of gibberellin-regulated peptides is controlled by gibberellins, which are a class of natural plant hormones produced by plants, fungi, and bacteria. Gibberellin (gibberellic acid) was discovered and described by E. Kurosawa in the ascomycete (rice parasite

Gibberella fujikuroi, which leads to a sharp increase in the length of rice stems) in 1926.[1] The endogenous content of gibberellin-regulated peptides and gibberellin is influenced by biotic (protozoa, bacteria, viruses, fungi) and abiotic factors (drought, floods, temperature, sodium concentration). A slight increase in temperature contributes to an increase in the content of endogenous gibberellin. At the same time, a wide range of exogenous gibberellins are actively used in agriculture to improve yields and increase crop production.

Gibberellin-regulated peptides are small, basic, water-soluble, cysteine-rich proteins with a molecular weight of about 8 kDa. A characteristic feature is that all these proteins contain 12 cysteines at the C-terminus, forming 6 disulphide bonds. The high cysteine content provides gibberellin-regulated peptides with high chemical, thermal, and proteolytic stability. Gibberellin-regulated protein allergy occurs more often in adolescents and adults and less often in children.[18-20] The most dangerous allergens are Pru p7 and Pru m7, as they cause anaphylactic reactions (Table 2).[21-24] The cross-reactivity between Pru p7, Pru m7, Cit s7, and Pun g7 is described. In contrast to the nonspecific lipid carrier protein, which is more abundant in fruit peel, gibberellin-regulated peptides are found in both the peel and pulp of vegetables and fruits. This type of allergy is dependent on the presence of a cofactor (taking medications such as Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), proton pump inhibitors, alcohol consumption, physical training, and menstruation).[18-20] Pru p7 is a gibberellin-regulated protein allergen found in the peel and pulp of peaches. It was first discovered and described in 2013. It cross-reacts with apricot, pomegranate, orange, and cypress pollen. The main prognostic symptom is facial swelling (especially in the eyelid area), and anaphylaxis often occurs. Biagioni *et al*. have developed a detailed algorithm for diagnosing this disease.[10] This requires a skin prick test for inhalation (including cypress pollen) and food allergens (including peach peel extract). In the case of a positive skin prick test for peach and cypress peel extract and a negative *in vitro* result for specific IgE to Pru p3, a preliminary diagnosis of allergy to Pru p7 is made. For confirmation, serum IgE to Pru p7 is additionally measured.

Pru m7 is an allergen isolated from apricots. The cross-reactivity between Pru m7 and Pru p7 has been proven. Notably, unlike Pru p7, Pru m7 caused allergic reactions more often in the presence of cofactors (16.7% and 84.6%, respectively). The main manifestation is swelling of the face, specifically the eyelids. Cit s7 is an allergen isolated from sweet oranges. The symptoms of allergy are much milder than the two previously mentioned types. A study found that 2 out of 12 patients (16.7%) had symptoms of urticaria and oropharyngeal syndrome, but none of the patients had anaphylactic shock. Light physical activity (slow walking, cycling, or running) was a cofactor for 4 out of 12 patients. During the ELISA test using patient serum, cross-reactivity between Cit s7, Pru p7, and Pru m7 was detected. Pun g7 is an allergen isolated from pomegranate. In a study of a large population group in Italy, the FABER test found that 0.5% of participants were sensitive to Pun g7. That is, this allergen is not as widespread as the previous ones, and a relatively small number of people are sensitised to it.[2]

In 2019, a new allergenic gibberellin-regulated peptide was identified from cypress pollen. The sensitization of gibberellin-regulated peptides in fruit is related to the sensitization of cypress pollen, with a percentage of sequence identity in cypress of 90% with fruit and 60% with vegetables. It was found that patients with food allergies have a lower quality of life because constant vigilance is required to avoid allergens.[25-27] In addition, such patients are constantly under stress due to worries about a possible anaphylactic reaction. Due to the insufficient study of gibberellin-regulated protein allergy, there is no pathogenetic treatment for this pathology. Therefore, it is difficult for patients to lead a full, active social life. To reduce the risk of allergies, it is important to consider the patient's age and, accordingly, the possible level of responsibility for their own health (Table 3).[28-31]

Quality allergy protection includes the avoidance of allergens, awareness of the symptoms of an allergic reaction, and knowledge of first aid.[32-36] Therewith, patients should have emergency equipment with them in case of an allergic reaction, specifically in case of anaphylactic shock. Thus, gibberellin-regulated protein allergy is a widespread problem due to severe clinical manifestations

and the presence of allergens in commonly consumed foods. An effective way to combat it is to avoid allergens and take care of one's health.

Discussion

Kuźmiński *et al*. described the characteristic features of nut allergy.[4] It was found that the term "nut allergy" includes allergies to almonds, Brazil nuts, peanuts, cashew nuts, hazelnuts, chestnuts, macadamia nuts, pecans, and walnuts. This type of allergy begins in childhood and, unlike many other types of food allergies, rarely disappears in adulthood and persists throughout life. The main complication of this disease is anaphylactic shock, which often causes death. At the same time, gibberellin-regulated protein allergy occurs more often in adulthood, and severe complications such as anaphylactic shock are much less common. To date, the following allergens present in almonds have been described: Pru du1 (albumin 2S, reserve protein), Pru du2 (conglutin, 7S globulin, reserve protein), Pru du3 (lipid transport protein), Pru du4 (profilin), Pru du5 (ribosomal protein S2), and Pru du6 (amandin). The main allergen in almonds, Pru du1, causes cross-reactions with other foods that contain this protein: walnuts, sunflower seeds, and peanuts. In addition, 33% of patients with almond allergy were found to be allergic to birch pollen. Peanuts contain the following allergens: Ber e1 (2S albumin) and Ber e2 (11S globulin). Ber e1 is responsible for severe allergic reactions; it is resistant to temperature and digestive enzymes; and it is involved in the cross-reaction between walnut (Jug r1) and pecan (Car i1). Peanuts (Ara h1), walnuts (Jug r2), hazelnuts (Cor a11), and cashews (Ana o1) have been described as having a comparable structure, which explains possible cross-reactions. The following allergens were found in hazel: Cor a1 (PR-10 protein), Cor a2 (profilin), Cor 6 (isoflavone reductase), Cor 8 (nonspecific LTP type 1), Cor 9 (11S legumin), Cor 11 (luminal binding protein), Cor 12 (oleosin with a molecular weight of 17 kDa), Cor 13 (oleosin with a molecular weight of 14-16 kDa), Cor a14 (2S albumin). Cor a1 causes cross-reactions with birch, alder, and hornbeam pollen. Cor a8 causes cross-reactions of lipid carrier proteins with peaches, peanuts, walnuts, and

cherries. Walnuts contain the following allergens: Jur r1 (2S albumin), Jur r2 (7S vicillin), Jur r3 (nonspecific lipid transport protein), and Jur r4 (11S globulin). The high 2S-dependent albumin concentrations cause cross-reactivity between walnuts and pecans, almonds, peanuts, and cashews. In an examination of 20 patients with food allergies to flowering fruits (*e.g*., apples, peaches, and apricots), 80% of them had a clinical reaction to nuts (walnuts and hazelnuts).

Pecoraro *et al*., Lyons *et al*., Yang *et al*., Dijkema *et al*. found that about 0.5% of the world's population is allergic to fish and seafood.[36-39] Patients with fish allergies are classified into the following groups: (A) polysensitised patients, who react to all types of fish due to sensitization to the panallergen b-parvalbumin; (B) monosensitised patients, who have a selective reaction to only one particular type of fish; (C) oligosensitised patients, who have an allergic reaction to several types of fish. The clinical picture is diverse, ranging from oral allergy syndrome and skin lesions to angioedema and anaphylaxis with respiratory/circulatory disorders.[40,41] The most common allergy is to fish fillets, and its allergens differ from those of fish caviar. This should be considered when selecting a suitable type of diet for such patients so as not to mistakenly limit the consumption of healthy, harmless foods. Eating untreated fish carries a risk of contracting *Anisakis simplex*. Anisakiasis is manifested by allergic reactions in the form of urticaria, angioedema, and anaphylactic shock.[42-44] This should be considered to avoid misdiagnosing food allergies in patients with parasitic diseases. *Anisakis simpleks* is a nematode that can cause human infection at stage 3 of its life cycle. This is possible by consuming contaminated raw, undercooked, and smoked fish and cephalopods. It is known that *A. simpleks* allergens are thermostable and have significant resistance to enzyme degradation.[7] Due to the difficulty of removing parasites from fish, sensitised patients are advised to consume only seafood from waters that are usually free of *A. simpleks* allergens and subject the seafood to heat treatment (60°C for more than 10 minutes or freezing for 24 hours at -20°C).

Inuo *et al*. described a case of allergy symptoms in a 15-year-old boy after eating strawberries during physical training.[45] The patient reported generalised urticaria and lip swelling caused by fast walking after consuming the above food product. The diagnostic prick test with fresh strawberries was

positive. The patient's serum was found to be positive for strawberry gibberellin-regulated peptide. Given the positive tests and the onset of symptoms as a result of brisk walking, it was concluded that the patient had an allergic reaction in response to exercise due to the consumption of a gibberellin-regulated protein in strawberries. This study also found that the presence of cofactors (physical activity, menstruation) in gibberellin-regulated protein allergy substantially worsens the course of the latter and leads to generalised reactions and severe complications.[46,47]

Urashima *et al*., Ramírez-Marín *et al.*, Rodriguez Bauza and Silveyra, Rey-Mariño and Francino observed that over the past 30 years, there has been a substantial increase in the incidence of atopic diseases: bronchial asthma, rhinitis, and food allergies.[48-51] Atopy is a hereditary pathological response of the immune system to environmental factors that are harmless to the general population. It is characterised by an increase in the release of specific IgE. Excessive hygiene, uncontrolled use of antibiotics, widespread use of pesticides in the agricultural and food industries, and air pollution from harmful emissions are all considered to be contributing to the increase in allergies. It has also been found that premature babies are more vulnerable to protein compounds that penetrate the incompletely formed intestinal barrier.

At the same time, the intestinal microbiome is the largest and most active component of the intestinal barrier and is important for the normal development of the immune response. The intestinal microbiome develops during the first 3 years, including intrauterine development and the next 2 years of a child's life.[5] The normal functioning of the intestinal mucosa is of immense importance, as this structure performs protective, nutritional, and immune functions. The intestinal barrier separates the intestinal lumen from the internal environment of the body. It is built from local microorganisms, epithelium, blood cells, lymphatic, and nervous tissue. At the same time, increased intestinal permeability in food allergies allows pathogenic substances to penetrate the intestinal barrier and stimulate the submucosal immune system. As a result, there is an increased release of inflammatory mediators, which leads to the destruction of the epithelial layer and increased intestinal permeability. Important ways to reduce the risk of any allergy are natural childbirth, breastfeeding, contact with

nature, pets, and the consumption of probiotics with food. Such simple recommendations can improve the immune defense of an individual and prevent a number of severe allergies and their complications in adulthood.

Everyday life can be severely disrupted by allergies in a number of ways. In addition to completely removing particular foods from one's diet, having an allergy also involves being on the lookout for any cross-contamination while food is being cooked or served in communal areas like restaurants. This continual watchfulness and the possibility of inadvertent intake can lead to a great deal of worry and anxiety. Peaches, for instance, are a fruit that is widely consumed worldwide, making it exceedingly difficult to avoid the allergy. Furthermore, due to cross-reactivity, peach allergies are frequently associated with reactions to similar fruits like apricots, cherries, and almonds. This has a significant negative influence on a person's nutritional intake and quality of life by drastically reducing the range of foods they can safely eat. Severe allergies to peaches always raise the possibility of anaphylaxis, a potentially fatal whole-body reaction that needs to be treated right away. One's everyday experiences and activities, including going on a trip or dining out, can be severely limited by this fear of experiencing a potentially fatal episode. The emotional and physical costs of dealing with a peach allergy demonstrate how a seemingly small food allergy may have a significant impact on a person's entire life.

Conclusions

An extensive review of gibberellin-regulated protein allergy, a newly identified and understudied food allergy, has been given in this paper. The main findings reveal that this allergy arises from a specific family of cysteine-rich antimicrobial peptides called gibberellin-regulated proteins found in various fruits, vegetables, and pollen. A defining characteristic is the cross-reactivity observed between different allergens, allowing sensitization to one to trigger reactions to others. Clinical symptoms of the allergy range from minor oral allergy syndrome, which involves itching, swelling, and rashes around the mouth, to potentially fatal systemic anaphylaxis, which involves breathing

difficulties and circulatory collapse. The allergy is primarily seen in adults and teenagers. Notably, it has been demonstrated that the presence of specific cofactors, such as exercise, menstruation, alcohol, and some drugs, significantly exacerbates and intensifies reactions. One distinct and poorly understood feature of the illness is its reliance on cofactors. These allergens have a significant potential for causing allergies because of their high thermal and proteolytic stability, which also makes them resistant to breakdown during cooking or digestion.

Avoiding foods that trigger allergies is currently the main management strategy for gibberellin-regulated protein allergy due to the lack of appropriate therapeutic options. But patients' quality of life is significantly reduced as a result, leading to heavy psychological, social, and financial costs. Anaphylactic reactions and unintentional allergen exposure must be avoided by maintaining constant watchfulness.

The results emphasise the necessity of more investigation to clarify the pathogenic pathways responsible for this allergy. Enhanced comprehension may facilitate the creation of focused treatments, mitigating the effects on patients' quality of life. Future research should also look for ways to more accurately detect and lessen the influence of cofactors in triggering severe reactions. It is essential to increase public and healthcare professional awareness of gibberellin-regulated protein allergy. Potentially lethal effects can be avoided with prompt recognition and the appropriate control of reactions. All things considered, more study is necessary to address the substantial unmet requirements related to this newly discovered food allergy.

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Table 1. The main types of allergic reactions according to Jell and Coombs.[11-15]

Name	**Type of antigen**	**Pathogenesis**	**Biologically active substances involved**	**Manifestations**
Anaphylactic/reaginic (reaction time 0-6 hours)	Food, non-infectious substances, medicines	Interaction of AH with IgG and IgE, fixed on histiocytes and mast cells	Histamine, an eosinophilic chemotactic factor of anaphylaxis	Anaphylactic shock, rhinitis, conjunctivitis, bronchial asthma, urticaria, atopic dermatitis
Cytotoxic/cytolytic (reaction time 24-72 hours)	Medicines, chemical, and organic substances	Interaction of IgE and IgG ABs with AGs of cell membranes or AGs adsorbed on them, resulting in activation of the complement system	Enzymes of the complement system, superoxide anion radical	Side effect of transfusion of incompatible blood, agranulocytosis
Immunocomplex Artius type (reaction time 24-72 hours)	Autoallergens	Interaction of IgM and IgG ABs and AGs, resulting in excessive formation of circulating immune complexes, activation of the complement system, infiltration of tissues by leukocytes, platelet aggregation and activation of lysosomal enzymes, which causes damage to the vascular endothelium	Complement, lysosomal enzymes, superoxide anion radical	Diseases of immune complexes, allergic glomerulonephritis, arteritis
Cellular/delayed type (reaction time 24-72 hours)	Infectious and chemical substances	Interaction of sensitised T-lymphocytes with hypertension, production of	Lymphokines	Contact dermatitis, transplant rejection

		inflammatory cytokines, activation of macrophages, monocytes, lymphocytes, their involvement in the site of hypertension, damage to surrounding tissues and formation of cellular infiltrate		reactions, reactions to tuberculin

AG, Antigen; AB, Antibody

Table 2. Allergens in gibberellin-regulated protein allergy.[21-24]

Source of the allergen	Name of the allergen	Allergen entry method
Peach tree	Pru p7	Alimentary
Pomegranate	Pun g7	Alimentary
Japanese apricot	Pru m7	Alimentary
Orange	Cit s7	Alimentary
Sweet cherry	Pru av7	Alimentary
Strawberries	Fra a3	Alimentary
Bell pepper	Cap a7	Alimentary
Cypress pollen	Cup s7	Inhalation

Table 3. Managing food allergies throughout life.[28-31]

Age group	Responsible persons	Features
Infants	Parents/guardians, close family circle, kindergarten staff	It is not immediately possible to recognise the symptoms of an allergic reaction, and it is difficult to identify the allergen due to the impossibility of collecting complaints and anamnesis from the patient.
Infants and toddlers	Parents/guardians, close family circle, kindergarten staff	The period of active recognition and exploration of the world around the patient, primarily through grasping reflexes and trying to taste everything.
Primary and secondary school children	Parents/guardians, close family circle, school staff, the patient	Relative independence and personal responsibility of the young patient for their own health and life.
Teenagers	The patient, parents/guardians, and the close group	A difficult period in the formation of personality, a craving for forbidden things, dangerous actions, often indifference to one's own health and life. The desire to try new things, often without considering the harmful consequences.
Young people	The patient, parents/guardians, and the close group	Start of an independent life, full responsibility for one's own actions, and the need to assess all possible risks. Frequent lack of financial capacity to ensure quality food and proper medical care.
Adults	The patient, their close group	Increased level of responsibility due to a permanent job, family, and many duties. Frequent lack of time to take care of one's own health.
Elderly people	Children, grandchildren, close family, the patient	Cognitive decline, often depressive behaviour, dependence on others for help and need for supervision.

Submitted: 21 February 2024

Accepted: 12 April 2024

Early access: 27 May 2024