Spectrum and frequency of food allergy in Kyiv`s adult citizens with allergic rhinitis: a cross-sectional study

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Abstract

Background: Food allergy affects 1-3% of adults worldwide. More than 160 foods can cause allergic reactions. Food allergy may preceed and stimulate allergic rhinitis.

Aim of the study was to assess the spectrum and frequency of sensitization to food allergens in patients with established allergic rhinitis from Kyiv, Ukraine.

Methods. The investigation was conducted as a cross-sectional study. 175 Kyiv adult patients with allergic rhinitis were enrolled to the trial. Sensitization to allergens and their components was determined by skin prick tests and in vitro detection of allergen specific IgE by ELISA in serum of the blood – multicomponent Allergy Explorer2- ALEX2 test.

Results. It was shown, that sensitization to following inhalant allergens was predominant: to timothy grass – in 50,3%, to ragweed - in 48,6%, to birch – in 44%, to wormwood – in 24%, to Alternaria alternatus mold – in 15,4% of patients. 131 (74,9%) participants have co-sensitization to at least one food allergen. Sensitization to following food allergens was predominant: to hazelnut – in 27,5%, to apple – in 26,3%, to peanut – in 21,7%, to celery – in 14,3%, to soy – in 13,1%, to fish carp – in 11,4%, to kiwi – in 9,1%, to crab – in 9,1%, to codfish – in 8,6%, to oyster – in 8,6%, to peach – in 8%, to lobster – in 8%, to carrot – in 7,4%, to anisakis – in 6,3%, to prawn – in 6,3%, to tiger prawn – in 5,7%, to beef – in 5,1%. It was found that the frequency of sensitization to cross-reactive proteins PR-10 was 20,5% (95% CI; 9,7%-33,9%) in patients with allergic rhinitis without food co-sensitization comparing to 51,1% (95% CI; 42,5%-59,7%) in participants with both allergic rhinitis and food co-sensitization, p<0,001; to nsLTP was 2,3% (95% CI; 0-8,9%) and 19,8% (95% CI; 13,4-27,2%), respectively, p=0,011.

Conclussion. In Kyiv adult population with allergic rhinitis approximately three quarters of patients have food co-sensitization, that may be the reason of exacerbations of allergic rhinitis after consuming vegetables, fruits and nuts due to cross-reactivity with inhalant allergens, that should be considered when manage such patients.

Introduction

Food allergy (FA) affects 1–3% of adults and 4–6% of children under 6 years. More than 160 foods can cause allergic reactions [1]. IgE-mediated food allergy is a serious human health problem affecting 1–10% of the population in developing countries, with variability depending on geographical area and age range [2]. Allergic reactions can range from mild itching to anaphylactic shock. Typically, food allergies include both IgE- and non-IgE-mediated immune disorders that occur after exposure to a food allergen. Although non-IgE-mediated food allergies correspond to pathological conditions of specific tissues, involving antigen-specific T cell responses (eg celiac disease), IgE-mediated allergies have various manifestations, including mild itching, gastrointestinal symptoms, and dangerous systemic anaphylaxis reactions.

In most cases, allergies are caused by the so-called major food allergens - "big 8": peanuts, milk, eggs, soy, wheat, fish, shellfish and nuts. These ingredients must be properly labeled in accordance with the Food and Drug Administration (FDA) [3], and the EU allergen labeling requirements provide for 14 allergens: wheat, crustaceans, eggs, fish, peanuts, soy, milk, nuts, celery, mustard, sesame seeds, lupines, mollusks, sulfites with a concentration of more than 10 mg/kg [4]. It is worth mentioning that allergens can be incorporated into food ingredients at the level of traces, provoking possible discrepancies between food content and labeling. In addition, a wide range of isoforms and posttranslational modifications (PTMs), as well as structural changes during processing can determine the allergenicity of proteins [5–7].

IgE-mediated FA affects approximately 3% of the population and has a strong impact on the daily lives of patients - the manifestations occur not only in the gastrointestinal tract, but also in other systems and organs. Studies have shown that food allergies coexist and are associated with an increase in the severity of asthma, allergic rhinitis and atopic dermatitis, which indicates that FA contributes to the chronicity and severity of allergic diseases. Eggs (2.7%), fish (1.6%), shellfish (1.3%), peanuts (1.3%) and tree nuts (1.2%) are the most commonly reported food allergens [8].

Cohort studies have shown that sensitization to food allergens develops in early childhood. The term "allergic sensitization" describes the induction of an allergic immune response at the first encounter with an allergen. There are different ways of allergic sensitization for FA. The first way (eg for milk, eggs), that is characteristic of oral allergens, in which sensitization occurs through the gastrointestinal tract. The second way (eg for the main allergen of birch pollen Bet v 1), that is characteristic of aeroallergens, in which sensitization occurs in the respiratory tract and creates the preconditions for the development of cross-reactions with homologous food allergens (eg with the main allergen of apples Mal d 1). As a result, symptoms are present in both the gastrointestinal tract and respiratory tract. The third way (so far research has been conducted only for peanuts) is percutaneous [9].

The aim of the present study was to assess the spectrum and frequency of food allergy with sensitization to different food allergens in patients with established allergic rhinitis from Kyiv, Ukraine.

Materials And Methods

Study population: participants were of both sexes, aged 18–69 years, with diagnosed allergic rhinitis. The inclusion criteria were: men and women, age 18–70 years, confirmed allergic rhinitis, no previous intake of antihistamines and glucocorticoids more than 4 weeks before participation in the investigation, a negative pregnancy test for women of reproductive age and signed informed consent. The exclusion criteria were: administration of any antihistamines and/or glucocorticoids for 4 weeks before the study, pregnancy and lactation, any acute diseases within 4 weeks before the trial, alcohol abuse, participation in other investigations.

Study design. The investigation was conducted as a cross-sectional study. A total of 175 participants with allergic rhinitis were selected to the study between the February 2021 to January 2022 on the basis of Department of clinical immunology and allergology with the section of medical genetics and

Department of internal medicine №1 of Bogomolets National Medical University, Kyiv, Ukraine. All participants were the Kyiv`s citizens.

Sensitization to allergens and their components was determined by skin prick tests (SPT) (Inmunotek, Spain) and in vitro detection of allergen specific IgE (sIgE) by ELISA in serum of the blood – multicomponent Allergy Explorer2- ALEX2 test (MacroArray Diagnostics, Vienna) allowing to detect sIgE to 295 allergens. The patient is considered sensitized to allergen in case of exceeding reference level of sIgE to at least one allergen extract or component (for example, Bet v1 in birch allergy).

Statistical analysis of the data was performed using SPSS software (version 23, IBM Corp., Armonk, NY, USA). The chi-squared test was used to determine the differences between expected frequencies. The difference was considered statistically significant at $p < 0.050$.

Results

The average age of participants was 33 years, men were 94 (53,7%), women were 81 (46,3%). It was shown, that sensitization to following inhalant allergens was predominant: to timothy grass – in 50,3% of patients, to ragweed - in 48,6%, to birch – in 44%, to wormwood – in 24%, to Alternaria alternatus mold – in 15,4% of patients (Table 1, Fig. 1).

Table 1
Sensitization to inhalant allergens.

Allergen (allergen extracts and components)	Number of patients, n	Percentage, %
Timothy grass (Phl p1, Phl p2, Phl p5.0101, Phl p6, Phl p7, Phl p12)	88	50,3
Ragweed (Amb a, Amb a1, Amb a4)	85	48,6
Birch (Bet v1, Bet v2, Bet v6)	77	44
Wormwood (Art v, Art v1, Art v3)	42	24
Alternaria alternatus mold (Alt a1, Alt a6)	27	15,4

In present study we revealed that 131 (74,9%) participants have co-sensitization to at least one food allergen, while 44 (25,1%) patients weren`t sensitized to any of the food allergens (from 154 food allergen extracts and components tested in this study). It was shown that sensitization to following food allergens was predominant: to hazelnut – in 27,5% of patients, to apple – in 26,3%, to peanut – in 21,7%, to celery – in 14,3%, to soy – in 13,1%, to fish carp – in 11,4%, to kiwi – in 9,1%, to crab – in 9,1%, to codfish – in 8,6%, to oyster – in 8,6%, to peach – in 8%, to lobster – in 8%, to carrot – in 7,4%, to anisakis – in 6,3%, to prawn – in 6,3%, to tiger prawn – in 5,7%, to beef – in 5,1%, to others – less than 5% (Table 2, Fig. 2).

Table 2
Sensitization to food allergens.

Allergen (allergen extracts and components)	Number of patients, n	Percentage, %
Hazelnut (Cor a1.0401, Cor a8, Cor a9, Cor a11, Cor a14)	48	27,4
Apple (Mal d1, Mal d2, Mal d3)	46	26,3
Peanut (Ara h1, Ara h2, Ara h3, Ara h6, Ara h8, Ara h9, Ara h15)	38	21,7
Celery (Api g1, Api g2, Api g6)	25	14,3
Soy (Gly m4, Gly m5, Gly m6, Gly m8)	23	13,1
Fish carp (Cyp c1)	20	11,4
Kiwi (Act d1, Act d2, Act d5, Act d10)	16	9,1
Crab (Chi spp.)	16	9,1
Codfish (Gad m, Gad m2 + 3, Gad m1)	15	8,6
Oyster (Ost e)	15	8,6
Peach (Pru p3)	14	8
Lobster (Hom g)	14	8
Carrot (Dau c, Dau c1)	13	7,4
Anisakis (Ani s1, Ani s3)	11	6,3
Prawn (Lit s, Pan b)	11	6,3
Tiger prawn (Pen m1, Pen m2, Pen m3, Pen m4)	10	5,7
Beef (Bos d_meat, Bos d6)	9	5,1

Additionally, to look for the possible difference between sensitization profiles of patients with only allergic rhinitis and patients with allergic rhinitis and co-sensitization to food allergens, we assessed sensitization to cross-reactive proteins, that are present in different allergen extracts and components, both inhalant and food. The following cross-reactive proteins have been assessed: PR-10 and nsLTP (Table 3). It was found that the frequency of sensitization to:

1. PR-10 was 20,5% (95% CI; 9,7%-33,9%) in patients with allergic rhinitis without sensitization to any food allergen comparing to 51,1% (95% CI; 42,5%-59,7%) in participants with both allergic rhinitis and food co-sensitization, $p < 0,001$;
2. nsLTP was 2,3% (95% CI; 0–8,9%) in patients with allergic rhinitis without sensitization to any food allergen comparing to 19,8% (95% CI; 13,4–27,2%) in participants with both allergic rhinitis and food co-sensitization, $p = 0,011$.

Table 3
The rates of sensitization to cross-reactive proteins.

Cross-reactive protein (allergen extracts and components containing such protein)	Participants with only allergic rhinitis (n = 44), n (%)	Participants with allergic rhinitis and food sensitization (n = 131), n (%)	Difference, p
PR-10 (Bet v1, Ara h8, Gly m4, Mal d1, Api g1, Dau c1, Cor a 1.0401)	9 (20,5%)	67 (51,1%)	< 0,001
nsLTP (Art v3, Ara h9, Act d10, Mal d3, Pru p3, Vit v1, Api g2, Api g6, Sola l6, Cor a8)	1 (2,3%)	26 (19,8%)	0,011

Discussion

The results of present study shown that in Kyiv adult population with allergic rhinitis the sensitization to timothy grass, ragweed, birch, wormwood and Alternaria alternatus mold was predominant and probably play causative role in development of seasonal allergic rhinitis exacerbations with corresponding clinical symptoms and features. Moreover, it was revealed in our investigation, that approximately three quarters of patients with allergic rhinitis also had co-sensitization to food allergens. The sensitization to hazelnut, apple, peanut, celery, soy, fish carp was predominant.

According to some authors, the prevalence of food sensitization among patients with allergic diseases is 37% and it does not differ significantly depending on gender or allergic disease. And the most common allergic disease among adults is allergic rhinitis – 59% [10]. It has also been shown that women are more prone to allergic rhinitis associated with food allergies than men [11].

In fact, allergic rhinitis is a rare manifestation of food allergies. It may be associated with a primary food allergy; however, it is more commonly associated with secondary food allergies, also known as pollen food syndrome (PFS). Thus, some vegetables and fruits can cause IgE-mediated food allergies (rice, citrus fruits, black lentils and bananas are identified as the main allergens that induce symptoms of allergic rhinitis), and others can cause symptoms of allergic rhinitis due to similarity in structure or homology with pollen. It has been shown that 17% of patients with pollen allergy (ie trees, weeds and grasses) may have a type I allergic reaction to certain vegetarian foods containing fruits and vegetables [11].

PFS is usually a mild type of food allergy that occurs when the mouth and throat come into contact with raw fruits or vegetables that contain epitopes that are also present in the pollen to which the subject is sensitized. Usually when these products are prepared or processed, they can be consumed without consequences in form of allergic symptoms. Common symptoms of PFS are redness, mild swelling or itching of the lips, tongue, inside of the mouth, soft palate and ears, itching and mild swelling of the throat. Sometimes people may experience symptoms in the esophagus or stomach: abdominal pain, nausea and even vomiting. Symptoms of allergic rhinitis may also include sneezing, runny nose, or, less

commonly, allergic conjunctivitis [12]. The most typical example of PFS is the development of oral symptoms when eating apples, hazelnuts, celery, and so on in patients with allergic rhinitis caused by birch pollen due to cross-reactivity. Other examples include hypersensitivity to wormwood, accompanied by symptoms after eating vegetables such as cabbage, cumin, parsley, coriander, anise and carrots, as well as some spices such as anise, pepper, black pepper, onion, garlic, cauliflower and broccoli. Maple pollen, hazelnut, peanut, fruits such as kiwis and peaches, and vegetables such as corn and lettuce, provoke allergic rhinitis symptoms in sensitive people after ingestion. Hypersensitivity to herbs and their classes, as well as their homology with other fruits, has not been studied in detail, but people who are sensitive to herbs are also sensitive to foods such as potatoes, melons, oranges, tomatoes and peanuts [11]. The most common triggers of PFS in adults are apples (21.1%), carrots (15.5%) and peaches (15.5%) [13]. In our present investigation we have compared the rates of sensitization to cross-reactive proteins PR-10 (containing in birch pollen, peanut, soy, apple, celery, carrot and hazelnut) and nsLTP (containing in wormwood, peanut, kiwi, apple, peach, grape, celery, tomato and hazelnut) in patients with only allergic rhinitis and patients with allergic rhinitis and co-sensitization to food allergens. We have revealed that rates of sensitization to PR-10 and nsLTP were significantly higher in patients with both allergic rhinitis and co-sensitization to food allergens comparing to patients with only allergic rhinitis. It should be noticed that these cross-reactive proteins are containing only in several allergen extracts and/or components of the allergen. So, patient may have allergy to birch, but may not have the sensitization to PR-10 protein, because it is included only in Bet v1 component of birch allergen. And this is why some patients may suffer from allergic rhinitis caused by birch and also have its exacerbations after consuming an apple (cross-reactive allergy due to presence of PR-10 in Bet v1 of birch and Mal d1 of apple), but other patients with birch allergy may eat apples without any consequences. So, such cross-reactive proteins may play role as a one of the causes of allergic rhinitis exacerbations and trigger symptoms after consuming some foods in patients with co-sensitization to several food allergens.

Conclusions

In Kyiv adult population with allergic rhinitis approximately three quarters of patients have co-sensitization to at least one food allergen. The higher rates of sensitization to cross-reactive proteins (presented in both inhalant and food allergens) were in patients with allergic rhinitis and food co-sensitization. So, presence of additional sensitization to several food allergens may be the reason of development of symptoms and features of allergic rhinitis after consuming vegetables, fruits and nuts due to cross-reactivity with inhalant allergens, that should be considered by the physicians when manage and treat the patients with allergic rhinitis.

Declarations

Ethics approval and consent to participate. Present clinical trial was performed in accordance with the Ukrainian laws, the requirements of Good Clinical Practice, and ethical principles of the Declaration of Helsinki. Written informed consent for participation in the study was obtained from all participants before

beginning of investigation. The trial`s protocol was approved by the Bioethical Committee of Bogomolets National Medical University, Kyiv, Ukraine.

Consent for publication. Not applicable.

Availability of data and materials. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests. The authors declare that they have no competing interests**.**

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Author`s contribution. TV, NA and KA: concept and design of investigation; TV, NA: assessment of the patients, collecting the data; TV, NA, KA: analyzation and interpretation of the results; TV, NA: statistical analysis, writing the text of the manuscript; TV, NA, KA: critical revising of the article, approving the final version of the manuscript.

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Figures

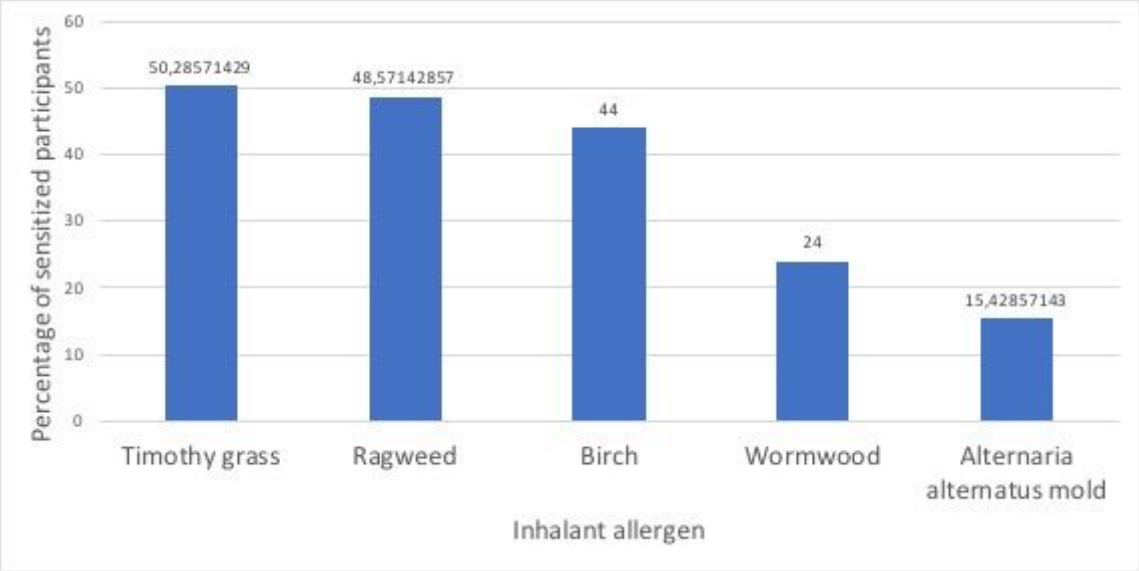

Figure 1

Frequency of sensitization to inhalant allergens.

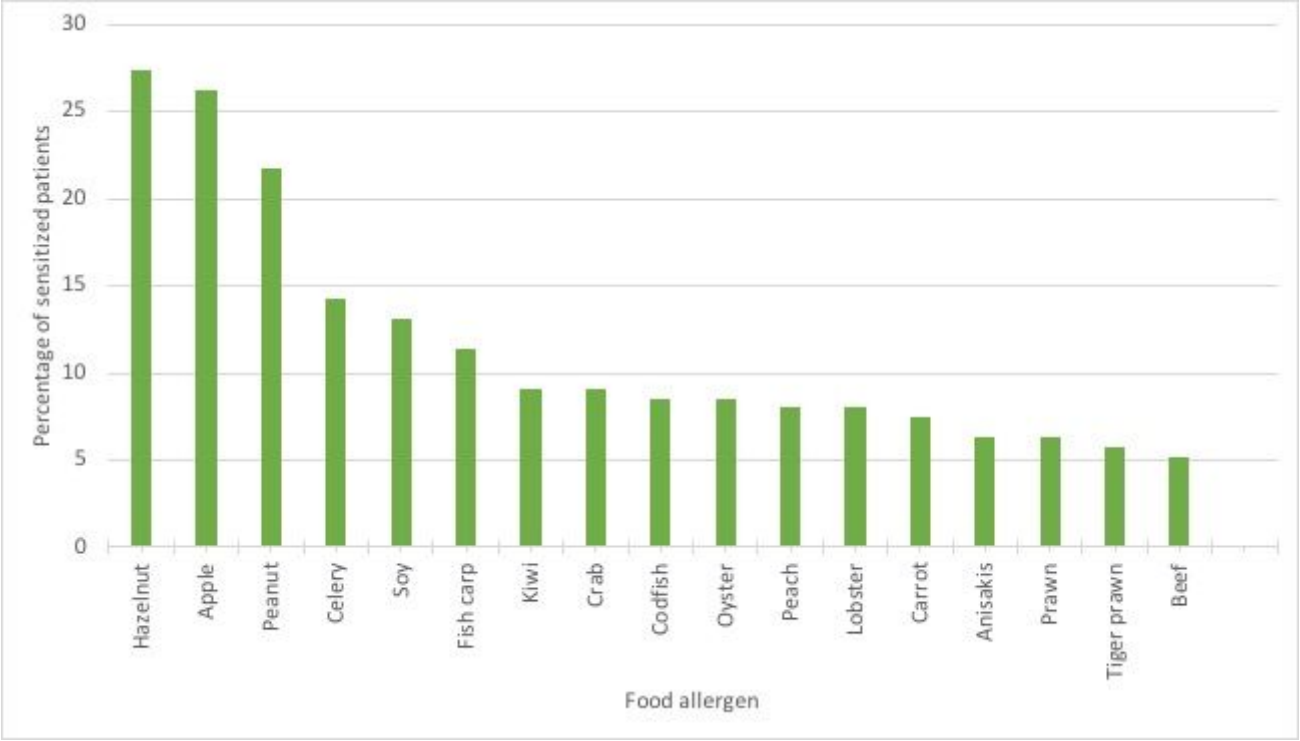

Figure 2

Frequency of sensitization to food allergens.