

Epidemiological survey of pediatric food allergy in Mashhad in Northeast Iran

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Abstract

Introduction: Food allergy is an increasing problem worldwide, but the foods responsible for food allergy are not the same in different countries, probably because of the role of genetic, cultural, and nutritional factors. The aim of this study was to determine the common food allergens in pediatric patients with different presentation of food allergy.

Methods: In this cross-sectional study, all of the patients were referred to pediatric allergy clinics affiliated with Mashhad University of Medical Sciences from September 2012 to August 2014. For patients with IgE-mediated food allergy that was diagnosed with clinical manifestations, the skin prick test was done. The results were analyzed by SPSS version 17 and statistical analysis was done with the chi-squared test and the t-test. P values < 0.05 were considered statistically significant.

Results: Three hundred seventy-one patients (53.9% male, 46.1% female) with ages in the range of three months to 18 years were studied. The most frequent food allergen in all patients with decreasing prevalence were egg white (17.8%), pepper (15.8%), curry (14.3%), egg yolk (14%), cow's milk (10%), and tomato (7.8%). The most common presenting symptoms were respiratory (allergic rhinitis 45%, asthma 32%), dermatologic (atopic dermatitis 30%, urticaria 8.3%), colitis (17.5%), and gastroesophageal reflux disease (GERD) (2%). According to the prevalence of food allergens in different age groups, we realized that, after the age of three years, the frequency of sensitization to egg white, egg yolk, cow's milk, wheat and cereals was decreased and allergy to pepper and curry was increased.

Conclusion: The prevalence of culprit foods that produce food allergies depends on several factors, including age, presenting manifestation, and where the patient lives. As many food allergies are outgrown, patients should be reevaluated regularly to determine whether they have lost their reactivity or not.

Keywords: food allergy, food allergen, pediatrics, skin prick test, Iran

1. Introduction

Food allergy is an increasing problem worldwide, affecting about 6% of children and 2% of adults (1). The prevalence of food allergy as well as other allergic diseases has risen in the last few decades (2). Allergen avoidance is one of key components in the management of allergies (3). Recognition of common food allergens in each

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geographical region is valuable for physicians to be able to remove only culprit allergens from the diet for a limited period of time. In the United States, the most common food allergens are cow's milk and eggs, while the most common allergens in Europe and Middle East countries are fruits and eggs, respectively (1-5). The most common food allergens among Iranian children with allergy (asthma, allergic rhinitis, atopic dermatitis, and urticaria) that were established with the prick test, were milk, eggs, and wheat flour, respectively (6). Furthermore, the most current cause of anaphylaxis in Iranian children was food (89.7%), with milk and wheat being the most common (7). Because, anaphylaxis is a life-threatening condition, identifying foods that cause this condition is very important (8). True identification and elimination of foods responsible for food allergy are better management approaches for food hypersensitivity reactions. Complete avoidance of common foods (egg, wheat, milk, soy, fish, and peanut) is not possible. Skin prick tests (SPT) are useful for demonstrating the foods responsible for IgE-mediated reactions, but there are no definite laboratory studies to help identify cell-mediated responses (3, 4). Elimination diets followed by food challenges can determine the foods responsible for cell-mediated food allergies (9). The purpose of this study was to determine the most common food allergens in children with various allergic symptoms, including atopic dermatitis, allergic rhinitis, asthma, anaphylaxis, and digestive problems in Mashhad, Iran. In Iran, we need further studies that demonstrate the overall prevalence of food allergies and the rate of hospital admissions for food-induced anaphylaxis - the most severe expression of food allergy.

2. Material and Methods

2.1. Research design

Three hundred and seventy-one patients with cutaneous (atopic dermatitis and urticaria), respiratory (asthma and allergic rhinitis) or gastrointestinal (diarrhea, vomiting, colitis) manifestations, who were referred to the Pediatric Allergy and Gastroenterology Clinics affiliated with Mashhad University of Medical Sciences from September 2012 to August 2014 were investigated for food allergies. Detailed histories were taken from all patients, and all had physical examinations. For IgE-mediated disorders, the allergy skin prick test (SPT) and for cell-mediated disorders exclusion diets, food challenge, and endoscopic examination were performed in addition to SPT.

2.2. Sampling

We determined the sample size from previous investigations of food allergies. We also scaled up the results to give the estimated number of patients with recorded diagnoses of food allergies in Iran.

2.3. Data collection and ethics

This study was approved by human ethics protocols with informed written consent from each patient (4). Also, the study was approved by the Ethics Committee of the Medical School at the Mashhad University of Medical Sciences. All participants were inhabitants of Khorasan Province in northeastern Iran. The age of the subjects ranged from three months to 18 years. All patients underwent routine allergy diagnosis tests, including clinical history, physical examination, and the skin prick test (SPT). A detailed checklist was completed by each participant to explain her or his symptoms. The skin prick test was done based on standard procedures, using purified allergen extracts with negative and positive controls being normal saline and histamine, respectively (10 mg/ml), as mentioned above. The extracts were placed on the volar surface of the forearm and subsequently introduced into the epidermis using a disposable hypodermic needle. The results were measured in 15 minutes. Data were excluded if the wheal reaction of negative control (saline) was larger than 2mm and the wheal reaction of positive control (histamine) was less than 3mm. A reaction was considered positive if the resulting wheal was at least 3mm larger than the negative control.

2.4. Statistical analyses

The results were analyzed by SPSS version 17 (New York, NY, USA), and statistical analysis was done with the chi-squared test and t-test. P values < 0.05 were considered statistically significant. The values of the quantitative variables were checked by the Kolmogorov-Smirnov test for normal distribution. Results with normal distribution were analyzed by parametric ANOVA or Student's t-test. Non-parametric Mann-Whitney and Kruskal-Wallis tests also were used for assessment of results with non-normal distributions.

3. Results

This study was performed on 371 patients 53.9% of whom were males and 46.1% were females. Patients younger than 2 accounted for 35.8% of the patients, while 34.6% were 2 to 7, 22.7% were 8 to 12, and 6.9% were 13-18. The mean age was 5.34. The most common presenting symptoms in our patients were allergic rhinitis (45%), asthma (32%), atopic dermatitis (30%), colitis (17.5%), and urticaria (8.3%). The presenting symptoms with lower

incidence were anaphylaxis (2%), GERD (2%), and recurrent infection (0.5%). In all studied patients, the most common foods responsible for food allergy were egg white (17.8%), pepper (15.8%), curry (14.3%), egg yolk (14%), cow's milk (10%), and tomato (7.8%). The less common food allergens in our study were cocoa (5%), orange (4.7%), peanut (4%), banana (4%), cereals (4%), soya (3.7%), grape (3.7%), almond (3.5%), wheat (3%), fish (2.8%), sesame (1.5%), and meat (0.7%). In our study, egg white, egg yolk, and cow's milk were the most common food allergens in patients younger than 2 and, as the child aged, the allergies were mostly outgrown and their frequency decreased. In patients older than 2, pepper and curry were the most common food allergens (Table 1). In this study we realized that the most common food allergens in patients with respiratory symptoms were pepper and curry, in patients with gastrointestinal manifestations, it was cow's milk, and in patients with skin problems, they were egg white and egg yolk (Table 2).

Table 1. Frequency of food responsible for food allergy according to the age

| Food allergens | Age groups, n (%) | | | |
|----------------|-------------------|------------|------------|-------------|
| | <2 years | 2-7 years | 7-12 years | 12-18 years |
| Egg white | 64 (48.1%) | 13 (10%) | 4 (4.7%) | 0 |
| Pepper | 12 (9%) | 25 (19.5%) | 10 (12%) | 8 (31.2%) |
| Curry | 9 (6.7%) | 20 (15.6%) | 8 (9.5%) | 5 (19.5%) |
| Egg yolk | 49 (36.9%) | 10 (7.8%) | 3 (3.5%) | 0 |
| Cow 's milk | 42 (31.6%) | 5 (3.9%) | 0 | 0 |
| Tomato | 7 (5.3%) | 7 (5.4%) | 6 (7.1%) | 3 (11.7%) |
| Cacao | 3 (2.2%) | 5 (3.9%) | 6 (7.1%) | 1 (3.9%) |
| Orange | 6 (4.5%) | 7 (5.4%) | 0 | 0 |
| Banana | 7 (5.3%) | 5 (3.9%) | 2 (2.4%) | 0 |
| Peanuts | 6 (4.5%) | 7 (5.4%) | 2 (2.4%) | 0 |
| Cereals | 12 (9%) | 0 | 3 (3.5%) | 0 |
| Soya | 7 (5.3%) | 4 (3.1%) | 0 | 2 (7.8%) |
| Grape | 1 (0.75%) | 4 (3.1%) | 5 (6%) | 2 (7.8%) |
| Nuts | 7 (5.3%) | 5 (3.9%) | 1 (1.2%) | 0 |
| Wheat | 6 (4.5%) | 2 (1.5%) | 0 | 0 |
| Fish | 0 | 4 (3.1%) | 4 (4.7%) | 0 |
| Sesame | 0 | 0 | 3 (3.5%) | 0 |
| Meats | 0 | 0 | 0 | 0 |

Table 2. Frequency of food responsible for food allergy according to the symptoms

| Food allergens | Symptoms, n (%) | | | |
|----------------|----------------------|---------------------------|---------------|-------------|
| | Respiratory symptoms | Gastrointestinal symptoms | Skin symptoms | Anaphylaxis |
| Egg white | 6 (2.1%) | 19 (26.4%) | 57 (39.5%) | 1 (5.2%) |
| Pepper | 45 (16%) | 10 (13.8%) | 17 (11.8%) | 1 (5.2%) |
| Curry | 48 (17%) | 10 (13.8%) | 10 (6.9%) | 3 (15.8%) |
| Egg yolk | 8 (2.8%) | 16 (22.2%) | 44 (30.5%) | 0 |
| Cow's milk | 3 (1%) | 43 (59.7%) | 29 (20.1%) | 1 (5.2%) |
| Tomato | 19 (6.7%) | 7 (9.7%) | 11 (7.6%) | 1 (5.2%) |
| Cacao | 17 (6%) | 0 | 6 (4.1%) | 2 (10.5%) |
| Orange | 15 (5.3%) | 2 (2.7%) | 3 (2%) | 0 |
| Banana | 11 (3.9%) | 9 (12.5%) | 7 (4.8%) | 0 |
| Peanuts | 9 (3.2%) | 2 (2.7%) | 7 (4.8%) | 1 (5.2%) |
| Cereals | 3 (1%) | 8 (11.1%) | 3 (2%) | 2 (10.5%) |
| Soya | 4 (1.4%) | 4 (5.5%) | 7 (4.8%) | 1 (5.2%) |
| Grape | 14 (5%) | 4 (5.5%) | 1 (0.7%) | 0 |
| Nuts | 3 (1%) | 7 (9.7%) | 11 (7.6%) | 0 |
| Wheat | 1 (0.3%) | 2 (2.7%) | 7 (4.8%) | 2 (10.5%) |
| Fish | 3 (1%) | 6 (8.3%) | 3 (2%) | 1 (5.2%) |
| Sesame | 3 (1%) | 0 | 3 (2%) | 1 (5.2%) |
| Meats | 0 | 0 | 3 (2%) | 0 |

4. Discussion

This study demonstrated that the most common food allergens in 371 patients who were referred to pediatric allergy clinics in Mashhad were egg white, pepper, curry, egg yolk, cow's milk, and tomato. However, other studies in another countries and in another geographical region in Iran had different results. In our study in Mashhad, the most common food allergen was egg white with the highest frequency among the children younger than 2 (48.1%). In research that was done by Pourpak in Tehran, cow's milk was the most common food allergen in almost all cases for children less than one year old (10). In contrast, Mukoyama identified egg, cow's milk, and wheat as the top three food allergens among children under the age of six in Japan. He reported that, when the child grows up, this list was changed to fish, shrimp, and black wheat (11). Alvarado discovered that fruits (54.2%), nuts (20%), and fish (14.35%) were the most common food allergens in Spanish children (12). Marrugo concurred with Alvarado in sensitization rate for fruits with 14.9% as the main trigger, but he ranked marine food and meat as the second and third most-common food allergens in Colombia (13). Rivas partially concurred with us, as egg was his top allergen in children under five years of age. (Ours was egg white.) Yet, his findings were compatible with Marrugo, ranking fruits and nuts at the top in the population older than five (14). Al-Hammadi also indicated that egg, fruits, and fish were the three top allergens in Asian children based on his findings. This list was followed by peanut, nuts, cow's milk, wheat, and vegetables (15). However, Kavaliunas blamed fruits, marine food, and milk (and dairy products) for the advent of food allergy in European children, in agreement with Alvarado and Marrugo's top allergy triggers (16).

Our second most-common food allergen was pepper, with 43 children between 2 to 18 years old affected. It was followed by curry with 33 children in the same age group. Pourpak found that tomato (36 children with 28.1% between 6 and 12 years old), egg white (28 children with 37.5% < 1 year old), and egg yolk (24 children with 33.3% < 1 year old) were placed in declining order of second, third, and fourth common food allergens (10).

The foods responsible for food allergy are different in the various countries because of the probable role of genetic, cultural, and nutritional factors. Food allergens are different in any age groups. In our study, compatible with another studies, the children outgrew their sensitivity to egg white, egg yolk, and cow's milk, while these are the most food allergens in children younger than 2. After children are 2 years old, the frequency of allergy to pepper, curry, cacao, and tomato increases slowly. These results occurred because, often, food allergies are not manifested to egg and milk until after 5 years of age (3).

In this study, 77% of patients who were referred to allergy clinics had asthma or allergic rhinitis. Their skin prick tests were positive for at-least one food allergen. The most common food allergens in this group were curry, pepper, tomato, cacao, orange, and grape. In these patients, the most common aeroallergen was *Salsola kali*. We know that cross reaction between allergen of *Salsola kali* (profiling) and fruit proteins in grape and melon, many children with this allergy show oral allergy syndrome after eating these fruits (17,18). Oral allergy syndrome is an IgE-mediated hypersensitivity that usually is confined to the oropharynx and consist of the rapid onset of oral pruritus, tingling of the lips, tongue, palate, and throat. Symptoms are generally short lived (3). In 30-40% of children with moderate to severe atopic dermatitis, food allergies occur. The skin prick test can help us to determine which food was responsible, and this test was sensitive, cheap, and available. Among our patients, 30% came with atopic dermatitis, and, in them, the most common food allergens were egg white, egg yolk, cow's milk, pepper, and tomato. This result is appropriate to other studies that were done in the past, such as in the study of Salehi in which the most common food allergens in children with atopic dermatitis were egg (39.22%) in < 2 years old, cow's milk (35.13%) and egg (32.43%) in children who were 2 to 6 years old, and peanut (25%) and egg (16.67%) in children older than 6 years old. Therefore, the prevalence of egg allergy is highly significant in patients with atopic dermatitis in Salehi's research in Tehran (19). Bergmann shows cow's milk, hen's egg, peanut, wheat, soy, nuts, and fish are responsible for > 90% of food allergies in children with atopic dermatitis (20). In Kim's research, the most common foods causing food hypersensitivity were egg and milk in patients with atopic dermatitis in Korea (21). Kwon confirmed the most-common food allergens in atopic dermatitis patients were egg and milk (22).

Gastrointestinal manifestations in our patients were colitis, abdominal pain, early satiety, and poor weight gain. In our study, the most common food allergens in patients with gastrointestinal manifestations were cow's milk, egg white, egg yolk, pepper, curry, cereals, and banana. In the last studies, sensitivity to cow's milk was the most common cause of food allergy in young infants, but it also has been associated with hypersensitivity to soya, egg, wheat, rice, chicken, and fish in older children (3). Cell-mediated hypersensitivities predominate (e.g.

gastrointestinal problems), making the standard prick skin test of little diagnostic value; therefore, challenge tests should be done to determine the foods responsible for these symptoms.

5. Conclusions

The prevalence of culprit foods that produce food allergies depends of several factors, including age, presenting manifestation, and where the patient lives. Since many food allergies are outgrown, patients should be reevaluated regularly to determine whether they have lost their reactivity to specific food allergens. Future studies must be designed rigorously using standardized methodology, including DBPCFC, to limit the potential sources of bias that could weaken the estimates of food allergies, and more high-quality studies are needed in other regions of Iran so that the results can be compared.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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