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ORIGINAL ARTICLE PEDIATRICS

Evaluation of clinical and demographic features of childhood food allergy: A single-center experience

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ABSTRACT

OBJECTIVE: Current evaluations of pediatric food allergies are very important, many studies have shown that the frequency of food allergies is increasing in the pediatric age group. In this study, we retrospectively investigated the epidemiology and clinical features to better understand the clinical effects of food allergy, to contribute to the literature on this subject, and to evaluate the data of our country.

METHODS: The epidemiological and clinical data of patients with food allergies diagnosed at the Erciyes University Pediatric Allergy Outpatient Clinic between 2014 and 2019 were analyzed. The outcomes were analyzed by a statistical analyzing program and compared with the literature.

RESULTS: As a result of our retrospective evaluation, we found that the mean age of 854 patients who were diagnosed with food allergy was 21.2±30.7 months (min 0 months, max 16.5 years). 512 (60%) of our patients were female, and 342 (40%) were male. The most common complaint was rash at the rate of 75.2% and followed by itching 27.6%, angioedema 10.5%, bloody defecation 10.5%, wheezing 8.4%, vomiting 8.3%, diarrhea 6.7%, frequent bronchiolitis 6.6%, cough 6.2%, and shortness of breath 4.4%. It was shown that 32.2% of the patient had multiple food allergies and the highest sensitivity rates were 65.9% with egg allergies and 39.2% with milk. In the classification, it was found that 75.1% of the patients who were followed up with food allergy had IgE-mediated food allergy, and 24.9% had a non-IgE-mediated food allergy.

CONCLUSION: The results of this study of a 5-year cross-sectional evaluation of the patients diagnosed with food allergy and followed up in our clinic may contribute to the growing body of literature on pediatric-age food allergy.

Keywords: Food allergy; IgE-mediated food allergy; Non-IgE food allergy; rash.

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Food allergy is the sum of the effects that develop after exposure to certain foods and re-occur at each exposure due to the immunological response of the individual [1, 2]. Although reactions to all kinds of foods can be seen, the most common food allergies are against cow's milk, eggs, nuts, soy, fish, and seafood. Food allergy, which is common in society, is an important public health problem.

In medical literature, the rate of food allergy based on individual responses varies between 3% and 35%, while an incidence of 1–10.8% has been proven by double-blind and placebo-controlled food challenges [2, 3]. In the United States, the prevalence of food allergy in children aged 1–5 and 6–19 years is 4.2% and 3.8%, respectively [4]. In studies from Turkey, it has been reported that the frequencies of food allergy were 0.8% in the 6–9-year-old age group in the Black Sea region, 2.4% in infants in Adana, and 7.7% in children attending nursery and kindergarten in Samsun [5–7]. In the present study, we presented a 5-year experience of pediatric food allergy at a single center.

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MATERIALS AND METHODS

This retrospective observational study was conducted by evaluating the files of 854 patients who were followed up with the diagnosis of food allergy in Erciyes University Faculty of Medicine Pediatric Allergy Outpatient Clinic between 2014 and 2019. The diagnosis of food allergy was achieved through clinical evaluation and skin prick tests. In addition, food challenge tests and serum-specific IgE (sIgE) analysis were performed in patients deemed necessary. The study was conducted with the approval of the Erciyes University Clinical Research Ethics committee with 2020/287 number on June 10, 2020. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed with a statistical software package (SPSS Inc. Released 2019), PASW Statistics for Windows, Version 26.0. New York, USA. The descriptive statistics of data were determined using mean, standard deviation, median, minimum and maximum, frequency, and ratio values. Categorical variables were summarized as numbers and percentages. The data normality was assessed using histogram and Shapiro–Wilk's test. To compare the differences among groups, a one-way analysis of variance was applied for quantitative data, and Chi-square test was applied for qualitative data. Bonferroni-adjusted z-tests were used for multiple comparisons. Data values were expressed using mean±standard deviation or median. Analyses were conducted using SPSS 26.0 statistical data analysis program. A $p<0.05$ was considered statistically significant.

Highlight key points

- Current evaluations about pediatric food allergies are crucial due to their effect on the quality of life of the patient and have shown that their frequency is increasing in many studies.
- A five-year experience of pediatric food allergy at a single center in Turkiye was presented.
- The clinical significance of diagnostic tests in food allergies exists only when evaluated together with the clinical presentation. For these reason, diagnosis of food allergy need to be performed thoroughly physical examination, taken detailed personal and family medical history and confirmed with diagnostic tests.

Table 1. Age and gender distribution of patients with food allergy

	Min–Max	Median	Mean±SD/n–%
Age (month)	0.0–199.0 (16.5y)	10.0	21.2±30.7
Sex			
Male			512±60.0%
Female			342±40.0%

Min: Minimum; Max: Maximum; SD: Standard deviation.

Table 2. There is no significant difference in gender between age groups

Age group	Male	Female	Total
0–23 m	393	281	674
24–71 m	83	40	123
6–18 year	36	21	57
Total	512	342	854

Chi-square test was used to compare the groups.

RESULTS

Erciyes University Pediatric Allergy Outpatient Clinic had 854 cases diagnosed with food allergy among 33.610 applications to clinic between 2014 and 2019. Food allergy was the initial diagnosis in 2.5% of outpatients. The mean age of the patients was 21.2±30.7 months. The youngest patient was less than a month old, and the oldest was 16.5 years old. The age distribution of the patients is given in Table 1. The numbers of male and female patients were 512 (60%) and 342 (40%), respectively. No significant difference in gender was present among age groups (Table 2).

The family history was scanned for any allergies, seasonal allergic rhinitis (SAR), and asthma. It was observed that 5.4% of the patients had a history of allergy in their mothers, 3% in their fathers, and 3.5% in their siblings. SAR was detected in the mother, father, and siblings of 6.1%, 5%, and 2.1% of the cases, respectively, while the asthma history was present in the mother, father, and siblings of 5.9%, 2.8%, and 3.6% of the cases, respectively.

It was observed that 32.2% of the patients had multiple food allergies. The most common allergy was against egg, with a rate of 65.9%. Milk allergy was determined in 39.2%, hazelnut in 12.5%, peanut in 8.4%, wheat in 6%, fish in 2.6%, soybean in 2.6%, sesame in 1.6%, and walnut in 1.5% of the patients. Less than 1% sensitivity was found against lentils, kiwi, banana, pistachio, potato,

Table 3. Evaluation of presenting symptoms of children diagnosed with food allergy

	n	%
Rash	642	75.2
Itching	236	27.6
Angioedema	90	10.5
Bloody stool	90	10.5
Vomiting	88	10.3
Wheezing	72	8.4
Mucus in stool	69	8.1
Diarrhea	57	6.7
Frequent bronchiolitis	56	6.6
Cough	53	6.2
Shortness of breath	38	4.4
Growth retardation/inability to gain weight	22	2.6
Rhinitis	19	2.2
Hyperemia around the mouth	13	1.5
Irritability	11	1.3
Nasal congestion	7	0.8
Sneeze	6	0.7
Conjunctivitis	4	0.5
Food rejection	4	0.5
Eosinophilia	2	0.2
Constipation	4	0.5
Nutritional problems	3	0.4
Abdominal pain	2	0.2
Bloatedness	2	0.2
Cyanosis	1	0.1
The feeling of being caught in the throat	1	0.1

chickpeas, chicken, and honey. Sensitivity to cocoa, sunflower seeds, beans, coconut, apricot, cherry, cinnamon, tomato, green pepper, eggplant, meat, strawberry, rice, and peas were detected in single cases (0.1%). None of the patients showed sensitivity to shellfish.

When the complaints of the patients were evaluated, the rash was observed as the most common complaint. In 84.9% of the allergic children with skin findings, atopic dermatitis, urticaria, and angioedema were observed in 58.4%, 20.4%, and 9.3% of them, respectively. It was determined that bloody and mucous stool complaints were often found together, as miscellaneous respiratory system symptoms that presented together. The presenting symptoms are given in Table 3.

Almost all of the patients were evaluated by complete blood count, and the mean eosinophil count was

Table 4. Significantly high eosinophil levels in the first 2 years of life

	Mean	SD	SE	Significance
0–23 m	610.4	673.519	26.337	0.014/0.005
24–71 m	431.2	399.520	37.255	0.014/0.98
6–18 year	328.6	326.749	45.312	0.005/0.98
Total	567.4	630.685	22.011	

SD: Standard deviation; SE: Standard error. To compare the differences among groups, a one-way analysis of variance (ANOVA) was applied, and Bonferroni-adjusted z-tests were used for multiple comparisons.

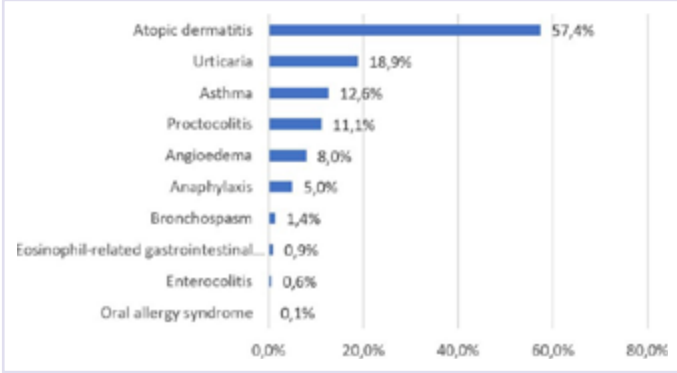

Figure 1. Classification of patients who are followed up with food allergy.

found to be 567.5±630.7. The percentage of eosinophils in the patients was evaluated as an average of 5.3±4.2%, the highest and lowest values were 40–0%, respectively. Children with food allergies were shown to have higher eosinophil counts in the first 2 years of life compared to other age groups (Table 4). The mean total IgE value was 392.8±703.1 IU/mL.

The patients were classified as IgE-mediated food allergies (19.8%), mixed-type food allergy (73.2%), and non-IgE-mediated food allergy (7%) (Fig. 1).

The prick test was positive in 75.1% of the patients. The rate of patients positive for one, two, three, four, five, and six agent(s) was 34.2%, 24.8%, 11.4%, 3.9%, 0.7%, and 0.1%, respectively (Fig. 2) Atopy patch test was used for patients with a negative prick skin test. The rates of patients positive for egg yolk, egg white, milk, wheat, soybean, and sesame were 17.4%, 11.9%, 6.4%, 2.5%, 1.2%, and 0.1%, respectively. High positivity (+3 or +4) on the atopy patch test was observed only in patients with egg sensitivity.

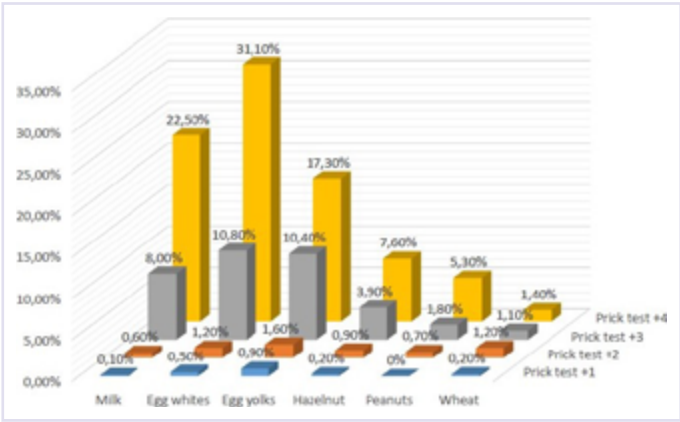

FIGURE 2. Evaluation of foods resulted positive through prick test.

Determination of food-sIgE levels in serum was performed in selected patients. sIgE levels were positive for milk in 3.9%, egg white in 2.1%, egg yolk in 1.3%, wheat in 0.6%, peanut in 0.4%, hazelnut in 0.4% and soybean in 0.1% of the patients.

The patients, who were evaluated as atopic by skin test, were classified as IgE-mediated (75.1%), while the ones negative for atopy as non-IgE mediated (24.9%). 71% of 563 patients followed up with egg allergy were IgE mediated, and 29% had non-IgE food allergy while 81% of 335 patients followed up with milk allergy were IgE mediated, and 19% had a non-IgE food allergy. All the patients who were followed up with hazelnut allergy, peanut allergy, and walnut allergy had IgE-mediated food allergies. The patients evaluated with atopy patch test were diagnosed with atopic dermatitis (62%), proctocolitis (22%), urticaria (10%), eosinophilic esophagitis (2%), and enterocolitis (2%).

When the patients were classified according to their presentation complaints and diagnoses, 20.8% of the patients who presented with rash were IgE mediated, 77.7% mixed, 1.5% non-IgE-mediated food allergy while 59.1% of the patients presented with angioedema were IgE mediated, 39.8% mixed, and 1% non-IgE-mediated food allergy. It was found that 2.3% of the patients who presented with bloody stools were IgE mediated, 49.4% mixed, and 48.3% were non-IgE-mediated food allergies.

DISCUSSION

Food allergy is an important health problem as it is frequently encountered in children and disrupts the quality of life [8]. Since food allergies usually start in the first 2 years of life when nutrition is very important for growth and development, it is critical to diagnose food allergies early and to follow up children with food allergies properly. Food allergy prevalence was found to be 8% in the pediatric age group, and severe reactions were reported in 38.7% of those cases [9]. Food allergies have been shown to be responsible for more than half of anaphylactic reactions in developed countries [10, 11]. In literature, no statistically significant difference was shown between prevalence and gender in epidemiological studies conducted on children with food allergy [5, 12].

Milk, eggs, peanuts, shelled tree nuts, fish, shellfish, soy, and wheat were shown to be responsible for 90% of the food allergy [13, 14]. Gupta et al. [9] showed that 30.4% of pediatric patients diagnosed with food allergy had multiple food allergies. In the present study, similar to the literature, it was shown that 32.2% of the pediatric patients had multiple food allergies. Unlike the literature results, egg was the most common food allergy and was shown the responsible allergen in 65.9% of the patients in the present study. For example, a study from Norway reported the incidence of egg allergy as 4.4% in children younger than 2 years [15]. In another study, Nwaru et al. [16] showed that the lifetime rate of egg allergy was 2.5%. Bayram reported that 26% of the patients aged 0–1 years in their study had egg allergy [12].

In our study, we demonstrated that 39.2% of the patients had milk sensitivity. Gupta et al. [9] reported that 21.1% of food allergy cases aged between 1 and 18 years were due to milk. Bayram found that milk allergy was present in 26% of the studied patients aged 0–1 years, in 19% aged 2–4 years, in 9% aged 4–7 years, and in 4% aged 8–14 years [12]. In Europe, the incidence of milk allergy under the age of 2 had been reported to be 0.54%, as confirmed by food challenge test [17].

In our study, 8.4% of the patients were diagnosed with peanut allergies. Gupta et al. [9] reported a rate of 25.2% peanut allergy as the most common cause of food allergy in patients between the ages of 1 and 18 years. Reaction to peanuts and other oily seeds was reported with a frequency of 1.1% in the United States, and around 3 million Americans were thought to be allergic to peanuts and/or seeds [18].

Fish protein that is a strong allergen for both children and adults, is among the most common foods that cause adverse reactions [19]. In our study, fish allergy was detected in only 2.6%, and no sensitivity to shellfish was found among those diagnosed with food allergy. Eggesbø et al.

[15] reported the frequency of fish allergy as 3% based on family statements. Gupta et al. [9] showed that 17.2% in the pediatric age group had a food allergy to shellfish. In a study conducted on the Turkish coastline, 2.5% of children with food allergy symptoms had shellfish and fish sensitivity [12]. In the present study, unlike the literature, the rate of fish allergy was lower than the previous results of studies conducted in different countries. This difference can be interpreted as the nutritional culture and local differences among countries. It has been shown that the fish consumption rates in Turkey were far below the world average, even though the country is a peninsula [20].

Although food allergies can present with different complaints, the most common complaint is the presence of a rash. Food allergy has been considered to be responsible for 20% of acute urticaria cases [21, 22]. In this study, 58.4% of the patients had atopic dermatitis, 20.4% urticaria, and 9.3% had angioedema findings. Branum and Lukacs reported that 27% of children with food allergies had atopic eczema or allergic skin findings and that rate was 8% in those without food allergy [23]. In our study, 75.2% of the patients had a rash, followed by itching with a rate of 27.6%. We suspect that itching might have been a less questioned complaint in addition to a difficult-to-express complaint in the pediatric age group, as the rate of itching was lower than the rash.

Asthma and seasonal allergy symptoms are more common in children with food allergies. However, isolated asthma and rhinoconjunctivitis due to food allergy were rare [24]. Food allergy-related rhinoconjunctivitis was not found in any patient in this study. Otherwise, the rate of asthma in children with food allergies was 12.6%. Branum and Lukacs showed that 29% of pediatric patients with food allergies had asthma, while it was 12% in those without food allergies [23]. Branum and Lukacs [23] also found respiratory symptoms in 30% of the children with food allergy while the rate was 9% in the group without food allergy.

Many patients with food allergies experience gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhea, etc.) [25]. In this study, gastrointestinal complaints were bloody stool in 10.5%, vomiting in 10.3%, diarrhea in 6.7%, food refusal in 0.4%, and throat discomfort with a sensation of stuck food in 0.1% of the patients.

Food allergy is one of the leading causes of out-of-hospital anaphylactic triggers in children and young adults [26]. In the literature, the incidence of food-induced fatal anaphylaxis in people with food allergies aged 0–19 years was estimated to be 3.25 per million [27]. Exercise is known to increase the severity of anaphylaxis by lowering its threshold [28]. In this study, anaphylaxis was observed in 43 patients (5%). None of the patients neither deceased due to anaphylaxis nor had exercise-induced anaphylaxis.

The clinical significance of diagnostic tests in food allergies exists only when evaluated together with the clinical presentation. In this study, 75.1% of the skin prick tests of the patients with food allergies were positive. Besides being very successful in showing IgE-mediated reactions, skin prick tests should be evaluated together with the clinical assessment. It is known that the sensitivity of the skin prick test is 90%, and the specificity is around 50% [29]. Kekki et al. [30] compared the skin prick test with the atopy patch test and showed that skin prick test positivity was associated with a high level of food-sIgE and early type reaction, while the total IgE levels were higher in those patients. It is known that prick test positivity is more frequently found in early-type reactions in patients followed up for food allergy, and patch test positivity is higher in late-type reactions [30]. Food allergies are classified by being IgE mediated and not IgE mediated [31]. In the classification, it was found that 75.1% of the patients who were followed up for food allergy had IgE-mediated food allergy, and 24.9% had a non-IgE-mediated food allergy.

Conclusion

Food allergy, which is a relatively common condition in children, is an important issue in pediatrics, considering the important effects on the quality of life of children and their families, as well as the economic burden on public health. Based on those consequences, it is important to know the local and global characteristics and clinical presentation of food allergy.

Ethics Committee Approval: The Erciyes University Clinical Research Ethics Committee granted approval for this study (date: 10.06.2020, number: 2020/287).

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Authorship Contributions: Concept – ENO, MC, FT; Design – ENO, MC, FT; Supervision – FT; Materials – ENO, MC, FT; Data collection and/or processing – ENO, MC, FT; Analysis and/or interpretation – ENO, FT; Literature review – ENO; Writing – ENO; Critical review – ENO, FT.

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