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ARAŞTIRMA RESEARCH ARTICLE

Evaluation of the clinical features of children diagnosed with IgE-mediated food allergy

IgE aracılı besin allerjisi tanısı konulan çocukların klinik özelliklerinin değerlendirilmesi

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ABSTRACT

Objective: The prevalence of food allergies differs among countries. In addition, data on allergic diseases that accompany food allergies are limited. We aimed to evaluate demographic, clinic, and phenotypic features in children diagnosed with IgE-mediated food allergies.

Materials and Methods: The charts for 186 children diagnosed with IgE-mediated food allergies at the allergy clinic between February 2008 and July 2013 were retrospectively reviewed.

Results: The most common food allergies in the children were egg whites (49.2%), cow's milk (42.3%), egg yolks (7.7%), peanuts (5.4%), soy (3.8%), hazelnuts (3.8%), sesame (3.8%), lentils (3.1%), and fish (3.1%). Isolated egg allergies were more common than isolated milk allergies in patients with asthma ($p< 0.0001$). Total IgE levels, peripheral eosinophil count, and history of gastrointestinal symptoms were higher in patients with multiple food allergies than in patients with mono-food allergies ($p< 0.01$, $p= 0.015$, $p< 0.001$, respectively). We found that the risk of developing asthma was 2.8-fold higher in patients diagnosed with food allergies and rhinitis (OR: 2.80, 95%; CI: 1.90-6.20; $p= 0.01$).

Conclusion: This study showed that the type, incidence, and clinical symptoms of IgE-mediated food allergies were heterogeneous.

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Key words: Food allergy, child, IgE-mediated hypersensitivity, egg, milk, peanut

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ÖZ

Giriş: Besin allerjisinin prevalansı ülkeler ve toplumlar arasında büyük farklılıklar gösterir. Ayrıca besin allerjisine eşlik eden diğer allerjik hastalıklar hakkındaki veriler de sınırlıdır. Çalışmamızda, IgE aracılı besin allerjisi tanısı konulmuş çocukların demografik, klinik ve fenotipik özelliklerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Allerji kliniğimizde Şubat 2008-Temmuz 2013 tarihleri arasında IgE aracılı besin allerjisi tanısı konulan çocukların dosyaları geriye dönük olarak incelendi.

Bulgular: Çocuklardaki en sık saptanan besin allerjileri sırasıyla; yumurta beyazı (%49.2), inek sütü (%42.3), yumurta sarısı (%7.7), yer fıstığı (%5.4), soya (%3.8), fındık (%3.8), susam (%3.8), mercimek (%3.1) ve balık (%3.1) idi. Astımlı hastalarda izole yumurta allerjisi, izole süt allerjisinden daha yüksek saptandı ($p< 0.0001$). Çoklu besin allerjisi olan hastalarda, tekli besin allerjisi olan hastalara göre, daha yüksek total IgE düzeyi, periferik kanda eozinofil sayısı ve sık gastrointestinal semptom öyküsü vardı (sırasıyla; $p< 0.01$, $p= 0.015$, $p< 0.001$). Besin allerjisi ve rinit tanısı konulan hastalarda astım gelişme riskinin 2.8 (OR: 2.80, %95 CI; 1.90-6.20; $p= 0.01$) kat daha fazla olduğunu tespit ettik.

Sonuç: Çalışmamızda IgE aracılı besin allerjisinin tipi, sıklığı ve klinik semptomlarının heterojen olduğu gösterilmiştir.

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Anahtar kelimeler: Besin allerjisi, çocuk, IgE aracılı aşırı duyarlılık, yumurta, süt, fıstık

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INTRODUCTION

The incidence of food allergies, an important public problem seen especially during childhood, is increasing. The mean incidence of food allergies is estimated to be 4-6% in children. Reactions due to immunoglobulin E (IgE)-mediated food allergies may affect one or more organs. Target organs in food allergies are the skin (eczema, urticaria, angioedema), the respiratory system (rhino conjunctivitis, asthma), the gastrointestinal system (abdominal pain, nausea, vomiting, diarrhea, bloody stool), and the cardiovascular system (anaphylactic shock). In general, the most common food allergens are cow's milk, eggs, soy, wheat, peanuts, and fish[1-4].

The most common foods that cause allergies in children and the incidence rates differ from country to country and among geographic regions, due to the varying ethnic, genetic, environmental, and cultural factors, societal feeding habits, and cooking methods[1-5]. In addition, the diet content for infants differs among countries. Accordingly, over-consumption of different foods that can cause allergies during early periods of life play a role in the development of a food allergy. In some countries, the most common food allergens related to cultural feeding habits are reported to be wheat, mustard, sesame, and kiwi[1,2,6,7]. Although peanuts are the most common food allergy in Western countries, fish allergies are common in the Mediterranean region, sesame in Israel, lentils in Spain, and bird's nest in Singapore[8-12]. In addition, seafood allergies, including shrimp and crustaceans, have been reported to be more common in the preschool age group in Asian countries; there is a similar propensity in South America[13].

In this study, we aimed to evaluate the demographic, clinic, and phenotypic features in children who had been diagnosed with IgE-mediated food allergy and then were followed up at our clinic.

MATERIALS and METHODS

A total of 186 patients who had been diagnosed with a food allergy and then followed up at our clinic between February 2008 and July 2013 were included in the study. Medical history, physical examination, clinical features, laboratory outcomes, and food allergens were retrospectively evaluated. Patients who presented with allergic complaints underwent a skin prick test and/or their food-specific IgE levels were measured. The skin prick test was performed in all patients. In children ≤ 2 years of age, the small panel included milk, egg yolks, egg whites, wheat, peanuts, hazelnuts, bananas, soy, fish, cocoa, and sesame. In patients > 2 years of age, an aeroallergens panel and a panel of 38 food allergens including milk, egg yolks, egg whites, wheat, peanuts, hazelnuts, bananas, soy, fish, sesame, cocoa, beef, chicken meat, walnuts, peas, strawberries, corn, rice, tomatoes, green peppers, potatoes, grapes, apples, oranges, lemons, pears, peaches, kiwis, red capsicum (Allergopharma, Reinbek, Germany) carrots, garlic, onions, apricots, melons, cumin, black pepper, pistachio nuts, and green beans (Alyostal ST-IR; Stallergenes SA, Antony, France) were tested. To provide standardization in the skin prick test, a non-traumatizing lancet or an applicator was administered on the volar surface of the forearm. After 15 min, the induration and erythema diameters were compared with the negative and positive controls; an induration diameter > 3 mm was considered a positive reaction. The prick-to-prick test with natural food and the skin prick test with commercially extracted foods was performed for foods such as milk, egg whites, strawberries, carrots, oranges, peaches, kiwis, and potatoes. However, no commercial lentil and chickpea extracts were available; therefore, only the prick-to-prick test with natural foods (crushed and diluted) was performed.

A total IgE level above +2 standard deviation (SD) according to age, elevated serum IgE levels, an increase in peripheral blood eosinophilic leukocytes to more than 0.450 ×x 10^9 eosinophils/L of blood, eosinophilia, and allergic disease in at least one of the patient's parents or siblings were accepted as familial atopy[14].

A diagnosis of food allergy was established in children who had the following features and presented to our clinic with allergic symptoms[15-18].

1. A diagnosis of food allergy was established without performing an oral provocation test in patients who had anaphylaxis history within the last 12 months with clinical history plus a serum-specific IgE level > 0.35 kU/L and/or a positive skin prick.
2. In patients without anaphylaxis history with clinical history plus a serum-specific IgE level > 0.35 kU/L and/or a positive skin prick, a 15-day elimination diet was applied, and then an oral food provocation test was carried out for that food. A food allergy was diagnosed in patients in whom allergic symptoms were observed.
3. A food allergy was diagnosed without an oral provocation test if the child had high predictive values for serum-specific IgE levels and/or skin prick results for some foods (cow's milk, eggs, peanuts, fish).

The open oral food challenge (OFC) test was performed in children under 2 years, while the double-blind placebo-controlled food challenge (DBPCFC) test was performed in children over 2 years old. The open provocation test was performed after all negative double-blind placebo-controlled food challenges. Oral provocation protocols were developed based on current knowledge in the literature[17-19]. All suspected and placebo foods were freshly prepared for each child for identical color, flavor, consistency, and odor.

Cow's milk was masked in corn flour (placebo), rice flour (placebo), a banana, or dairy-free chocolate pudding. Eggs were hidden in corn flour (placebo), rice flour (placebo), potato puree, or oatmeal. Wheat and soy were masked in rice flour (placebo), applesauce, or dairy-free chocolate pudding. Hazelnuts, peanuts, walnuts, and oatmeal grains (placebo) were masked in chocolate pudding or applesauce. Fruits were masked in pear puree (placebo) and added to a mixture of crushed fresh mint, parsley, and dill. Boiled legumes (lentils, chickpeas, and green peas) were masked in rice flour (placebo), oat flour (placebo), applesauce, rolled oats, and dairy-free chocolate pudding. Beef, a seasoning mix (cumin, black pepper, thyme, rosemary, mustard, and pepper), onion, garlic, and turkey meat (placebo) were prepared as grilled meat patties. Similarly, fish, a seasoning mix (cumin, black pepper, thyme, rosemary, mustard, and pepper), onion, garlic, and turkey meat (placebo) were prepared as grilled meat patties and given to patients. Finally, canned tuna was used as placebo in the provocation test with fish. This study was approved by the ethics committee of Firat University.

Statistical Analysis

Statistical analyses were performed with SPSS 21.0 for Windows (IBM SPSS Statistics, Chicago, IL). The median and interquartile range for all data including age, age of onset of symptoms, eosinophil counts, and total IgE showing abnormal distribution were calculated, and all statistical comparisons were performed using the Mann-Whitney U test. A value of $p< 0.05$ was considered significant for all analyses. We performed univariate and multivariate logistic regression analyses to establish the factors associated with asthma. The factors that were significant in the univariate regression analysis or resulted in a shift in the odds ratio (OR; > 0.2) for the relationship were then included as covariates in the multiple regression analysis.

RESULTS

Sensitization to foods was found in 186 patients who presented to our clinic with allergic complaints through the skin prick test and/or specific IgE outcomes. The most frequent positivity was egg whites (53.8%; n= 100), cow's milk (46.2%; n= 86), egg yolks (12.4%; n= 23), peanuts (10.8%; n= 20), and soy (7%; n= 13). Following the clinical and provocation tests, food allergies were diagnosed in 130 of 186 (69.8%) patients in whom test sensitization was observed. The most common allergies were egg whites (49.2%; n= 64), cow's milk (42.3%; n= 55), egg yolks (7.7%; n= 10), peanuts (5.4%; n= 7), soy, hazelnuts, and sesame (3.8%; n= 5), and fish and lentils (3.1%; n= 4) (Table 1). The mean age of the patients was 1.0 (0.2-17) years, and the mean age of symptom onset was 0.7 (0.1-12) years. Familial atopy history was observed in

Table 1. Frequency of food allergens in children with IgE-mediated food allergy (n= 130)

Foods	Diagnosis of food allergy n (%)
Egg white	64 (49.2)
Cow's milk	55 (42.3)
Egg yolk	10 (7.7)
Peanut	7 (5.4)
Soy	5 (3.8)
Hazelnut	5 (3.8)
Sesame	5 (3.8)
Fish	4 (3.1)
Lentil	4 (3.1)
Cocoa	3 (2.3)
Banana	3 (2.3)
Chicken meat	3 (2.3)
Beef	3 (2.3)
Pistachionut	3 (2.3)
Chickpea	3 (2.3)
Pea	2 (1.5)
Potato	2 (1.5)
Kiwi	2 (1.5)
Wheat	1 (0.8)
Peach	1 (0.8)
Orange	1 (0.8)
Walnut	1 (0.8)
Carrot	1 (0.8)
Strawberry	1 (0.8)

68.5%, elevated serum total IgE in 50.8%, and elevated peripheral eosinophil count in 57.7% of the patients. Patients' complaints at the time of admission included skin symptoms (97.7%; n= 127, eczema, urticaria, and angioedema), respiratory symptoms (38.5%; n= 50, wheezing, dyspnea, cough, rhinitis, and conjunctivitis), gastrointestinal symptoms (13.8%; n= 18, vomiting, nausea, oral pruritus, abdominal cramping, and diarrhea), cardiovascular symptoms (2.3%; n= 3, hypotension and tachycardia), and neurological symptoms (2.3%; n= 3, dizziness, headache, and confusion). In addition to food allergies, atopic dermatitis was found in 63.2% (n= 84), asthma in 32.3% (n= 62), urticaria in 27.8% (n= 37), rhinitis in 8.3% (n= 11), and anaphylaxis in 6.1% (n= 7) (Table 2) of the patients. In terms of food allergies according to age group, 77.4% (n= 48) of the egg allergies, 84.3% (n= 43) of the cow's milk allergies, and 80% (n= 8) of the egg yolk allergies were seen in the 0 to 2-year-old age range. In contrast, 71.4% (n= 5) of the peanut allergies, 100% (n= 4) of the fish allergies, and 77.7% (n= 7) of the tree nut (hazelnuts, pistachio nuts, walnuts) allergies were observed in patients between 6.1 and 18 years old.

Asthma was statistically higher in patients with an isolated egg allergy than in those who had an isolated milk allergy ($p< 0.0001$) (Table 3). In addition, the total IgE level, peripheral eosinophil count, and gastrointestinal symptoms were statistically higher in patients who had multiple food allergies than in patients with mono-food allergies ($p< 0.01$, $p= 0.015$, $p< 0.001$, respectively) (Table 4). The incidence of developing asthma was 2.8-fold higher in patients with food allergy–associated rhinitis [OR: 2.80, 95% confidence interval (CI): 1.90–6.20; $p= 0.01$]. The risk of developing asthma was lower in children who had atopic dermatitis, urticaria, and milk allergies (Table 5).

Table 2. Characteristics of the patients with food allergy

Characteristic	Food allergy
Gender n (%)	
Male	83 (63.8)
Female	47 (36.2)
Family history of allergy n (%)	
No	41 (31.5)
Yes	89 (68.5)
Presenting symptoms n (%)	
Cutaneous symptoms	127 (97.7)
Respiratory symptoms	50 (38.5)
Gastrointestinal symptoms	18 (13.8)
Cardiovascular symptoms	3 (2.3)
Neurological symptoms	3 (2.3)
Concomitant allergic diseases n (%)	
Atopic dermatitis	84 (63.2)
Asthma	62 (32.3)
Ürticaria	37 (27.8)
Rhinitis	11 (8.3)
Anaphylaxis	7 (6.1)
Serum total IgE levels n (%)	
Normal	64 (49.2)
Increased	66 (50.8)
Peripheral eosinophil count n (%)	
Normal	55 (42.3)
İncreased	75 (57.7)
Aeroallergen sensitivity n (%)	
Grass pollen	19 (14.6)
Tree pollen	7 (5.4)
House-dust mite	6 (4.6)
Meanage (years)*	1.0 (0.2-17)
Age of on set of symptoms (years)*	0.7 (0.1-12)
Serum total IgE levels (IU/mL)*	21.8 (0.9-1057)
Peripheral eosinophil count (mm^3)*	485 (45-1578)

* Median (interquartile ranges)

DISCUSSION

Epidemiological studies on the relationship of food allergies with atopic dermatitis, allergic rhinitis, and asthma are limited[1]. Studies on food allergies have focused on indicators of the development of food allergies and the role and incidence of food allergies in specific diseases (e.g., atopic dermatitis, asthma, anaphylaxis). It has been reported that egg allergies are associated with the development of asthma[5,20-22]. In this study, we also found that egg allergies were more common than isolated milk allergies in patients with asthma.

Various incidence rates for mono- and multiple-food allergies in children have been reported. In general, 30% of children with allergies develop allergies to more than one food[5]. In agreement with the literature, in this study we found that 29.2% of the children developed multiple food allergies. More serious clinical phenotypes are seen in children with multiple food allergies than in those with mono-food allergies, such as elevated total IgE level, high eosinophil count, increased risk of anaphylaxis, severe atopic dermatitis manifestation, and malnutrition due to extreme dietary restrictions[5].We found that the total IgE level and the peripheral eosinophil count were higher in children with multiple food allergies than in children with mono-food allergies. In addition, the risk of developing

Table 3. Comparison of the characteristics in children with isolated cow's milk and egg allergies

	Isolated cow's milk (n= 32)	Isolated egg (n= 40)	p valvue
Gender n (%)			
Male	23 (71.9)	25 (62.5)	NS≠
Female	9 (28.1)	15 (37.5)	
Age of on set of symptoms (years)*	0.9 (0.2-8)	1.0 (0.3-5.5)	NS¥
Family history of allergy n (%)	25 (78.1)	27 (67.5)	NS≠
Serum total IgE levels (IU/mL)*	11.3 (0.9-278)	17.4 (1.1-453)	NS¥
Increased serum total IgE levels n (%)	11 (34)	18 (45)	NS≠
Peripheral eosinophil count (mm^3)*	415 (60-1340)	485 (5.0-1260)	NS¥
İncreased peripheral eosinophil count n (%)	16 (50)	24 (60)	NS≠
Concomitant allergic diseases n (%)			
Atopic dermatitis	21 (65.6)	31 (77.5)	NS≠
Asthma	3 (7.5)	16 (50)	0.0001≠
Ürticaria	7 (21.9)	7 (17.5)	NS≠
Presentation symptoms n (%)			
Skin	32 (100)	40 (100)	NS≠
Respiratory	14 (43.8)	11 (27.5)	NS≠

* Median (interquartile ranges)
¥ Kruskal Wallis test
≠ X^2 -test

Table 4. Comparsion of the characteristics in children with one food allergy and more than one food allergy

	Allergy to one food	Allergies to more than one food	p value
Gender n (%)			
Male	59 (71.1)	24 (28.9)	NS≠
Female	33 (70.2)	14 (29.8)	
Age of on set of symptoms (years)*	1.52 (0.1-10)	2.04 (0.1-12)	NS¥
Family history of allergy n (%)	65 (70.7)	24 (63.2)	NS≠
Serum total IgE levels (IU/mL)*	15.7 (0.9-453.0)	112.0 (3.4-1057.0)	0.01¥
Increased serum total IgE levels n (%)	42 (47.7)	22 (57.9)	NS≠
Peripheral eosinophil count (mm^3)*	468 (50-1340)	648 (80-1578)	0.015¥
Increased peripheral eosinophil count n (%)	47 (51.1)	28 (73.7)	0.02≠
Concomitant allergic diseases (%)			
Atopic dermatitis	62.0	65.8	NS≠
Asthma	32.6	34.2	NS≠
Allergic rhinitis	6.5	13.2	NS≠
Ürticaria	28.3	26.3	NS≠
Presentation symptoms (%)			
Skin	97.8	97.4	NS≠
Respiratory	38	39.5	NS≠
Gastrointestinal	5.4	34.2	0.001≠

* Median (interquartile ranges)
¥ Kruskal Wallis test
≠ X^2-test

Table 5. Logistic regression analysis for asthma in children with food allergy

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p valvue
Gender	1.10 (0.86-4.26)	NS		
Age of onset of symptoms (years)	1.20 (0.92-1.26)	NS		
Family history of allergy	0.99 (0.28-3.52)	NS		
Cow's milk	0.71 (0.16-0.31)	0.001		
Egg white	2.82 (0.69-11.44)	NS		
Peanut-Treenuts	6.13 (0.34-10.9)	NS		
Serum total IgE levels	2.81 (0.84-9.34)	NS		
Peripheral eosinophil count	0.58 (0.15-2.22)	NS		
Atopic dermatitis	0.55 (0.42-0.74)	0.04	0.42 (0.32-0.79)	0.005
Ürticaria	0.27 (0.17-0.88)	0.03	0.21 (0.13-0.74)	0.04
Rhinitis	3.90 (2.10-7.60)	0.01	2.80 (1.90-6.20)	0.01
More than one food allergy	1.22 (0.76-1.90)	NS		

asthma is reportedly higher in children with multiple food allergies[23,24]. We observed more gastrointestinal symptoms in children with multiple food allergies than in those with mono-food allergies, but there was no significant difference between asthma and respiratory symptoms. The incidence of developing asthma was 2.8-fold higher in patients with food allergy–associated rhinitis. This finding was a result of the atopic march mechanism in allergic children. Furthermore, we found that the risk of developing asthma was lower in children with atopic dermatitis, urticaria, and cow's milk allergies. Many studies have reported a correlation between atopic dermatitis and increased risk of developing asthma[25,26]. However, this result could not be generalized for the general population in our study because it was not a cohort study and was conducted in a specific group that had an IgE-mediated food allergy. This correlation should be confirmed with future studies.

The most common food causing allergy in children varies from country to country and among geographic regions. Egg allergies are more common than cow's milk allergies in the Oceanic countries (Australia, New Zealand) and Asia[27]. Cow's milk allergies have been reported as the most common food allergy in children on the American continent and in the Middle East. However, the incidence of the most common food allergens varies in Europe[1,2,22]. In our study, eggs were the most common food allergens. Traditionally, in Turkey, similarly to Middle Eastern cuisine, dairy products and eggs in addition to red meat, wheat products, spices, and legumes are frequently consumed. Yavuz et al. reported that egg allergies were the most common allergy in Turkish children who had food allergies[5]. Han et al. found that the most common sensitization were eggs (51.5%) followed by cow's milk (31.2%) and peanuts (16.2%) in children under 4 years old with atopic dermatitis[28]. Various factors are crucial in the development of food allergies. Recent studies have focused on the effects of genetic factors. Polymorphisms have been defined in many candidate genes, and these genes interact with environmental factors[2,4]. Epigenetic effects may play a role in the detection of eggs as the most common food allergy in our results. Egg whites are a more common allergy than egg yolks. Egg white allergies were found in 49.2% of our patients with food allergies, while egg yolk allergies were found in only 7.7%.

Cow's milk was the second most common food allergy in this study. Yavuz et al. found that the most common allergy was eggs (57.8%) followed by cow's milk (55.9%) in Turkish children in various age groups who have food allergies. Since bovine serum albumin, an allergic protein, is found in milk and bovine meat, cross-reactivity is seen[5]. Bovine meat allergies are possible in patients who have cow's milk allergies or vice versa. However, the possibility of cow's milk allergies is higher in patients who have bovine meat allergies. In one study, association of cow's milk allergy was observed in 8 of 11 (72.7%) children who had bovine meat allergies. In contrast, despite a positive skin test in 84% of children with cow's milk allergies, a positive reaction on the DBPCFC test with bovine meat was observed in only

20%[29]. In our study, associated cow's milk allergies were found in two of three (66.6%) patients who had a red meat allergy. These data show that we should consider cow's milk allergies in patients who have red meat allergies. However, in a study by Orhan et al. with children in the 6 to 9-year-old age group living in northeastern Turkey, the most common food allergy was bovine meat followed by cocoa and cow's milk[30]. The researchers did not find cow's milk allergies in any children who had red meat allergies.

Although milk and eggs are the most common food allergies worldwide, the third most common allergy differs among countries[1]. For example, the third most common food allergy has been reported as peanuts in the United States and Switzerland, wheat in Japan and Germany, tree nuts in Spain, and sesame in Israel[31].However, in our study, the third most common food allergy was peanuts. In addition, grass and cerealpollen allergies were found in 6 of 7 (85.7%) patients who had peanut allergies. It has been reported that pollen sensitization and related incidence of rhinitis development increased in children with peanut allergies. It has also been reported that a skin reaction, which was defined as positive with peanuts, might result from the cross-reaction between pollen and peanuts or primary peanut sensitization in children who have pollen allergies[5]. Furthermore, there was an association of hazelnut allergies in three patients, pistachio allergies in two patients, and walnut allergy in one patient among the seven patients in whom we found peanut allergies.

In this study, hazelnuts, soy, and sesame were the fourth most common food allergy. Turkey is a major global producer of hazelnuts, and hazelnut consumption is high. In the literature, it has been reported that peanut and tree nut allergies were most commonly seen in young adults and adolescents[2]. In this study, 71.4% of the peanut allergies and 77.7% of the tree nuts allergies were seen in the 6.1- to 18-year-old age range. The prevalence of sesame allergies has recently reportedly increased in some countries[10]. In the Middle East, including our region, sesame is among the five most common food allergies. Because dietary sesame is regularly consumed in Israel, sesame ranks third among the foods that cause allergy after cow's milk and eggs, and the second among foods that cause anaphylaxis after cow's milk[6,10]. In this study, sesame allergies were observed in five children, and three of these patients were under 2 years old. This result may depend on including sesame products in the infant's diet (such as tahini halva, tahini molasses) and the breast feeding mother's diet. We found soy allergies in five of our patients through the oral provocation test. In addition, we found soy allergies in four (7.3%) children with cow's milk allergies, and the results were parallel to the results in the literature[32,33].

Lentil and fish allergies ranked fifth in our patients diagnosed with food allergies. Yavuz et al. reported that lentils were the sixth most common food allergy in Turkish children who were diagnosed with food allergies[5]. In addition, lentil allergies have been reported as the fifth most common food allergy in children in Spain[9]. As in the Middle East, Mediterranean countries, India, Bangladesh, and some Asian countries, lentils are frequently consumed as an important nutrient for infants and older children. In addition, cross-reactivity is highly variable in the legume family, including lentils. Although allergic reaction to multiple legumes is rare among children in North America, multiple legume reactions have been frequently diagnosed in children in the Mediterranean region and India[34,35]. Yavuz et al. reported that isolated lentil allergies were infrequent and other legume allergies were associated with most lentil allergies (83%) in Turkish children[36]. We foundpeanut, chickpea, and green pea allergies in 75% of the patients who were allergic to lentils. Cross-reactivity among legumes varies among individuals in different countries and with different dietary habits. However, researchers have reported that fish allergies depend on geographic feeding habits, the methods used in preparing and cooking fish,and the type and quantity of the fish eaten in the local diet. In our study, fish allergies were the fifth most common food allergy. Fish allergies were the third most common food allergy after cow's milk and egg allergies in children under 2 years old in Spain[37].

This study has limitations. First, the population consisted of selected children with IgE-mediated food allergy who had been referred to our tertiary university clinic. In addition, all children included in this study were children who had allergic symptoms. Thus, the incidence of food allergy might not reflect the true prevalence of food allergy in the general population. Second, the open provocation test was used instead of a double-blind placebo-controlled oral provocation test, which is the gold standard for children under 2 years old. However, no suspicion in the diagnosis of food allergy in the majority of the cases with obvious symptoms was found in the children's medical history, and allergen sensitization was demonstrated on skin tests, food-specific IgE measurements, and subsequent observation of objective symptoms in the open provocation tests. Furthermore, this study was conducted in the eastern

region of Turkey, which is less developed compared to the western region and has different dietary and cultural characteristics, and this study was a limited study conducted with children who have food allergies.

In conclusion, this study showed that the type, incidence, and clinical symptoms of IgE-mediated food allergies were heterogeneous. Egg white allergies were the most common allergy, and isolated egg allergies were more common than isolated milk allergies in patients with asthma. In addition, the majority of patients diagnosed with food allergies presented with skin symptoms. In light of these results, future studies on food allergies should focus on the effects of genetic, cultural, dietary, and environmental factors on the development of food allergies and correlations with other allergic diseases.

REFERENCES

1. *Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, et al. The prevalence of food allergy: A meta-analysis. J Allergy Clin Immunol 2007;120:638-46.*
2. *Sicherer SH, Sampson HA. Food allergy. J Allergy Clin Immunol 2010;(Suppl 2):S116-S25. doi:10.1016/j.jaci.2009.08.028.*
3. *Prescott S, Allen KJ. Food allergy: riding the second wave of the allergy epidemic. Pediatr Allergy Immunol 2011;22:155-60. doi: 10.1111/j.1399-3038.2011.01145.x.*
4. *Lack G. Epidemiologic risks for food allergy. J Allergy Clin Immunol 2008;121:1331-6. doi: 10.1016/j.jaci.2008.04.032.*
5. *Yavuz ST, Sahiner UM, Buyuktiryaki B, Soyer OU, Tuncer A, Sekerel BE, et al. Phenotypes of IgE-mediated food allergy in Turkish children. Allergy Asthma Proc 2011;32:47-55. doi: 10.2500/aap.2011.32.3481.*
6. *Dalal I, Binson I, Reifen R, Amitai Z, Shohat T, Rahmani S, et al. Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel. Allergy 2002;57:362-5.*
7. *Mattila L, Kilpeläinen M, Terho EO, Koskenvuo M, Helenius H, Kalimo K. Food hypersensitivity among Finnish university students: association with atopic diseases. Clin Exp Allergy 2003;33:600-6.*
8. *Sicherer SH, Munoz-Furlong A, Burks AW, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. J Allergy Clin Immunol 1999;103:559-62.*
9. *Crespo JF, Pascual C, Burks AW, Helm RM, Esteban MM. Frequency of food allergy in pediatric population from Spain. Pediatr Allergy Immunol 1995;6:39-43.*
10. *Cohen A, Goldberg M, Levy B, Leshno M, Katz Y. Sesame food allergy and sensitization in children: the natural history and long- term follow-up. Pediatr Allergy Immunol 2007;18:217-23.*
11. *Martinez San Ireneo M, Ibanez MD, Sanchez JJ, Carnés J, Fernández-Caldas E. Clinical features of legume allergy in children from a Mediterranean area. Ann Allergy Asthma Immunol 2008;101:179-84.*
12. *Goh DL, Lau YN, Chew FT, Shek LP, Lee BW. Pattern of food-induced anaphylaxis in children of an Asian community. Allergy 1999;54:84-6.*
13. *Prescott SL, Pawankar R, Allen KJ, Campbell DE, Sinn JKh, Fiocchi A, et al. A global survey of changing patterns of food allergy burden in children. World Allergy Organ J 2013;6:21. doi: 10.1186/1939-4551-6-21.*
14. *Pardo J, Carranza C, Muro A, Angel-Moreno A, Martín AM, Martín T, et al. Helminth-related Eosinophilia in African immigrants, Gran Canaria. Emerg Infect Dis 2006;12:1587-9.*
15. *Hill DJ, Heine RG, Hosking CS. The diagnostic value of skin prick testing in children with food allergy. Pediatr Allergy Immunol 2004;15:435-41.*
16. *Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. J Allergy Clin Immunol 2001;107:891-6.*
17. *Lieberman JA, Sicherer SH. The diagnosis of food allergy. Am J Rhinol Allergy 2010;24:439-43. doi: 10.2500/ajra.2010.24.3515.*
18. *Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, Bock SA, Sicherer SH, Teuber SS; Adverse Reactions to Food Committee of American Academy of Allergy, Asthma&Immunology. Work Group report: oral food challenge testing. J Allergy Clin Immunol 2009;123(Suppl 6):S365-S83. doi: 10.1016/j.jaci.2009.03.042.*
19. *Yum HY, Yang HJ, Kim KW, Song TW, Kim WK, Kim JH, et al. Oral food challenges in children. Korean J Pediatr 2011;54:6-10. doi: 10.3345/kjp.2011.54.1.6.*
20. *Kotaniemi-Syrjanen A, Reijonen TM, Romppanen J, Korhonen K, Savolainen K, Korppi M. Allergen-specific immunoglobulin E antibodies in wheezing infants: the risk for asthma in later childhood. Pediatrics 2003;111:e255-61.*
21. *Tariq SM, Matthews SM, Hakim EA, Arshad SH. Egg allergy in infancy predicts respiratory allergic disease by 4 years of age. Pediatr Allergy Immunol 2000;11:162-7.*
22. *Bekkers MB, Aalberse RC, Gehring U, Kerkhof M, Koppelman GH, de Jongste JC, et al. Hen's egg, not cow's milk, sensitization in infancy is associated with asthma: 10-year follow-up of the PIAMA birth cohort. J Allergy Clin Immunol 2013;132:1427-8. doi: 10.1016/j.jaci.2013.07.053.*
23. *Nickel R, Lau S, Niggemann B, Grüber C, von Mutius E, Illi S, et al; MAS Group. Messages from the German Multicentre Allergy Study. Pediatr Allergy Immunol 2002;13(Suppl 15):7-10.*
24. *Schroeder A, Kumar R, Pongracic JA, Sullivan CL, Caruso DM, Costello J, et al. Food allergy is associated with an increased risk of asthma. Clin Exp Allergy 2009;39:261-70. doi: 10.1111/j.1365-2222.2008.03160.x.*
25. *Kulig M, Bergmann R, Klettke U, Wahn V, Tacke U, Wahn U. Natural course of sensitization to food and inhalant allergens during the first 6 years of life. J Allergy Clin Immunol 1999;103:1173-9.*
26. *Bergmann RL, Edenharter G, Bergmann KE, Forster J, Bauer CP, Wahn V, et al. Atopicdermatitis in early infancy predicts allergic airway disease at 5 years. Clin Exp Allergy 1998;28:965-70.*
27. *Tan JW, Joshi P. Eggallergy: an update. J Paediatr Child Health 2014;50:11-5.*
28. *Han DK, Kim MK, Yoo JE, Choi SY, Kwon BC, Sohn MH, et al. Foodsensitization in infants and young children with atopic dermatitis. Yonsei Med J 2004;45:803-9.*
29. *Verfel SJ, Cooke SK, Sampson HA. Clinical reactivity to beef in children allergic to cow's milk. J Allergy Clin Immunol 1997;99:293-300.*

30. *Orhan F, Karakas T, Cakir M, Aksoy A, Baki A, Gedik Y. Prevalence of immunoglobulin E-mediated food allergy in 6-9-year-old urban schoolchildren in the eastern Black Sea region of Turkey. Clin Exp Allergy 2009;39:1027-35. doi: 10.1111/j.1365-2222.2009.03263.x.*

31. *Fiocchi A, Brozek J, Schunemann H, Bahna SL, von Berg A, Beyer K, et al. World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines. Pediatr Allergy Immunol 2010;21(Suppl 21):1-125. doi: 10.1111/j.1399-3038.2010.01068.x.*

32. *Bock SA, Atkins FM. Patterns of food hypersensitivity during sixteen years of double-blind, placebo-controlled food challenges. J Pediatr 1990;117:561-7.*

33. *Zeiger RS, Sampson HA, Bock SA, Burks AW Jr, Harden K, Noone S, et al. Soy allergy in infants and children with IgE-associated cow's milk allergy. J Pediatr 1999;134:614-22.*

34. *Bernhisel-Broadbent J, Sampson HA. Cross allergenicity in the legume botanical family in children with food hypersensitivity. J Allergy Clin Immunol 1989;83:435-40.*

35. *Ibáñez MD, Martínez M, Sánchez JJ, Fernández-Caldas E. Legume cross-reactivity. Allergol Immunopathol (Madr) 2003;31:151-61.*

36. *Yavuz ST, Sahiner UM, Buyuktiryaki B, Tuncer A, Yilmaz EA, Cavkaytar O, et al. Role of specific IgE in predicting the clinical course of lentil allergy in children. Pediatr Allergy Immunol 2013;24:382-8. doi: 10.1111/pai.12080.*

37. *Pascual CY, Reche M, Fiandor A, Valbuena T, Cuevas T, Esteban MM. Fish allergy in childhood. Pediatr Allergy Immunol 2008;19: 573-9. doi: 10.1111/j.1399-3038.2008.00822.x.*