

## PAPER DETAILS

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AUTHORS: Ugur Altas,Elif Akman,Zeynep Meva Altas,Fatih Çiçek,Mehmet Yasar Özkars

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# Determination of the frequency of food allergen sensitivity in children with atopic dermatitis

Uğur Altaş<sup>1</sup>, Elif Akman<sup>2</sup>, Zeynep Meva Altaş<sup>3</sup>, Fatih Çiçek<sup>4</sup>, Mehmet Yaşar Özkars<sup>1</sup>

<sup>1</sup>Department of Pediatric Allergy and Immunology, Ümraniye Training and Research Hospital, University of Health Sciences, İstanbul, Turkey

<sup>2</sup>Department of Pediatrics, Ümraniye Training and Research Hospital, University of Health Sciences, İstanbul, Turkey

<sup>3</sup>Public Health Specialist, Ümraniye District Health Directorate, İstanbul, Turkey

<sup>4</sup>Department of Pediatric Allergy and Immunology, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Turkey

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## ABSTRACT

**Aims:** We aimed to evaluate the frequency of food allergen sensitivity in children with atopic dermatitis (AD).

**Methods:** The study is a descriptive study in a retrospective design. Children aged 0-18 years with AD were included in the study. The sociodemographic characteristics, laboratory parameters and the frequency of food allergen sensitivity were evaluated. Allergen sensitization was defined as a positive allergen-specific IgE or skin prick test.

**Results:** The data of 295 patients with AD were evaluated. Food allergen sensitivity was detected in 34.2% (n=101) of them. Of the patients 21.4% (n=63) had a single food allergen sensitivity, whereas 12.9% (n=38) had multiple food allergen sensitivity. Egg was the most common food allergen (n=78, 26.4%). Patients with single food allergen sensitivity and multiple food allergen sensitivity were both significantly younger than those without food allergen sensitivity ( $p<0.001$  for both). Total IgE values of AD patients with multiple food allergen sensitivity were significantly higher than those with single allergen sensitivity and those without food allergen sensitivity ( $p=0.002$  and  $p=0.003$ , respectively).

**Conclusion:** A significant relationship was found between age, total IgE values and the presence of food allergen sensitivity in atopic dermatitis patients. Factors that may be associated with the development of food allergen sensitivity should be considered in the treatment and management of the disease in children with AD.

**Keywords:** Atopic dermatitis, children, allergy, food allergen sensitivity

## INTRODUCTION

Atopic dermatitis (AD) is one of the most commonly seen skin diseases among children.<sup>1</sup> Atopic dermatitis is a chronic, recurrent and highly itchy dermatitis.<sup>2</sup> The prevalence of AD is increasing all over the world.<sup>3,4</sup> Atopic dermatitis usually develops in early childhood and is usually associated with elevated IgE values, eosinophils, and other allergic diseases.<sup>5</sup>

In the pathogenesis of AD, genetic factors, immune dysregulation, disruption of the skin's barrier function, environmental factors, and nutrients play important roles.<sup>1</sup> The pathophysiological mechanisms of allergic diseases are similar to each other.<sup>6</sup> Atopic march; is the clinical definition in which AD that develops at an early age is accompanied by other allergic diseases such as food allergies, asthma and allergic rhinitis in older ages.<sup>7</sup>

Food allergy occurs as a result of immunological reactions against food proteins. Allergies to milk, eggs,

soy, shellfish, and nuts are the most commonly observed types of food allergies.<sup>8</sup> The frequency of food allergies is increasing, and it is more commonly seen in children than adults.<sup>9</sup> In a meta-analysis study, the point prevalence of food allergy determined with specific IgE sensitivity was reported as 16.6% (95% CI 12.3-20.8). In the same study, the prevalence of food allergy determined with the skin prick test was reported as 5.7% (95% CI 3.9-7.4).<sup>10</sup>

There are studies that demonstrate a causal relationship between atopic dermatitis and the development of food allergies.<sup>11</sup> Food allergen-specific IgE positivity is observed in approximately half of patients with AD. Positive symptoms are observed in approximately one-third of patients with severe AD during the oral food test.<sup>12</sup> Similarly, type 2 inflammation is observed in patients with AD and those with food allergies.<sup>13</sup> In addition, with the deterioration of the barrier function of the skin in AD patients, the development of food sensitivity can be observed by absorbing the allergen nutrients by the

**Corresponding Author:** Uğur Altaş, druguraltas@gmail.com



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skin and reaching the lower layers of the skin.<sup>13,14</sup> Some food allergy cases are accompanied by an impaired skin barrier even if AD is not present.<sup>15</sup>

It is important to evaluate possible allergy-related conditions in patients with AD and to predict the emergence of other allergic phenotypes in the future. Knowing the frequency of food allergy in patients with AD will help to better plan the prioritized approach and treatments in the management of the disease. In this context, we aimed to evaluate the frequency of food allergen sensitivity in children with atopic dermatitis in our study.

## METHODS

The study was carried out with the permission of Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date:04.07.2023, Decision No: 240). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study is a descriptive study in a retrospective design. Children with AD who applied to our pediatric allergy and immunology outpatient clinic between May 2022 and May 2023 were included in the study. Since the study was retrospective in design, data from all patients diagnosed with atopic dermatitis in the hospital database within a 1-year period were analyzed for the study. Patients with a diagnosis of a skin disease other than AD were excluded from the study.

## Measures

Children's sociodemographic characteristics (age, gender), laboratory parameters (eosinophils, total IgE values), food allergen sensitizations were examined.

For the food allergen-specific IgE measurements, ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) was used. Specific IgE values, equal to or greater than 0.35 kU/L, were considered as positive. Skin prick test was performed to the patients who had negative results for allergen specific IgE. Epidermal skin prick tests were performed with the use of allergen extracts (ALK-Abello, Madrid, Spain) along with a positive control (10 mg/dl of histamine phosphate) and a negative control (0.9% sterile saline). Horizontal and vertical measurements were performed for the indurations. Indurations were considered positive, if the average diameter at least 3 mm greater than the negative control.

Allergen sensitization was defined as a positive allergen-specific IgE or skin prick test. The food allergen sensitization was confirmed with clinical history (including dietary history, maternal dietary history for breastfed infants) and physical examination of patients, and food elimination and food provocation tests.

## Statistical Analysis

SPSS (Statistical Package for Social Sciences for Windows 25.0 program was used for the analysis and the recording of data. Descriptive data was presented with median values, interquartile range, numbers (n) and percentages (%). For the comparison of continuous variables that non-normally distributed; Kruskal Wallis test was used for more than two groups and Mann Whitney U test was used for two groups. The statistical significance level was set at  $p < 0.05$ .

## RESULTS

In the study, data from 295 pediatric patients diagnosed with atopic dermatitis (AD) were evaluated. Among these patients, 52.9% (n=156) were male, and 47.1% (n=139) were female. The median age was 3 years (1-7). Eosinophil and total IgE values of the patients were examined. The median values of absolute eosinophils and eosinophils (%) were 360.0 103/ $\mu$ L (210.0-600.0) and 4.2% (2.6-6.9), respectively. The median total IgE value was 88.0 IU/ml (22.0-304.0) ([Table 1](#)).

Table 1. Eosinophil and total IgE values of atopic dermatitis patients	
	Median (IQR)
Eosinophil (10 <sup>3</sup> /ul)	360.0 (210.0-600.0)
Eosinophil (%)	4.2 (2.6-6.9)
Total IgE (IU/ml)	88.0 (22.0-304.0)
IQR:Interquartile range	

The sensitization to food allergens in AD patients was evaluated. Egg allergy was the most common allergen among the patients (n=78, 26.4%). The frequencies of sensitization to cow's milk, peanut and hazelnut allergens were 12.2% (n=36), 9.5% (n=28) and 4.1% (n=12), respectively. Three patients had walnut and two patients had pistachio allergen sensitization ([Table 2](#)).

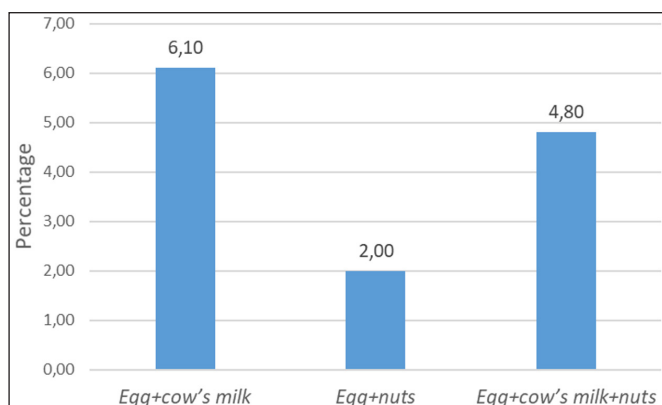
Table 2. Distribution of food allergen sensitization in atopic dermatitis patients		
Allergen sensitization	n	%
Egg	78	26.4
Cow's milk	36	12.2
Peanut	28	9.5
Hazelnut	12	4.1
Walnut	3	1.0
Pistachios	2	0.7

The frequency of single and multiple food allergen sensitization in AD patients was also evaluated in the study. Food allergen sensitization was detected in 34.2% (n=101) of the patients. Of the patients 21.4% (n=63) had a single food allergen sensitization. Of the patients 12.9% (n=38) had multiple allergen to sensitization ([Table 3](#)).

Both egg and cow's milk allergen sensitization was seen in 6.1% (n=18), egg and nuts allergen sensitization was seen in 2.0% (n=6), and egg, cow's milk and nuts allergen sensitization was seen in 4.8% (n=14) of patients with multiple allergen sensitization (Figure).

**Table 3.** Frequency of single and multiple food allergen sensitization in atopic dermatitis patients.

Allergen sensitization	N	%
No	194	65.8
Yes	101	34.2
Single allergen sensitization	63	21.4
Multiple allergen sensitization	38	12.9



**Figure.** Frequency of multiple food allergen sensitization.

A significant relationship was found between age, total IgE values and the presence of food allergen sensitization in AD patients. Patients with single food allergen sensitization and multiple food allergen sensitization were both significantly younger than those without food allergen sensitization ( $p < 0.001$  for both). There was no significant difference between the median age values of those with single food allergen sensitization and multiple food allergen sensitization ( $p = 0.878$ ). Total IgE values of AD patients with multiple food allergen sensitization were significantly higher than those with single allergen sensitization and those without food allergen sensitization ( $p = 0.002$  and  $p = 0.003$ , respectively). There was no significant difference in total IgE values between those without food allergen sensitization and those with single food allergen sensitization ( $p = 0.606$ ). There was no significant relationship between eosinophil values and the presence of food allergen sensitization ( $p > 0.05$ ) (Table 4).

## DISCUSSION

Atopic dermatitis is one of the most common skin diseases in children. Food allergies are also common, especially in early childhood. Foods are triggers in approximately 20-30% of patients with moderate to severe AD.<sup>17</sup> In this context, we evaluated the frequency of food allergen sensitization in children with AD.

There is increasing evidence in the literature that AD predisposes to food allergy.<sup>18,19</sup> It is recommended that food allergen-specific skin tests or specific IgEs be performed in all children under 5 years of age, especially those with moderate to severe AD who do not respond to topical treatment.<sup>18</sup> In our study, 34.2% (n=101) of the children had food allergen sensitization. The frequency of food allergen sensitization was found to be mostly against eggs (26.4%), cow's milk (12.2%), and peanuts (9.5%). In a study in the literature, the frequency of food allergy in children with AD was reported as 27%. In the same study, allergies to eggs (21%), peanuts (15%) and milk (8%) were the most common, similar to our study.<sup>20</sup> In a study conducted in our country, the frequency of food allergen sensitization in children with AD was reported as 59%. In the same study, the most common allergens were egg white (39%), egg yolk (31%), cow's milk (13%) and wheat flour (5%).<sup>21</sup> The fact that the frequency of food allergen sensitization was found to be lower in our study than in the other study in our country may be due to the fact that clinical severity scores of AD patients were not performed in our study. In addition, according to studies, food allergen sensitization was reported more frequently in patients with more severe AD than in mild AD patients. The difference between study results may also be related to the clinical severity of AD patients.<sup>21,22</sup> In a study conducted in our country in 2012, the frequency of food allergen sensitization in children with asthma and rhinitis was observed to be 5.8%. When compared with the results of our study (34.2%), it can be considered that over the years, there has been an increase in food allergen sensitivity in children. There is a need for community-based prospective studies in this field.

**Table 4.** The relationship between single and multiple food allergen sensitization and age, eosinophil and total IgE in atopic dermatitis patients

	No sensitization (n=194)	Single allergen sensitization (n=63)	Multiple allergen sensitization (n=38)	P value*
	Median (IQR)	Median (IQR)	Median (IQR)	
Age (years)	5.0 (2.0-8.0)	2.0 (1.0-4.0)	2.0 (1.0-3.0)	<0.001
Eosinophil ( $10^3/\mu\text{l}$ )	350.0 (210.0-540.0)	400.0 (180.0-730.0)	415.0 (220.0-620.0)	0.371
Eosinophil (%)	4.1 (2.6-6.7)	4.7 (2.5-7.8)	4.5 (2.5-7.0)	0.515
Total IgE (IU/ml)	82.0 (19.0-301.0)	52.0 (20.0-211.0)	201.0 (88.0-400.0)	0.005

IQR: Interquartile range, \*Kruskal Wallis test



In our study, 21.4% of the patients had single food allergen sensitization, and 12.9% had multiple allergen sensitization. The majority of those with multiple allergen sensitization exhibited a combination of egg and milk allergen sensitization. In a study conducted in our country, 38% of children with AD had an allergy to a single food, whereas multiple allergen sensitization was found in 21% of AD patients.<sup>21</sup> Although the frequency of single and multiple food allergen sensitization was found to be higher than in our patients, the ratio of the frequency of single and multiple food allergen sensitization to each other is similar to that in our study.

In our study, the ages of both patients with single and multiple food allergen sensitization were significantly lower than those without food allergy. There was no difference in age between those with multiple food allergen sensitization and those with a single food allergen sensitization. In a study, children with AD with food allergen sensitization were mostly in the younger age group, although statistical significance was not observed.<sup>21</sup> Similarly, in a different study, the risk of developing food allergy was reported to be higher in AD patients under the age of 2 years.<sup>23</sup> Since the development of food allergen sensitization is seen at younger ages in AD patients, especially younger age groups should be followed up for the development of allergy in clinical follow-up.

In our study, total IgE values of AD patients with multiple food allergen sensitization were significantly higher than those with single allergen positivity and those without food allergen sensitization. Since IgE plays a role both in the pathogenesis of AD and in the pathogenesis of food allergy,<sup>5,24,25</sup> it is expected that total IgE levels are higher in AD patients with food allergen sensitization, and this elevation is more pronounced in those with multiple food allergen sensitization. In the light of our study results; there is a need for multicenter studies to evaluate some clinical factors such as the clinical severity of AD and the duration of the disease, and to clarify other factors that may be associated with the development of food allergen sensitization in AD patients.

### Limitations and Strengths

The fact that our study was conducted in a single center creates a limitation in terms of the generalizability of the results. In addition, the lack of clinical severity scores of AD patients may have caused to find a lower rate of food allergen sensitization in AD patients compared to the literature. This is another limitation of our study. In addition, the evaluation of the frequency of food allergen sensitization in children with AD, the presence of multiple food allergen sensitization and the factors associated with the presence of food allergen sensitization contributes to the literature with a broad perspective. This is the strength of the study.

## CONCLUSION

In the study we conducted in children with AD, approximately one out of every three children (34.2%) had food allergen sensitivity. The frequency of multiple food allergen sensitivity was 12.9%. The frequency of food allergen sensitivity was found to be mostly against eggs (26.4%), cow's milk (12.2%), and peanuts (9.5%). A significant correlation was found between age, total IgE values and the presence of food allergen sensitivity in AD patients. Children with food allergen sensitivity had significantly lower age and higher total IgE values. Factors that may be associated with the development of food allergen sensitivity should be considered in the treatment and management of the disease in children with AD. Thus, preventive measures can be taken more quickly and practically in children who are more prone to the development of food allergies.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date:04.07.2023, Decision No: 240).

**Informed Consent:** Because the study was conducted retrospectively, no written informed consent form was obtained from parents and the patients.

**Referee Evaluation Process:** Externally peer reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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