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Original Article

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Evaluation of clinical and laboratory findings in patients with atopic dermatitis: A retrospective study

Abstract

Aim: Atopic dermatitis (AD) is a chronic, itchy inflammatory skin disease. This study aimed to examine the clinical features, investigate laboratory test results, and evaluate disease prognosis using allergy tests in patients with AD.
Materials and Methods: This retrospective study analyzed patient demographics, clinical characteristics, and laboratory data, including serum eosinophils, serum total IgE, other immunoglobulin (Ig) levels, skin prick test results, and patch test results.
Results: A total of 564 patients were diagnosed with AD, of whom 343 (60.8%) were boys. Skin prick tests were positive in 138 (35.1%) patients. Eosinophilia was more common in patients with food sensitivity within the first year of life ($p<0.001$). Patch test hypersensitivity was observed in half of the 32 patients tested. During follow-up, tolerance developed in 67.4% of 123 patients. Girls developed tolerance to foods earlier than boys ($p=0.005$). Sensitivity to inhaled allergens was higher in patients who developed tolerance after 2 years of age compared to those who developed tolerance before 2 years ($p=0.001$).
Conclusion: Elevated serum eosinophil counts in AD patients within the first year of life may indicate a higher risk of food sensitivity. Atopy patch tests may help clarify food allergies, and clinicians should consider that AD patients are at risk for aeroallergen sensitivities in addition to food sensitivities.

Keywords: Atopic dermatitis, food allergy, skin test, patch test, immunglobulin E

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by intense itching and recurrent eczematous lesions (1). The estimated prevalence of AD in children is 15-20% (2). Diagnostic tools such as serum total immunoglobulin (Ig) E, serum allergen-specific IgE, skin prick test (SPT), and atopy patch test (APT) are commonly used to detect potential allergen hypersensitivity. The allergic hypersensitization process, known as the "atopic march," often begins with AD and food allergy (FA) in early childhood and may progress to aeroallergen sensitivity, asthma, and allergic rhinitis later in life (1,3,4). Clinical studies indicate that approximately 35% of children with AD have concurrent food allergies (5).

This study aimed to determine the demographic and clinical characteristics of patients diagnosed with AD in our outpatient clinic, examine their laboratory findings (serum eosinophil count, serum total IgE, IgA, IgG, and IgM levels, as well as SPT and APT results), and evaluate the disease prognosis.

MATERIALS AND METHODS

This retrospective study included AD patients aged 1 month to 18 years who visited the Pediatric Immunology and Allergy Outpatient Clinic at Dokuz Eylül University Faculty of Medicine between January 2016 and 2019. All patients met the Hanifin and Rajka diagnostic criteria for AD (5). Patients with chronic diseases and immune deficiencies were excluded. The clinical

and demographic characteristics, as well as the laboratory parameters of the patients, were retrospectively recorded from the hospital data system. Patients were grouped based on their SPT results as either SPT-positive or SPT-negative. Food tolerance was evaluated in patients with hypersensitivity to four primary foods: milk, egg, wheat, and soy. Full tolerance was defined as the patient's ability to consume these foods without adverse reactions. Based on the age of tolerance development, patients were further classified into two groups: those who developed tolerance at 2 years of age or younger (≤2 years) and those who developed tolerance after 2 years of age (>2 years). Ethics approval was obtained from the Local Ethics Committee of Dokuz Eylül University.

A serum total IgE level of 45 IU/mL or higher was defined as high IgE, and a total eosinophil count of 470 cells/mm³ or higher was defined as eosinophilia (6).

SPT results were evaluated in patients who had abstained from antihistamines and systemic steroids for at least one week prior to testing. Indurations greater than 3 mm compared to the negative control were considered positive. The allergens tested included house dust mites (Dermatophagoides farinae and D. pteronyssinus), mold fungi (Alternaria, Cladosporium, Aspergillus fumigatus), animal antigens (cat and dog), pollens (grass mix, weed, mugwort, and tree pollens including alder, poplar, birch, beech, olive), and food allergens (milk, egg yolk, egg white, wheat, and soy) (Alk-Abello®, Hørsholm, Denmark).

For the APT, allergens (fresh milk, egg white and yolk, soy) were placed into the chambers of an IQ Ultimate™ patch (Chemotechnique MB, Vellinge, Sweden). Each chamber had a volume of 32 µL and an internal area of 64 mm². The allergen-filled chambers were applied to the patient's back using adhesive hypoallergenic tape.

Patients were initially evaluated 48 hours after application, 20 minutes after removing the patches. A second evaluation was conducted 24 hours later (72 hours after the test initiation). Evaluations followed the European Task Force on Atopic Dermatitis guidelines, with reactions of 2+ or higher considered positive (7).

Serum IgA, IgM, and IgG levels were classified based on Turkish pediatric age norms: values below -2 SD were considered low, values above +2 SD were considered high, and intermediate values were deemed normal (8).

Statistical Analysis

Data analyses were conducted using SPSS software (version 22.0). The Shapiro-Wilk and Kolmogorov-Smirnov tests were applied to assess data normality. If any group did not meet the assumption of normality, nonparametric testing methods were used.

Logistic regression analysis was performed to identify factors influencing the development of food tolerance. Categorical data between the two groups were compared using the chi-square test, while the Mann-Whitney U test was employed to compare continuous variables that did not follow a normal distribution. A significance level of 95% confidence interval (CI) and a p-value<0.05 were considered statistically significant.

RESULTS

A total of 564 patients with AD were included in the study, of whom 343 (60.8%) were boys. The mean age of patients at their first visit to our clinic was 15.34±13.33 months, with 329 patients (58.3%) aged 1 year or younger.

All patients presented with skin rash, with itching being the most common accompanying symptom, reported by 31% of patients. Gastrointestinal symptoms accompanied skin symptoms in 11.9% of cases, respiratory symptoms in 20.2%, and both gastrointestinal and respiratory symptoms in 1.6% of cases (Table 1).

Table 1. The clinical and demographic characteristics of patients with AD

Gender		Girls, n (%)	Boys, n (%)	Total, n (%)
Age on admission	0-12 mo	122 (21.6)	207 (36.7)	329 (58.3)
	13-24 mo	48 (8.5)	72 (12.8)	120 (21.3)
	25-60 mo	51 (9)	64 (11.4)	115 (20.4)
Mode of delivery	VD	124 (22)	96 (17)	220 (39)
	C/S	141 (25)	203 (36)	344 (61)
Time of birth	Term	199 (35.3)	307 (54.4)	506 (89.7)
	Premature	22 (3.9)	36 (6.4)	58 (10.3)
Family history of allergic disorders	Yes	134 (23.7)	197 (35)	331 (58.7)
	No	87 (15.4)	146 (25.9)	233 (41.3)

Eosinophilia was present in 291 (53.1%) of the 549 patients with available blood counts at admission. Among the 527 patients with measured serum total IgE levels, 218 (41.3%) had elevated IgE levels. Elevated IgE was observed in 144 male patients (27.3%), with significantly higher levels in male patients compared to females (p=0.02). Additionally, patients aged 2 years and older showed significantly higher IgE levels (p<0.001).

In patients with low Ig G, A, or M levels at admission, these levels normalized during follow-up. No cases of immunodeficiency were identified. There was no significant correlation between low Ig levels at admission and food hypersensitivity (p>0.05).

The data on eosinophil counts and Ig levels are summarized in Table 2.

Table 2. The laboratory data of patients with atopic dermatitis at the time of admission

Laboratory data		n	%
Eosinophil count[a]	**Normal**	258	46.9
	High	291	53.1
Eosinophil percent[a]	**<4%**	320	58.3
	≥4%	229	41.7
Serum total IgE level[b]	**Normal**	309	58.6
	High	218	41.4
Serum IgA level[c]	**Normal**	252	97.3
	Low	7	2.7
Serum IgG level[d]	**Normal**	150	89.3
	Low	18	10.7
Serum IgM level[e]	**Normal**	154	95.7
	Low	7	4.3

a: distribution for 549 patients, b: distribution for 527 patients, c: distribution for 259 patients, d: distribution for 168 patients, e: distribution for 161 patients, whose data could be reached

SPT was performed on 393 (69.7%) patients at the time of admission, with hypersensitivity to at least one allergen detected in 138 (35.1%) of these patients. Among the SPT-positive patients, hypersensitivity to food allergens was identified in 109 (79%), hypersensitivity to aeroallergens in 15 (10.9%), and both food and aeroallergens in 14 (10.1%). The distribution of allergen hypersensitivities by age at presentation is shown in Figure 1.

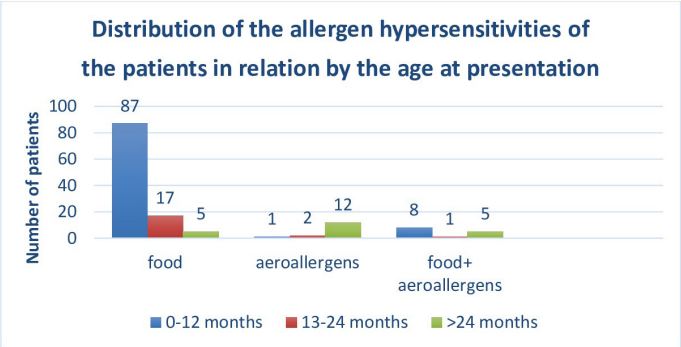

Figure 1. The distribution of allergen hypersensitivities by age at presentation

The most common food hypersensitivities were to egg (21.3%) and milk (12.2%). The most frequent aeroallergen hypersensitivities were to cat dander (11 patients), grass pollens (9 patients), and house dust mites (9 patients), in rank order. SPT results indicated that food allergen hypersensitivity was significantly higher in patients within the first year of life compared to those older than 1 year (p<0.001).

The mean age of patients with aeroallergen hypersensitivity on SPT was 29.28±18.78 months. Aeroallergen sensitivity was significantly more common in patients aged 2 years and older compared to those under 2 years (p<0.001).

Eosinophilia was significantly more common in patients with FA diagnosed within the first year of life compared to those without FA in the first year (p<0.001). However, no significant association was observed between total IgE levels and FA within the first year (p>0.05).

Overall, both eosinophil counts and serum total IgE levels were significantly higher in the SPT-positive group compared to the SPT-negative group (p<0.001). Hypersensitivity detected by SPT showed no correlation with gender, delivery type, gestational age at birth, or family history of allergic disorders (Table 3).

Table 3. Evaluation of patients according to skin prick testa results

		Positive (n/%)	Negative (n/%)	p-value
Gender	**Female**	54 (13.8)	99 (25.2)	0.52
	Male	84 (21.3)	156 (36.7)	
Mode of delivery	**VD**	44 (11.2)	98 (25)	0.22
	C/S	94 (24)	157 (39.8)	
Time of birth	**Term**	126 (32)	230 (58.5)	0.43
	Premature	12 (3.1)	25 (6.4)	
Eosinophil countb	**Normal**	52 (13.4)	143 (37.1)	<0.001
	High	82 (21.2)	109 (28.3)	
Serum total IgEc	**Normal**	59 (15.6)	153 (40.4)	<0.001
	High	79 (20.8)	88 (23.2)	
Family history of allergic disorders	**Positive**	86 (21.9)	156 (39.7)	0.45
	Negative	52 (13.2)	99 (25.2)	

a: Distribution for 393 patients who underwent skin prick test, b: Distribution for 386 patients whose eosinophil level was measured, c: Distribution for 379 patients whose serum Total IgE levels were measured

Among the 32 patients with suspected FA at admission but negative SPT results, half (16 patients) were positive for APT. Of these APT-positive patients, 10 showed sensitivity to egg, 4 to milk, and 2 to soy. Serum total IgE levels were within normal range in 81.2% of these patients. Gastrointestinal symptoms were the most common accompanying findings alongside skin symptoms in this group.

Full tolerance to allergenic foods developed within the first 72 months in 83 (67.4%) of 123 patients with FA, with 49 (39.9%) achieving tolerance within the first 2 years of life. The median age for tolerance development was 22 months (range: 7–72 months). Among patients who developed tolerance, 54 (65%) were determined to be tolerant following food provocation tests conducted in our clinic, while 29 (34.9%) achieved tolerance through consumption of allergenic foods at home without adverse reactions.

Tolerance development occurred significantly earlier in girls than in boys, with a median age of 19 months (range: 8–58 months) for girls and 23 months (range: 7–72 months) for boys (p=0.005). Food tolerance was found to be 4.3 times more likely in girls than in boys (OR 4.33, 95% CI, 1.58–11.86, p=0.004). Aeroallergen hypersensitivity was significantly higher in patients who developed tolerance after 2 years of age compared to those who developed tolerance by age 2 (p=0.001).

There was no significant correlation between age at presentation, serum total IgE level, eosinophil count, and tolerance development (p=0.06, p=0.11, p=0.88, respectively). However, patients with eosinophilia at admission were more likely to develop tolerance within the first 2 years (p=0.01).

DISCUSSION

In our study, we analyzed the findings of patients diagnosed with AD and observed that food sensitization was more prevalent than inhalant sensitization during the first year of life, as determined by skin prick test results. Furthermore, serum eosinophil levels were significantly elevated in patients with food sensitization.

The prevalence of AD continues to rise globally, with rates varying between 5% and 20% across different geographic regions (9). In a birth cohort study conducted in Adana, Türkiye, 59.3% of infants with AD were male (10). Other studies have also indicated a higher prevalence of FA among male individuals (11,12). Consistent with these findings, the majority of AD patients in our study were boys (male-to-female ratio: 1.55:1), and boys made up a significant proportion of patients with food sensitivity.

A study on children with AD reported that the most common symptoms were dry skin (64.2%) and itching (62.9%) (13). In our study, rash was present in all patients, with itching as the second most common complaint at 31%. We attribute the lower rate of reported itching in our study to the younger age of our patient cohort, as the majority were under 1 year old, an age at which children may not effectively express itching as a symptom.

Most patients with AD exhibit elevated serum total IgE levels and peripheral blood eosinophilia (14). Hon et al. (15) reported elevated total IgE levels in patients with eczema and positive SPT hypersensitivity. Similarly, a study from Türkiye found that both eosinophil percentages and serum IgE levels were significantly higher in children with food hypersensitivity, especially those aged 0–6 months (16). Akan et al. (17) demonstrated a relationship between eosinophilia and allergic sensitization in AD patients.

In our study, total IgE and eosinophil counts were significantly higher in patients with food hypersensitivity, with eosinophilia showing particular significance in children under 1 year old compared to total IgE. Therefore, detecting eosinophilia in pediatric patients with suspected FA in primary care may warrant referral to allergy clinics for further investigation.

The prevalence of FA in patients with AD has been reported to range between 30% and 40% in various studies. One study found food hypersensitivity in 21% of AD patients (16). In our study, food sensitivity was present in 31.2% of patients, with egg being the most common allergen (21.3%). Similarly, Bregmann et al. (18), reported egg white as the most common allergen in AD patients, and a study from Türkiye also identified egg hypersensitivity as the most prevalent, followed by milk hypersensitivity (16).

It has been noted that food hypersensitivity tends to decrease with age, while aeroallergen hypersensitivity, particularly to cat dander, increases (19). Consistent with these findings, our study found significantly higher rates of food allergen hypersensitivity in the first year of life, with aeroallergen hypersensitivity becoming more prevalent after age two (p<0.001). Additionally, aeroallergen hypersensitivity was more common among patients who developed food tolerance after age two. Thus, we recommend ongoing clinical follow-up for potential aeroallergen hypersensitivity, even in patients who achieve food tolerance over time.

Early diagnosis and treatment may allow for timely intervention in respiratory allergic diseases that can develop later in life. Additionally, treatment approaches such as immunotherapy, which may positively influence prognosis, could be considered for suitable patients.

In our study, food tolerance developed more frequently within the first two years among FA patients who presented with eosinophilia. However, tolerance developed later in male AD patients with high total IgE levels, suggesting that male gender and elevated IgE may play a more significant role in delayed tolerance development than eosinophilia alone. Further comprehensive studies are recommended to better understand these associations.

A study reviewing non-IgE and mixed IgE-mediated food allergies found high specificity (91.5%) but low sensitivity (57.4%) for APT in patients with gastrointestinal symptoms

(20). Similarly, Sirin Kose et al. (21) reported that while APT is diagnostically reliable in AD patients, it shows low sensitivity in those with gastrointestinal symptoms. In our study, APT was applied to SPT-negative AD patients, revealing food hypersensitivity in half of the tested individuals. Among these patients, gastrointestinal symptoms were the most common complaint accompanying the rash. These findings suggest that APT may serve as an alternative diagnostic tool for food hypersensitivity in AD patients, particularly those with suspected FA and gastrointestinal symptoms.

Celiksoy et al. (22) found that hypogammaglobulinemia was more common in children with AD than in healthy controls. Another study examining eight children with AD and hypogammaglobulinemia reported that, although these patients had low serum IgG levels in infancy, they recovered clinically within two years of admission and did not develop permanent immunodeficiency (23). Similarly, in our study, all patients with low serum Ig levels at admission achieved normal levels during follow-up, and none were diagnosed with immunodeficiency. Additionally, we found no significant association between low Ig levels and the development of food hypersensitivity.

In the study by Martinez et al. (24), 52% of children under 2 years with egg allergy developed tolerance within a 35-month follow-up period. Similarly, a cohort study found that 49.3% of children with egg allergy achieved tolerance by 72 months (25). In our study, 67.4% of patients with FA developed tolerance within the first 72 months, with egg being the most frequently tolerated allergen (69%).

Limitations

The primary limitations of this study are its single-center design and retrospective nature.

CONCLUSION

Eosinophilia in pediatric AD patients, particularly within the first year of life, may serve as an early indicator of potential allergen hypersensitivities, underscoring the importance of referral to specialized allergy clinics for comprehensive evaluation. Additionally, in some AD cases, food allergies undetectable by SPT can be identified through APT, offering a valuable alternative diagnostic tool.

Our findings indicate that over half of the patients with food allergies develop tolerance by age six. However, these patients may remain at risk for new allergen sensitivities and respiratory allergic disorders in later childhood, warranting continued clinical follow-up.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The Ethics Committee of Dokuz Eylül University Faculty of Medicine; No.2019/03-15 dated 02/2019.

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