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ASSOCIATION OF EOSINOPHIL AND TOTAL IGE VALUES WITH ALLERGY TEST RESULTS IN PATIENTS WITH ATOPIC DERMATITIS

ATOPİK DERMATİT TANILI HASTALARIN EOZİNOFİL VE TOTAL IgE DEĞERLERİNİN ALERJİ TEST SONUÇLARIYLA İLİŞKİSİ

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ABSTRACT

Objective: Atopic dermatitis (AD) is a chronic, recurrent, allergic inflammatory skin disease that may have a genetic predisposition. Eosinophilia is a common finding in patients with atopy. In our study, we aimed to investigate the relationship between eosinophil and IgE levels and allergy test results in patients with atopic dermatitis.

Methods: In this descriptive study, the files of patients diagnosed with atopic dermatitis and followed up in our Pediatric Allergy and Immunology Clinic between January 2021 and December 2022 were retrospectively reviewed. Age, gender, eosinophil, total IgE and specific IgE (for food and inhaled allergens) values were analyzed in the study. Skin prick test (SPT) was also performed in patients who had negative results for allergen-specific IgE.

Results: The absolute eosinophil count, eosinophil (%) and total IgE values of patients sensitized to at least one of the food and aeroallergens were significantly higher than those without allergen sensitization. The cut-off point of total IgE in predicting allergen sensitization was found to be 91.5 by ROC analysis. The sensitivity and specificity values for the cut-off point of total IgE were 73.3% and 72.9%.

Conclusion: In this study, allergen sensitization was detected in 3 out of every 4 AD patients with total IgE and eosinophil values above the cut-off point we analyzed. Accordingly, we think that total IgE and eosinophil values are successful in predicting allergen sensitization. In clinics where specific IgE or SPT cannot be performed, eosinophil and total IgE values in whole blood will be useful for preliminary diagnosis.

Keywords: Total IgE, eosinophils, ROC analysis

ÖZ

Amaç: Atopik dermatit (AD), genetik yatkınlık gösterebilen kronik, tekrarlayan, alerjik inflamatuar bir cilt hastalığıdır. Eozinofili, atopi hastalarında yaygın bir bulgudur. Çalışmamızda, atopik dermatit tanılı hastalarda eozinofil ve IgE değerlerinin alerji test sonuçları ile olan ilişkisini incelemeyi amaçladık.

Yöntem: Tanımlayıcı tipte olan çalışmada; Ocak 2021- Aralık 2022 tarihleri arasında atopik dermatit tanısı olan ve Çocuk Alerji ve İmmünoloji Kliniği'mizde takipli hastaların dosyaları retrospektif olarak incelendi. Çalışmada yaş, cinsiyet, eozinofil, total IgE ve spesifik IgE (gıda ve inhaler alerjenler için) değerleri analiz edilmiştir. Hastalarda gıda ve aeroallerjenleri tespit etmek için alerjen spesifik IgE testi yapılmıştır. Alerjen spesifik IgE testi negatif olan hastalara deri prick testi de uygulanmıştır.

Bulgular: Besin ve aeroalerjenlerin en az birisi için duyarlılığı olan hastaların mutlak eozinofil sayısı, eozinofil (%) ve total IgE değerleri alerjen duyarlılığı olmayanlara göre anlamlı olarak daha yüksekti. Hastaların total IgE değerlerinin alerjen duyarlılığını öngörme kapasitesi için ROC analizi yapıldı. Yapılan ROC analizi ile total IgE'nin alerjen duyarlılığını öngörmedeki kesim noktası 91,5 olarak bulundu. Total IgE'nin kesim noktası için sensitivite ve spesifite değerleri %73,3 ve %72,9 bulundu.

Sonuç: Çalışmada, total IgE ve eozinofil değerleri analiz ettiğimiz kesim noktasının üzerinde olan yaklaşık her 4 AD hastasının 3'ünün (%72,2) alerjen duyarlılığı tespit edildi. Buna göre total IgE ve eozinofil değerlerinin alerjen duyarlılığını öngörmede başarılı olduğunu düşünmekteyiz. Spesifik IgE veya deri prick testi bakılamayan kliniklerde ön tanı açısından tam kanda bakılan eozinofil ve total IgE değerleri faydalı olacaktır.

Anahtar Kelimeler: Total IgE, eozinofil, ROC analizi

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Introduction

Atopic disease pathogenesis involves the participation of basophils and eosinophils, along with Immunoglobulin E (IgE). Effector cells engaged in allergic inflammation can be activated by IgE, a fundamental molecule.[5] In the acute phase of atopic disease, particularly at the onset or during exacerbation, IgE is excessively produced due to an increased generation of T helper 2 cytokines in the majority of patients with atopic dermatitis (AD).[6] During the development of related diseases, eosinophils migrate to the affected sites and perform their cellular functions under the influence of the local microenvironment. It has been documented that eosinophils play a crucial role in allergic diseases and combating parasitic infections.[7] Recent studies have explored inflammatory cytokines and biomarkers in several disease contexts.[8, 9]

Our study aimed to explore the correlation between IgE levels, eosinophil counts, and allergy test outcomes in individuals diagnosed with atopic dermatitis. Eosinophils are a cell type that is frequently increased in allergic reactions and total IgE levels are generally accepted as a marker reflecting allergic sensitization. In this context, understanding how eosinophil and IgE levels correlate with allergy test results in patients with AD may be effective in both the pathophysiology of the disease and the development of patient-specific treatment strategies.

Methods

Study type and design

In this retrospective analysis, the records of patients diagnosed with atopic dermatitis and under the care of our Pediatric Allergy and Immunology Clinic from January 2021 to December 2022 were comprehensively examined. During this period, patients with available records and diagnosed with atopic dermatitis were included in the study. The diagnosis of atopic dermatitis was made according to the Hanifin-Rajka diagnostic criteria. Approval for the study's conduct was secured from the Ethics Committee of Umraniye Training and Research Hospital on January 26, 2023, with decision number 24.

Measures

The study involved the analysis of age, gender, eosinophil count, total IgE and specific IgE values (for both food and inhaler allergens). A specific IgE test for allergens, including food and inhalers, was conducted. The patients' IgE and eosinophil values were measured during their initial visit when they had complaints. The eosinophil count was determined from the peripheral blood smear or counter and values higher than 4% were considered eosinophilia. Allergen specific IgE measurements, ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) was used. Specific IgE levels were measured for inhaled allergens (house dust mite, cat epithelium, pollen), food allergens (cow's milk, egg white and food mix (milk, egg white, wheat, peanut, soya, fish) Specific IgE values, equal to or greater than 0,35 kU/L, were considered as positive. Epidermal SPT 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. Patients who underwent SPT were tested for inhaled allergens including house dust mite, cat epithelium, tree mix, cockroach, alternaria and cladosporium. Among food allergens, cow's milk, egg white, egg yolk, wheat, peanut, hazelnut, walnut, chicken, red meat were tested. SPT were administered to patients with negative allergen-specific IgE results. Allergen positivity was defined as a positive outcome in either the allergen-specific IgE test or the SPT.

Statistical Analysis

The SPSS for Windows 25.0 program was employed for the statistical analysis and record of data. Descriptive results, including median, interquartile range (IQR), numbers (n), and percentages (%), were presented. The normal distribution was assessed using both visual (graphics) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). In cases of non-normally distributed data, the Mann–Whitney U test was applied to compare two independent variables. The Chi-square test was utilized to compare categorical data. Receiver Operating Characteristics (ROC) curve analysis was conducted to evaluate the predictive capacity of total IgE, eosinophils (absolute), and eosinophils (%) values for specific IgE test positivity concerning food and aeroallergens. Sensitivity and specificity values were computed for cut-off points. A significance level of $p<0,05$ was considered for statistical significance.

Results

The study assessed data from 486 pediatric patients diagnosed with AD. Among the patients, 53.9% (n=262) were male. The median age of the participants was 2.0 years (1.0-5.0). Table 1 presents the median values for absolute eosinophils, eosinophils (%), and total IgE, which were 290.0 10^3/uL (180.0-500.0), 3.4% (2.1-5.4), and 77.0 IU/ml (17.0-241.0), respectively. Aeroallergen sensitisation was present in 71 (14.6%) patients, food allergen sensitisation was present in 99 (20.3%) patients, and both food and aeroallergen sensitisation were present in 17 (3.5%) patients. While 129 (26.5%) of the patients had signs of allergic rhinitis (AR), 65 patients (13.3%) had asthma symptoms and 113 (23.2%) had food allergy symptoms (Table 1).

Patients with sensitization to at least one food or aeroallergen exhibited significantly elevated values in absolute eosinophil count, eosinophil (%), and total IgE compared to those without allergen sensitization ($p<0.001$). No notable correlation was observed between

age and the presence of allergen sensitization (p=0.195) (Table 2).

Tablo 1. Demographic and obstetric data of the participants

	n (%)
Gender	
-Male	262 (53.9)
-Female	224 (46.1)
.	**Median (IQR)**
Age (years)	2.0 (1.0-5.0)
Eosinophils (absolute) (10^3/Ul)	290.0 (180.0-500.0)
Eosinophils (%)	3.4 (2.1-5.4)
IgE (IU/ml)	77.0 (17.0-241.0)
	n (%)
Aeroallergen sensitivity	71.0 (14.6)
Food allergen sensitivity	99.0 (20.3)
Both food and aeroallergen sensitivity	17 (3.5)
Symptoms	
-Allergic rhinitis	129 (26.5)
-Asthma	65 (13.3)
-Food allergy	113 (23.2)

IQR:Interquartile range,

Conducting ROC analysis aimed to assess the predictive capability of total IgE values for allergen sensitization. The analysis revealed a cut-off point of 91.5 for total IgE in predicting allergen sensitization. The Area Under the Curve (AUC) (95% CI) was determined as 0.785 (0.772-0.843) (p<0.001) through ROC analysis. Sensitivity and specificity values for the identified cut-off point of total IgE were 73.3% and 72.9%, respectively.

In the ROC analysis for eosinophil values, the AUC was low (0.622 and 0.633, respectively). Therefore, the cut-off points for absolute and % eosinophil values were 500.0 and 5.0%, respectively. Patients with at least one of the absolute eosinophil and eosinophil (%) values above the cut-off point and total IgE above 91.5 were considered criteria positive. Allergen sensitization was detected in 72.2% (n=65) of criteria positive patients (n=90) (p<0.001) (Table 3).

Discussion

Immunoglobulin E, eosinophils, and basophils are involved in the pathogenesis of atopic disease. IgE is a key molecule that can activate effector cells involved in allergic inflammation.[5]

Table 2. Association of allergen sensitization with age, eosinophils and total IgE

	Allergen Sensitization				
	No		**Yes**		**p value**
	Median	IQR	Median	IQR	
Age (years)	2.0	1.00-5.00	2.0	1.0-6.0	0.195
Eosinophils (absolute)(10^3/uL)	250.0	170.0-430.0	380.0	210.0-630.0	<0.001
Eosinophils (%)	2.9	1.9-4.6	4.0	2.6-7.4	<0.001
Total IgE (IU/ml)	33.0	9.0-100.0	194.0	87.0-479.0	<0.001

IQR:Interquartile range

In our investigation, patients exhibiting sensitization to at least one food or aeroallergen displayed significantly elevated absolute eosinophil count, eosinophil (%), and total IgE values compared to those without allergen sensitization. A study by Özkars in the literature indicated higher eosinophil count and IgE levels in atopic dermatitis patients with food allergy compared to those without food allergy.[10]

Table 3. Association between criteria positivity and allergen sensitization

	Allergen sensitization n (%)		**P value**
Criteria positivity* n (%)	No	Yes	
Yes	25 (27.8)	65 (72.2)	<0.001
No	274 (69.2)	122 (30.8)	

* Absolute eosinophils >500, eosinophils (%) >5, total IgE >91.5

In contrast, İlhan et al.'s study on patients with atopic dermatitis found no parallel correlation between food sensitivity and IgE.[11] Lee et al. suggested that AD patients with concomitant allergic rhinitis were more likely to have higher serum IgE levels, attributing it to the proportional relationship between allergen-specific IgE levels and total serum IgE levels.[12] Saglam et al. discovered that median values of eosinophils (both absolute and %) and total IgE were higher in atopic disease patients with positive skin test and positive specific IgE test results compared to those with negative results.[13] Altaş et al.'s study on atopic dermatitis patients revealed higher total IgE levels in those with positive allergy test results compared to those without positive results.[14] Our study corroborates the efficacy of IgE level and eosinophil values as reliable markers for predicting allergies.

Eosinophils are believed to contribute to tissue damage in the pathogenesis of AD by releasing reactive oxygen metabolites and cytotoxic granules.[15] Borres et al.[16] indicated a connection between eosinophilia in peripheral blood and the presence of atopic disease or the likelihood of subsequent development. Our study examined absolute eosinophil count, eosinophils (%), and median values of total IgE. In Jenerowicz et al.'s study on atopic dermatitis patients, the absolute eosinophil count

was reported as 290.0 ± 205.7, eosinophil percentage as 6.3 ± 5.6%, and IgE and absolute eosinophil count were higher in patients with positive SPT compared to those with negative results.[17] Similar findings were observed in our study, with these values occurring at comparable rates.

Our study found a cut-off point of 91.5 in the ROC analysis, assessing the predictive capacity of total IgE values for allergen sensitization. The Area Under the Curve (AUC) was determined as 0.785, with sensitivity and specificity values of 73.3% and 72.9%, respectively. Jenerowicz et al., in their study, employed ROC curve analysis to assess the predictability of measured parameters in distinguishing AD patients from healthy individuals, finding an AUC value of 0.678 for peripheral blood eosinophilia determined by absolute eosinophil count.[17] Saglam et al. conducted ROC curve analysis to assess the predictive capability of eosinophil (absolute), eosinophil (%), and total IgE values for test positivity, which included results from both the SPT and/or specific IgE positivity. The total IgE cut-off point was 104.5 for all patients (AUC: 0.789), with sensitivity and specificity at 72.0% and 71.9%, respectively. In patients with atopic dermatitis, the total IgE cut-off point was 86.5. Notably, our study observed a higher total IgE cut-off point in atopic dermatitis patients compared to Saglam et al.'s study, although sensitivity and specificity rates were comparable.[13]

In conclusion, our findings suggest that total IgE and eosinophil values serve as reliable indicators of atopy in patients showing signs of allergy based on history and physical examination. This allows for patient monitoring until access to more detailed and costly tests, such as specific IgE and SPT, becomes feasible.

Result and Recommendations

In the study, allergen sensitization was detected in 3 out of every 4 AD patients (72.2%) with total IgE and eosinophil values above the cut-off point we analyzed. This suggests that total IgE and eosinophil values effectively predict allergen sensitization. The effectiveness of these laboratory parameters should be acknowledged in both the diagnosis and ongoing monitoring of atopic dermatitis. The risk of developing food allergy is lower in mild atopic dermatitis. Therefore, in mild AD patients, eosinophil and total IgE values in whole blood can be interpreted in terms of allergy in clinics that do not have access to allergy test or specific IgE. Since our patients were generally in the young age group, we did not differentiate by age group, but further studies can be performed with a larger patient group.

Compliance with Ethical Standards

Approval for the study's conduct was secured from the Ethics Committee of Umraniye Training and Research Hospital on January 26, 2023, with decision number 24.

Conflict of Interest

The author declares no conflicts of interest.

Author Contribution

All the authors equally contributed to this work.

Financial Disclosure

None

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