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Original Article PEDIATRICS

Evaluation of the predictive value of total IgE and absolute eosinophil levels on allergy test positivity

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ABSTRACT

OBJECTIVE: Atopic diseases are the most common chronic conditions in childhood. The best treatment for allergic disease is possible with early diagnosis. The purpose of the study was to assess the predictive value of total immunoglobulin E (IgE) and eosinophil levels for allergy test positivity in patients diagnosed with asthma, allergic rhinitis (AR), atopic dermatitis (AD), and food allergy (FA).

METHODS: Pediatric patients between 0 and 18 years old diagnosed with asthma, AR, AD, and FA were included in the study. Demographic characteristics of the patients, total IgE, eosinophil (absolute and %) values, specific igE (SPIGE), and skin prick test (SPT) results were recorded.

RESULTS: The data of 2665 patients were evaluated in the study. Of the patients, 58.6% were male, whereas 41.4% were female. The median age of the children was significantly higher both in SPT-positive and SPIGE-positive patients ($p<0.001$). If the criteria positivity is accepted as total IgE value is ≥104.5 (for AD: 86.5, asthma: 116.5, AR: 120.5, FA: 42.5) and absolute eosinophil ≥500 and/or eosinophil (%) ≥5%; test positivity was higher for each disease and all patients ($p<0.001$).

CONCLUSION: Total IgE and eosinophil levels can be used to identify atopy in patients with symptoms of AD, asthma, and AR. Total IgE and eosinophil values are suitable and easily obtainable parameters for better evaluation of health-care resources for the diagnosis and follow-up of atopic illnesses.

Keywords: Allergy test positivity; eosinophil levels; total IgE.

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Atopy is the genetic predisposition for the production of antibody immunoglobulin E (IgE) as a response to low-dose common environmental factors such as pollen, house dust mites, and food allergens. An atopic individual has a high probability of developing one or more of the diseases such as atopic dermatitis (AD), asthma and allergic rhinoconjunctivitis, and food allergies [1, 2].

Allergic march is used to express the natural course of atopic diseases. A baby born to atopic parents and carrying the genetic burden of atopy has the ability to respond and sensitize to allergens, it encounters from the 1st days of its life. Usually, the first allergic disease to be seen is AD, followed by clinical findings of food allergy (FA). FA, which is present in most of the cases with AD, has an important role in the pathogenesis of the disease. In the later years of life, sensitivity to respiratory allergies develops, and bronchial asthma and allergic rhinitis (AR) findings are added to the table [3].

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Allergic illnesses are the most commonly seen chronic conditions in childhood period. Epidemiological data show that allergic diseases are increasing in parallel with the changing lifestyles and conditions in developed and developing countries. Therefore, the need for allergy testing is increasing [2, 4–6].

The best treatment for allergic disease is possible with early diagnosis. Children are often first evaluated by primary care physicians. In some children, the symptoms are typically suggestive of allergic diseases, such as seasonal AR and conjunctivitis. In some children, allergy should be considered a differential diagnosis; for example, recurrent vomiting in infants. At this stage, it is necessary to determine who, when, and how allergy diagnostic tests will be performed [4].

Allergy is a hypersensitivity reaction to a specific allergen and is started with immunological mechanisms [7]. IgE starts and augments the inflammatory process and in this way the allergic reaction [8, 9]. Eosinophilia is seen with various situations. Some of these conditions are asthma, atopic diseases, helminth infections, drug hypersensitivity reactions, and neoplasms [10]. IgE and eosinophil values have different roles on the disease process. In this process, while IgE is the cause of allergic asthma; eosinophilia can be interpreted as a result of this whole process [9].

The aim of our study was to assess the predictive value of total IgE and eosinophil levels for allergy test positivity in patients diagnosed with asthma, AR, AD, and FA.

Highlight key points

- The predictive value of total immunoglobulin E (IgE) and eosinophil levels for allergy test positivity in patients diagnosed with asthma, allergic rhinitis (AR), atopic dermatitis (AD) and food allergy (FA) were evaluated.
- If the criteria positivity is accepted as total IgE value is ≥104.5 (IU/ml) (for AD: 86.5, asthma: 116.5, AR: 120.5, FA:42.5) and absolute eosinophil ≥500 (cells/μL) and/or eosinophil (%) ≥5%; test positivity was found to be significantly higher for each disease group and all patients.
- Total IgE and eosinophil values are suitable and easily obtainable parameters for better evaluation of health care resources for the diagnosis and follow-up of atopic illnesses.

Table 1. Sociodemographical and laboratory features of the patients

	n	%
Gender		
Female	1104	41.4
Male	1565	58.6
	Median (min–max)	
Age (years)	5 (0–17)	
Eosinophil (absolute) (1/μL)	270 (0–17720)	
Eosinophil (%)	3.1 (0–54.6)	
Total IgE (IU/mL)	92 (0–16076)	

IgE: Immunoglobulin E; Min: Minimum; Max: Maximum.

MATERIALS AND METHODS

This retrospective study was conducted in the Pediatric Allergy and Immunology Department of our hospital, from August 2021 to March 2022. The same Umraniye Training and Research Hospital Clinical Research Ethics Committee approval was taken for conducting the study (31.03.2022/112). Informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki.

Children aged 0–18 years with a diagnosis of asthma, AR, AD, and FA are included in this study. Among these patients, children with complete blood count, total IgE measurement, specific igE (SPIGE), and skin prick tests (SPT) (aeroallergen: house dust mite, pollen, cat; food: milk, eggs, and peanuts) recorded in their files were included in the study. Children with viral infections, parasitic infestations, immunocompromised states, and chronic pulmonary diseases were excluded from the study.

The name, surname, age, gender, and diagnosis of the patients were recorded. The samples were collected by venopuncture, and the serum was separated by centrifugation for total IgE measurements. Eosinophil (absolute) and eosinophil (%) values were determined by examination of the complete blood count. Total IgE measurements were made by nephelometric method (Siemens Healthcare Diagnostics Products; Marburg, Germany). Fluorescent enzyme immunoassay method (UniCAP, Phadia; Uppsala, Sweden) was used for SPIGE measurements. 0.35 kU/l was accepted as the cutoff value for SPIGE results. Skin tests of the patients were performed on the forearm. In the test, histamine (10 mg/mL) was used as positive control; teomin (Laboratoire Stallergens, France) was used as the negative control. Aeroallergen and food allergen (Laboratoire Stallergens, France) were used as allergen. The tests were evaluated after 15–20 min. An induration of at least 3 mm greater than the negative control was considered positive.

Table 2. Relationship between the test positivity and patients' age and laboratory features

	SPT positivity		SPIGE positivity		Test positivity*	
	Negative	Positive	Negative	Positive	Negative	Positive
Age (years)	4 (0–17)	7 (0–17)	4 (0–17)	5 (0–17)	4 (0–17)	5 (0–17)
p-value**	<0.001		<0.001		<0.001	
Eosinophil (absolute) (1/μL)	260 (0–17720)	350 (0–1830)	230 (0–17720)	370 (0–5670)	220 (0–17720)	370 (0–5670)
p-value**	<0.001		<0.001		<0.001	
Eosinophil (%)	3 (0–54.6)	4.4 (0–22)	2.7 (0–54.6)	4.4 (0.0–48.9)	2.5 (0.0–54.6)	4.4 (0–48.9)
p-value**	<0.001		<0.001		<0.001	
Total IgE (IU/mL)	79.9 (0–16076)	224 (1.0–6589)	53 (0–6727)	216 (1.0–16076)	43 (0–6727)	216 (1.0–16076)
p-value**	<0.001		<0.001		<0.001	

SPT: Skin prick test; SPIGE: Specific immunoglobulin E; Min: Minimum; Max: Maximum; *: SPT positivity and/or SPIGE positivity; **: Mann–Whitney U test.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, New York: IBM Corporation. Demographic and clinical characteristics of the patients were presented using descriptive analyses as percentages (%), frequencies (n), medians, minimum, and maximum values. Conformity of continuous variables to normal distributions was examined by visual (histogram and probability graphs) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Mann–Whitney U test was used in cases where normal distribution was not observed for the comparison of the two independent groups. The Chi-square test was used for the analyses of categorical variables. The capacity of serum total IgE, eosinophil (absolute), and eosinophil (%) values in predicting test positivity (SPT and/or SPIGE positivity) analyzed using receiver operating characteristics (ROC) curve analysis. When a significant cutoff value was observed, sensitivity and specificity were presented. While evaluating the area under the curve (AUC) and all statistical tests, $p<0.05$ was considered a statistically significant result.

RESULTS

The data of the 2665 patients were evaluated in the study. Of the patients, 58.6% were male, whereas 41.4% were female. Median age was 5.0 (0–17) years. The median values of the absolute eosinophil, % eosinophil, and total IgE were 270 (cells/μL) (0–17720), 3.1 (0–54.6), and 92 (international units [IU]/mL) (0–16076), respectively (Table 1).

In the evaluation of SPIGE, 33.3% in total, 23.3% with aeroallergens, and 12.6% with food allergens were detected. The highest rate of aeroallergens was determined for house dust mite with 20% and the highest rate of food allergens was determined for egg with 10.5%.

In prick tests, 13.3% in total, 12.7% with aeroallergens, and 0.7% with food allergens were detected. The highest rate of aeroallergens was determined for house dust with 12.3%, and the highest rate of food allergens was determined for egg with 0.6%.

The median age of the patients was significantly higher both in SPT-positive and SPIGE-positive patients when compared to negative patients ($p<0.001$). Median age was higher also in patients having either SPT or SPIGE-positive results or both (test positivity) ($p<0.001$). Eosinophil (absolute and %) and total IgE median values were also higher in patients with positive test results when compared to negative patients ($p<0.001$) (Table 2).

The capacity of serum total IgE, eosinophil (absolute), and eosinophil (%) values in predicting test positivity (SPT and/or SPIGE positivity) analyzed using ROC curve analysis. The cutoff value for the total IgE was 104.5 (IU/mL) (AUC [95% CI]: 0.789 [0.771–0.806]) among all patients ($p<0.001$). Sensitivity and specificity were 72.0% and 71.9, respectively. Other cutoff values, sensitivity and specificity, and AUC are also presented in Table 3.

If the criteria positivity is accepted as total IgE value is ≥104.5 (IU/mL) (for AD: 86.5, asthma: 116.5, AR: 120.5, and FA:42.5) and absolute eosinophil ≥500 (cells/μL) and/or eosinophil (%) ≥5%; test positivity was found to be significantly higher for each disease group and all patients ($p<0.001$) (Table 4).

TABLE 3. ROC analysis of the laboratory values

	Sensitivity (%)	Specificity (%)	AUC	95% CI	p
Total IgE (IU/mL)					
All patients					
Cut-off: 104.5	72.0	71.9	0.789	0.771–0.806	<0.001
AD					
Cut-off: 86.5	73.1	71.9	0.787	0.747–0.827	<0.001
Asthma					
Cut-off: 116.5	72.7	72.6	0.803	0.778–0.829	<0.001
AR					
Cut-off: 120.5	72.4	72.4	0.803	0.783–0.824	<0.001
FA					
Cut-off: 42.5	73.4	72.8	0.797	0.755–0.840	<0.001
Eosinophil (absolute) (1/µL)					
All patients					
Cut-off: 275	63.6	61.5	0.662	0.640–0.683	<0.001
AD					
Cut-off: 295	61.1	59.4	0.622	0.572–0.672	<0.001
Asthma					
Cut-off: 285	65.3	62.6	0.679	0.647–0.711	<0.001
AR					
Cut-off: 265	65.9	63.9	0.690	0.664–0.716	<0.001
FA					
Cut-off: 305	58.0	59.8	0.606	0.550–0.661	<0.001
Eosinophil (%)					
All patients					
Cut-off: 3.25	64.4	63.4	0.677	0.656–0.698	<0.001
AD					
Cut-off: 3.45	60.2	58.6	0.644	0.595–0.693	<0.001
Asthma					
Cut-off: 3.25	65.5	65.1	0.689	0.657–0.721	<0.001
AR					
Cut-off: 3.25	67.5	66.7	0.711	0.686–0.716	<0.001
FA					
Cut-off: 3.35	61.5	60.2	0.631	0.576–0.686	<0.001

AD: Atopic dermatitis; AR: Allergic rhinitis; FA: Food allergy; AUC: Area under curve; CI: Confidence interval.

DISCUSSION

In our study, the predictive value of allergy test positivity of total IgE, absolute, and percent eosinophil levels in patients diagnosed with asthma, AR, AD, and FA was evaluated. When total IgE, absolute, and percent eosinophil values were compared separately with test positivity (SPT positivity and/or SPIGE positivity), a statistically significant correlation was detected. Total igE, absolute, and % eosinophil's values were thought to have a high predictive value for allergies.

Allergy can be suspected with a careful history and a good physical examination, but some specific tests may be needed for a definitive diagnosis. The gold standard for the determination of specific allergens is the ImmunoCAP® immunoassay, but this method can be expensive and requires specialist equipment and skill. Despite the low negative predictive value of the total IgE level, many

Table 4. Frequency of test positivity of the patients having criteria positivity

Criteria positivity	Test positivity									
	AD		Asthma		AR		FA		All patients	
	n	%	n	%	n	%	n	%	n	%
Positive	78	79.6	214	78.7	319	79.6	54	74.0	425	77.0
Negative	138	34.8	287	34.7	443	35.5	115	32.8	672	33.7
p-value*	<0.001		<0.001		<0.001		<0.001		<0.001	

AD: Atopic dermatitis; AR: Allergic rhinitis; FA: Food allergy; Criteria positivity: Total IgE value is ≥104.5 (IU/mL) (for AD: 86.5, asthma: 116.5, AR: 120.5, FA: 42.5) and absolute eosinophil ≥500 (1/ µL) and/or eosinophil (%) ≥5%; Test positivity: Skin prick test and/or specific IgE positivity; *: Pearson Chi-square test.

immunologists use this test for the initial evaluation of patients with suspected allergies [11–13].

IgE levels have played an important role in the evaluation of patients with allergic disease for many years [14, 15], although insufficient sensitivity has been reported [16]. The prevalence of allergic diseases continues to increase worldwide, and therefore many studies are being conducted on the total IgE level and its relationship to atopy and allergic diseases [17–19]. Both doctors and parents want children with allergic diseases to be diagnosed quickly [16, 20, 21].

In asthma, the inflammation and repair process leads to remodeling of the airway. There is strong evidence that eosinophils play an important role in the pathophysiology of allergic and non-allergic asthma. In eosinophil value in blood, it is an indirect marker of airway inflammation in asthma. In addition, the absolute eosinophil count in peripheral blood is a widely used laboratory value to indicate the allergic etiology of the disease [22].

Accurate diagnosis facilitates the selection of appropriate management strategies, such as immunotherapy or allergen avoidance. Conversely, the value of a negative allergy diagnosis should not be underestimated. Because this can avoid trials with various inappropriate drugs, unnecessary avoidance measures [23].

In our study group, 58.6% were males and 41.4% were children, and the median age was 5 (0–17) years. The median age of the patients was significantly higher both in SPT-positive and SPIGE-positive patients when compared to negative patients ($p<0.001$). The median age was higher also in patients having either SPT or SPIGE-positive results or both (test positivity) ($p<0.001$). It was thought that allergy tests could be a better diagnostic tool as age increases.

In this study, when total IgE levels were compared with SPT and sp SPIGE test positivity separately and together, it was found to be significantly higher in all cases. It was concluded that the total IgE level is a good diagnostic tool to predict allergy. In some studies, it has been concluded that routine measurements of serum IgE levels in allergic patients or in patients with suspected allergic disease are helpful in evaluating the presence and severity of atopic sensitization. However, eosinophil (absolute and %) and median values were also higher in patients with positive test results when compared to negative patients ($p<0.001$). These results are in accordance with the previous studies [6, 14, 24]. Elevated IgE in early childhood period appears to be an early predictor of the subsequent appearance of allergen- SPIGE and allergic disease [25].

100 IU/mL total IgE is considered as breakpoint in all age groups except infants. The sensitivity of total IgE in allergic diseases due to multiple allergens is higher than in any type of allergy when the cutoff value is accepted as 195 IU/mL [6].

In our study, cutoff values were determined as 104.5 for total IgE, 275 for absolute eosiophil and 3.25 for eosinophil percentage in all patients.

The lowest cutoff value for total igE was found in the FA group, and the highest cutoff value was found in the asthma group. Absolute eosinophil cutoff values were close to each other in the allergic disease groups that we studied. The highest value was found in the FA group and the lowest value in the AR group. Percent eosinophil cutoff values were almost similar, and the highest value was in the AD group.

In one study, non-allergic patients with a total serum IgE >150 IU)/mL had a five-fold higher risk of developing asthma [26].

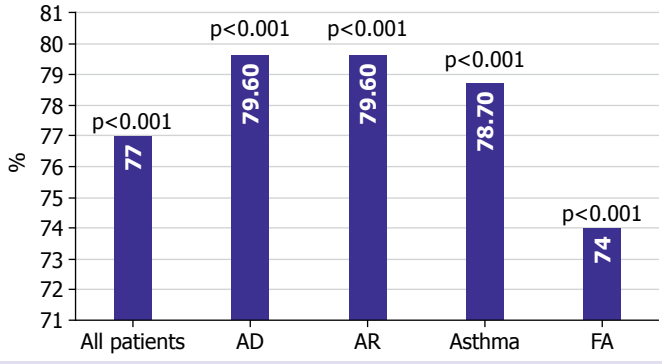

FIGURE 1. Frequency of test positivity of the patients having criteria positivity.

AR is associated with positive skin test reactions (or allergen-SPIGE antibodies) but independent of total IgE levels [27]. Measurement of total IgE has low sensitivity (44%) in identifying patients with current AR [28]. In addition, AR may also exist even with normal IgE levels [29].

In our study, a statistically significant correlation was found when the positivity criteria determined by the study for each atopic disease (AD, asthma, and AR) and FA were compared with the test positivity (SPT positivity and/or SPIGE positivity) (Fig. 1). We considered that total igE and eosinophil values, especially when evaluated together, were successful in predicting allergy.

It is very important to take a good history in allergic diseases, but it does not make a definitive diagnosis. Tests such as total IgE, skin prick and skin patch tests, and double-blind placebo-controlled food challenge test may be required to support the diagnosis. An increase in total IgE and eosinophils strongly suggests that the person is sensitive to the allergen(s) [5].

The results obtained in our study revealed that total IgE and eosinophil values are reliable parameters in demonstrating the presence of atopy in patients with complaints and physical examination findings suggestive of allergy, who applied to the general pediatric outpatient clinic. Thus, it allows patients to be followed in this direction before or until they perform specific tests, which are relatively difficult to reach and expensive.

In our study, either allergy skin test was performed or SPIGE level was checked in the blood. Both tests were not performed on each patient at the same time. This is one of the limitations of our study. However, the fact that our study was conducted in a single center may have limited the results of the study in terms of evaluating similar patient profiles. In further studies, similar multicenter and population-based clinical studies may be beneficial in terms of more practical recognition of atopic diseases. Another limitation of ours is that the clinical classification of the patients was not evaluated in the study. There may be differences in the diagnostic predictions of eosinophil and IgE parameters in allergic diseases in patients with mild or severe clinical severity. In future studies, this situation can be taken into consideration and evaluations can be made. Although our study was carried out in a single center; it has made an important contribution to the literature in this field with its high sample size and examination of the diagnostic value of eosinophils and IgE in terms of more than one allergic disease. This is the strength of our study.

Conclusion

Our study with a large sample size adds an important aspect to the literature. Our results have practical information about the approach to pediatric patient groups with allergic complaints. In our study, if the criteria positivity is accepted as total IgE value is ≥104.5 (for AD: 86.5, asthma: 116.5, and AR: 120.5, FA: 42.5) and absolute eosinophil ≥500 and/or eosinophil (%) ≥5%; test positivity was higher for each disease and all patients. The presence of atopy could be decided by evaluating total IgE and eosinophil levels. These tests could be used to identify diseases such as AD, asthma, and AR that have allergic pathogenesis. Total IgE and eosinophil values are suitable parameters for better evaluation of health-care resources for the diagnosis and follow-up processes of atopic illnesses. Especially in centers where clinical facilities are less, a more practical diagnosis can be made with the blood eosinophil and IgE values of children who are thought to be have atopic diseases.

Ethics Committee Approval: The Umraniye Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 31.03.2022, number: 112).

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