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ORIGINAL ARTICLE

Retrospective investigation of the relationship between clinical and laboratory parameters and allergy tests in children with allergic rhinitis

Uğur Altaş[1] **Eray Tunce**[2] **Zeynep Meva Altaş**[3] **Fatih Çiçek**[4] **Mehmet Yaşar Özkars**[1]

1 University of Health Sciences Turkey, Istanbul Ümraniye Training and Research Hospital, Department of Pediatric Allergy and Immunology, Istanbul, Turkey
2 University of Health Sciences Turkey, Istanbul Ümraniye Training and Research Hospital, Department of Pediatrics, Istanbul, Turkey
3 Ümraniye District Health Directorate, Istanbul, Turkey
4 University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital, Department of Pediatric Allergy and Immunology, Istanbul, Turkey

Abstract

Background: It was aimed to investigate the relationship between neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), eosinophil-lymphocyte ratio (ELR), serum total immunoglobulin E (IgE) values and allergy test positivity in patients with allergic rhinitis (AR).

Methods: The study is a descriptive study with a retrospective design. Data on patients aged 10-18 years with a diagnosis of AR were investigated retrospectively. Age, gender, hemogram parameters (leukocyte, eosinophil, lymphocyte, platelet), total IgE values, allergy history and allergy test positivity were evaluated. A p value of less than 0.05 was considered as a statistically significant result.

Results: In the study, the data of 230 pediatric patients with AR were analyzed. The median age of the children was 13 years (10-18). Of the patients 57.4% (n=132) were male, 42.6% (n=98) were female. All laboratory values, except PLR, of the patients with positive allergy test were higher than the patients with negative allergy test. This elevation in WBC, neutrophil, absolute eosinophil, eosinophil percentage, total IgE and ELR values was statistically significant ($p<0.05$). When the cut-off point for ELR was 0.066; sensitivity was 78.8% and specificity was 70.4%. When the cut-off point for total IgE is 134.5; sensitivity was 75.8%, specificity was 74.1% ($p<0.001$)

Conclusions: According to study results, 3 out of every 4 patients with positive allergy test can be detected by ELR and total IgE values. Since allergy tests cannot be performed in every clinic, it is extremely important to evaluate the success of more practical and accessible blood tests in predicting allergy test positivity.

Keywords: Allergic Rhinitis, Children, Allergy Test, Laboratory Parameters.

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Corresponding Author:
Uğur Altaş, University of Health Sciences Turkey, Istanbul Ümraniye Training and Research Hospital, Department of Pediatric Allergy and Immunology, Istanbul, Turkey
E-Mail: druguraltas@gmail.com

INTRODUCTION

Rhinitis is presented with symptoms such as nasal congestion, runny nose, sneezing, and itching, arising from an underlying inflammatory process and/or a dysfunctional nasal mucosa (1). Allergic rhinitis (AR) causes a significant burden of disease worldwide (2, 3). For this reason; diagnosis, treatment, and follow-up of allergic rhinitis with laboratory parameters are extremely important for the control of the disease.

Allergic rhinitis refers to an immunoglobulin E (IgE)-mediated reaction against allergens that starts clinically from the nasal mucosa (4, 5). In addition to the nasal inflammation observed in allergic rhinitis, there is also a systemic inflammation (6). In patients with AR, early and late allergic responses triggered by allergens are mediated by a number of inflammatory cells. Within minutes of contact with the allergen, IgE-dependent mast cells degranulate and release synthesized inflammatory mediators. TH2 lymphocytes and eosinophils play a role in immunological processes in both nasal and bronchial tissue. Eosinophils are the dominant cells in the chronic inflammation that is the typical feature of the late-phase allergic response (7).

Neutrophils, lymphocytes, and platelets are important blood parameters that play a role in inflammation. Today, these laboratory parameters are used to evaluate many infectious and inflammatory conditions and are easy to apply and accessible (8). There are data showing that these parameters should be evaluated for the diagnosis and follow-up process of allergic rhinitis as in other allergic diseases (9-11).

Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and eosinophil-lymphocyte ratio (ELR) values are calculated by dividing the blood lymphocyte value, respectively. Many studies in the literature have reported that NLR, PLR, and ELR parameters can be used as inflammatory markers in chronic inflammatory diseases (12-14). In a study conducted in pediatric patients diagnosed with allergic rhinitis in the literature; NLR of children with AR was found to be higher than the control group (14). In a study conducted in adult patients with a diagnosis of allergic rhinitis, ELR was reported to be significantly higher than the control group (12). In another similar study, eosinophil values were elevated in pediatric patients having AR when compared with the control group without AR (15).

In our study, we aimed to investigate the relationship between NLR, PLR, ELR, serum total immunoglobulin E (IgE) values that can be measured from peripheral blood, and allergy test positivity in patients with allergic rhinitis.

MATERIALS and METHODS

Study design, type and sample

The study is a descriptive study with a retrospective design. Data on pediatric patients aged 10-18 years with a diagnosis of allergic rhinitis who applied to the Ümraniye Training and Research Hospital Pediatric Allergy and Immunology outpatient clinic between January 2022 and December 2022 were investigated retrospectively from the hospital's database. No sample size was calculated; all patients with allergic rhinitis who applied to our clinic within a year were included in the study.

Measures

Children's sociodemographic characteristics such as age and gender, hemogram parameters (leukocyte, eosinophil, lymphocyte, and platelet), total IgE values, allergy history, and allergy test positivity were evaluated in the study.

The diagnosis of allergic rhinitis was made when at least 2 of the main symptoms of runny nose, nasal congestion, nasal itching, and sneezing were present for more than 1 hour in a day and for at least 2 consecutive days. These findings were questioned in the outpatient clinic examination of the patients, and the diagnosis of allergic rhinitis was made based on the clinical history and physical examination. Allergen-specific IgE test was performed in order to detect allergens in the patients. Skin prick test was also applied to the patients who had negative results for allergen-specific IgE. Allergy test positivity was defined as a positive allergen-specific IgE or skin prick test. Patients who were both negative were defined as the allergy test negative patient group.

Allergic rhinitis is classified according to symptom duration and severity. Patients with AR symptoms lasting less than 4 days a week or less than 4 weeks are classified as having intermittent AR; Those with symptoms lasting more than 4 days per week and longer than 4 weeks were classified as having persistent AR. While AR patients with at least one of the signs of sleep disturbance, impairment in daily activities, recreational and/or sports activities, deterioration in school or work performance, and disturbing symptoms are classified as moderate-severe AR; patients with none of these findings were classified as mild AR (16).

Statistics

The analysis and the recording of the data were performed with SPSS (Statistical Package for Social Sciences for Windows 25.0) program. Descriptive data were represented as median, minimum, maximum values, numbers (n) and percentages (%). The categorical data was analyzed with the chi-square test. Conformity of continuous variables to the normal distribution was investigated with visual (histograms and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Mann Whitney U test was used to compare continuous variables that did not have a normal distribution. The capacity of serum total IgE, ELR, NLR and PLR values in predicting test positivity (skin prick test or specific IgE positivity) analyzed using ROC (Receiver Operating Characteristics) curve analysis. When a significant cutoff value was observed, the sensitivity and specificity were presented. A p value <0.05 was accepted as the significance level.

Ethics

The study was approved by the Health Sciences University Ümraniye Education and Research Hospital Ethics Committee on 11/05/2023 with decision number 140.

RESULTS

In the study, the data of 230 pediatric patients with AR were analyzed. The median age of the children was 13 years (10-18). Of the patients 57.4% (n=132) were male, 42.6% (n=98) were female. When the AR clinic of the patients was evaluated, most of the patients were persistent moderate-severe (38.3%, n=88) (Table 1).

Table 1. Age, gender and disease clinic of the patients

Age (years), median (min-max)	13 (10-18)	
Gender, n (%)	Female	98 (42.6)
	Male	132 (57.4)
Disease clinic, n (%)	Intermittent Mild	58 (25.2)
	Intermittent Moderate-Severe	18 (7.8)
	Persistent Mild	66 (28.7)
	Persistent Moderate-Severe	88 (38.3)

When the allergy test positivity of the patients was evaluated, house dust mite allergy was the most common, followed by cat and pollen allergies, respectively. House dust mite allergy was positive in 66.1% (n=152) of the patients. The percentage of patients with positive cat and pollen allergy tests were 22.6% (n=52) and 13.0% (n=30), respectively. Two patients had cow's milk allergies and 6 had peanut allergies. Inhalant allergen sensitivity was accompanied by all eight food allergy cases. There was no patient with egg allergy. The number of monosensitized cases was 92 (59.7%), and the number of polysensitized cases was 62 (40.3%). The patient's allergy test positivity and laboratory values such as WBC, neutrophil, and eosinophil are shown in Table 2.

Table 2. Laboratory parameters and allergy test positivity of the patients

Laboratory parameters	*Median (min-max)*
WBC (10^3 mm^3)	7600.0 (4600.0-19510.0)
Neutrophil (10^3/uL)	3920.0 (1800.0-14960.0)
Eosinophil (10^3/uL)	260.0 (31.0-2930.0)
Eosinophil (%)	3.4 (0.2-24.1)
Lymphocyte (10^3/uL)	2670.0 (1000.0-5270.0)
Platelet (10^3 mm^3)	298000.0 (209.0-566000.0)
Total IgE (IU/mL)	178.0 (3.0-2472.0)
*Allergy test positivity**	*n (%)*
House dust mite	152 (66.1)
Cat	52 (22.6)
Pollen	30 (13.0)
Cow's milk	2 (0.9)
Peanut	6 (2.6)
Egg	0 (0)
Monosensitized cases	92 (59.7)
Polysensitized cases	62 (40.3)

** Percentages were proportioned to the total number of patients (n=230). WBC:White blood cell, IgE: Immunoglobulin E*

There were 154 (67.0%) patients with positive allergy tests. Of the 154 patients with positive allergy tests, 120 (77.9%) had positive specific IgE test and 34 (22.1%) had a positive skin prick test. Allergy test was negative in 76 patients (33.0%). In the study, AR patients with positive allergy test (allergen specific IgE or skin prick test positive) and allergy test negative test (specific IgE and skin prick test negative) were compared. All laboratory values, except PLR, of the

patients with positive allergy tests were higher than the patients with negative allergy tests. The elevation in WBC, neutrophil, absolute eosinophil, eosinophil percentage, total IgE and ELR values in patients with test positive AR was statistically significant (p<0.05) (Table 3).

Table 3. Laboratory values of patients with and without allergy test positivity

	Test Positive AR (n=154)	Test Negative AR (n=76)	P value
	Median (min-max)	Median (min-max)	
WBC (10^3 mm^3)	7995.0 (4600.0-19510.0)	7270.0 (5040.0-11100.0)	0.009
Neutrophil (10^3/uL)	4075.0 (1800.0-14960.0)	3780.0 (2430.0-7840.0)	0.048
Eosinophil (10^3/uL)	330.0 (40.0-2930.0)	140.0 (31.0-870.0)	<0.001
Eosinophil (%)	4.2 (0.3-24.1)	2.0 (0.2-10.6)	<0.001
Lymphocyte (10^3/uL)	2700.0 (1000.0-5270.0)	2560.0 (1340.0-3980.0)	0.981
Platelet (10^3 mm^3)	302000.0 (209.0-474000.0)	283000.00 (216000.0-566000.0)	0.475
Total IgE (IU/mL)	248.0 (15.0-2472.0)	31.0 (3.0-882.0)	<0.001
NLR	1.5 (0.7-6.1)	1.3 (0.9-3.3)	0.068
PLR	110.8 (0.08-220.5)	110.9 (62.3-191.0)	0.806
ELR	0.13 (0.02-0.81)	0.05 (0.01-0.49)	<0.001

WBC:White blood cell, AR:Allergic rhinitis, IgE: Immunoglobulin E, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, ELR:Eosinophil-lymphocyte ratio

When the relationship between disease severity and laboratory parameters was examined, absolute eosinophil, eosinophil (%) and ELR values were significantly lower in patients with moderate-severe AR (p=0.023, p=0.006, p=0.008, respectively) (Table 4).

Table 4. Relationship between disease severity and laboratory parameters

	Mild AR (n=124)	Moderate-Severe AR (n=106)	P value
	Median (min-max)	Median (min-max)	
WBC (10^3 mm^3)	7550,0 (4680.0-16230.0)	7895.0 (4600.0-19510.0)	0.208
Neutrophil (10^3/uL)	3800.0 (2220.0-12700.0)	4200.0 (1800.0-14960.0)	0.216
Eosinophil (10^3/uL)	300.0 (31.0-2930.0)	200.0 (50.0-2930.0)	0.023
Eosinophil (%)	3.9 (0.3-12.5)	2.3 (0.2-24.1)	0.006
Lymphocyte (10^3/uL)	2520.0 (1000.0-5270.0)	2710.0 (1550.0-4400.0)	0.066
Platelet (10^3 mm^3)	295000.0 (209.0-474000.0)	304500.00 (212000.0-566000.0)	0.121
Total IgE (IU/mL)	223.0 (11.0-1802.0)	148.5 (3.0-2472.0)	0.065
NLR	1.5 (0.8-6.1)	1.5 (0.7-4.6)	0.907
PLR	110.8 (0.08-220.5)	110.0 (62.3-189.3)	0.775
ELR	0.13 (0.01-0.80)	0.07 (0.02-0.81)	0.008

WBC:White blood cell, AR:Allergic rhinitis, IgE: Immunoglobulin E, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, ELR:Eosinophil-lymphocyte ratio

ROC analysis was performed to evaluate the prediction of allergy test positivity by NLR, PLR, ELR and total IgE values. The area under the curve was 0.592, 0.499, 0.784 and 0.794 for NLR, PLR, ELR and total IgE values, respectively (Table 5).

Table 5. ROC analysis of NLR, PLR, ELR and total IgE values

Parameters	Area Under Curve	P value	95% Confidence Interval	
			Lower Bound	Upper Bound
NLR	0.592	0.049	0.503	0.681
PLR	0.499	0.990	0.410	0.589
ELR	0.784	<0.001	0.709	0.858
Total IgE	0.794	<0.001	0.715	0.872

ROC: Receiver Operating Characteristics, IgE: Immunoglobulin E, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, ELR:Eosinophil-lymphocyte ratio

Since the area under the curve is sufficient for ELR and total IgE; the cut-off point for predicting allergy test positivity of ELR and total IgE values was analyzed by ROC analysis. When the cut-off point for ELR is 0.066; sensitivity was 78.8% and specificity was 70.4%. When the cut-off point for total IgE is 134.5; sensitivity was 75.8%, specificity was 74.1% (p<0.001) (Figure 1).

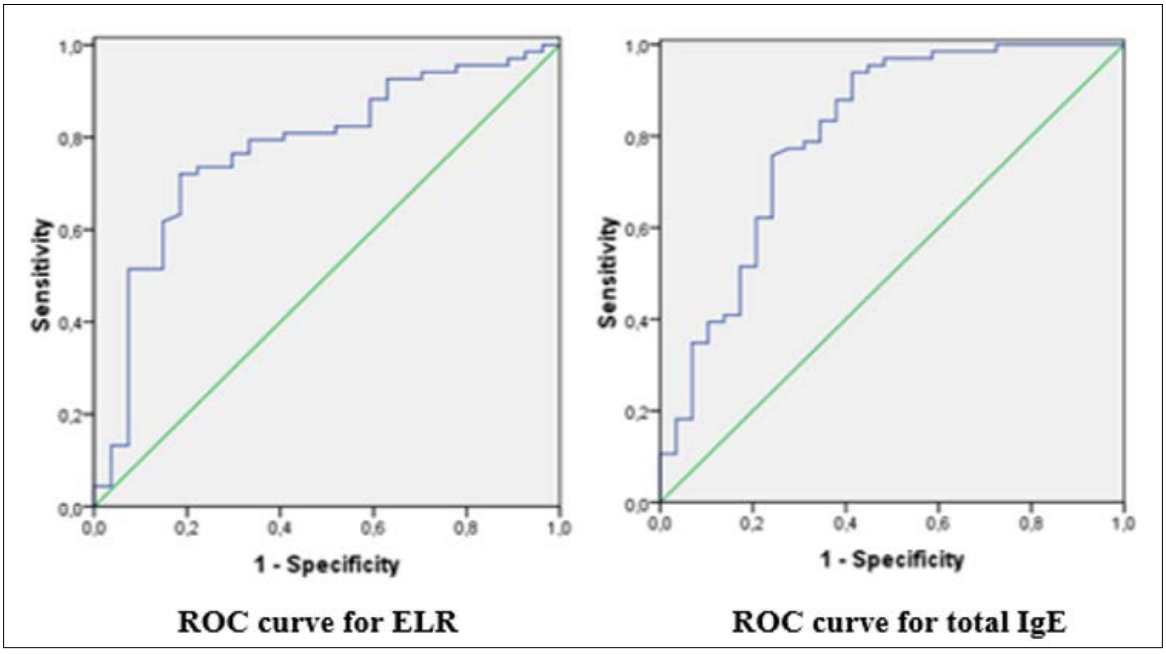

Figure 1. ROC curve for ELR and total IgE

DISCUSSION

In cases where inflammation accompanies chronic diseases, an increase in laboratory parameters indicating inflammation in the blood can be observed in patients. Easily accessible and practical tests such as complete blood count are used in the follow-up of many diseases. Evaluation of complete blood count parameters in AR patients and the level of NLR, ELR, and PLR parameters that can be evaluated with these parameters will provide practicality in disease management. In the study carried out in this context; the relationship between laboratory parameters and allergy test positivity was evaluated in AR, which is one of the allergic diseases accompanied by inflammation.

Environmental allergens enter the body through the upper respiratory tract. For this reason, the nasal mucosa is exposed to many environmental allergens. Aeroallergens such as house dust mites and pollens are often responsible for the pathogenesis of allergic respiratory diseases such as asthma and allergic rhinitis (17). When allergy test positivity was evaluated in AR patients in our study, house dust mite tests was the most common, followed by cat and pollen allergy tests, respectively. Similarly, in the literature, house dust mite allergy sensitivity has been observed most frequently in pediatric patients with allergic rhinitis (18). In studies conducted in our country, sensitivity to house dust mite was found most frequently in children (19-21).

In a study conducted in our country, the eosinophil levels were significantly increased in AR patients, and lymphocyte levels were low in children with AR. In the same study, it was reported that ELR could be used in the diagnosis and follow-up of pediatric AR patients (22). In our study, all laboratory values of patients with positive allergy test were higher than those with negative allergy test, except PLR. This elevation in WBC, neutrophil, absolute eosinophil, eosinophil percentage, total IgE and ELR values were statistically significant. In the literature, it has been reported that blood eosinophil and total IgE values are high in AR patients (23). Eosinophils are the most dominant cells in the pathogenesis of allergic inflammation. Eosinophils are elevated in blood and nasal secretions of atopic individuals (12). IgE release is also seen during inflammatory processes in allergic diseases (24). For these reasons, higher eosinophils and total IgE are expected in patients with a positive allergy test.

Studies in the literature have shown that eosinophilia is associated with allergen sensitivity and can be used as a sensitivity marker (12, 25). The number of studies that set a cut-off point for predicting allergen sensitivity is limited in the literature. In this context, in our study, ROC analysis was used to determine the cut-off point in predicting allergy test positivity for ELR and total IgE values. In our study, when the cut-off point for ELR was 0.066; sensitivity was 78.8% and specificity was 70.4%. For Total IgE, when the cut-off point was 134.5; sensitivity was 75.8% and specificity was 74.1%. These results can be interpreted as the ELR and total IgE values of approximately 3 out of every 4 patients with positive allergy tests are above the cut-off points of 0.066 and 134.5, respectively. In a study conducted in our country, when the ELR was over 0.09 in predicting allergen sensitivity, the sensitivity was reported as 61.8% and the specificity as 73.3% (26). In a study conducted in our country in adult AR patients, sensitivity and specificity were reported as 76.6% and 69.4%, respectively, when ELR was above 0.067 (12). The fact that the ELR cut-off point, which we found in predicting allergen sensitivity in our study, was similar to the literature shows that ELR can be used as a marker to predict allergy test positivity.

Strengths and limitations

Studies evaluating the relationship between complete blood count parameters and total IgE values, as well as NLR, PLR, ELR parameters, and allergy test positivity in pediatric patients with a diagnosis of allergic rhinitis are limited in the literature. One of the strengths of our study is that it makes an important contribution to the literature in this field. Another strength of our study is that we present data with our ROC analysis showing that eosinophil and total IgE values can be evaluated with a cutoff value in predicting allergy test positivity. In addition to the strengths of our study, it was conducted in a single center creating a limitation in terms of the generalizability of the results. Besides, the absence of a healthy control group in the study also creates a limitation.

Conclusions

Evaluation of laboratory parameters is extremely important in the diagnosis and follow-up of AR patients. In our study, laboratory parameters of pediatric patients with AR were evaluated. WBC, neutrophil, absolute eosinophil, eosinophil percentage, total IgE and ELR values were statistically significantly higher in patients with positive allergy tests. In addition, in the ROC analysis performed to evaluate the prediction of allergy test positivity by laboratory values; at a cut-off value of 0.066 for ELR,

the sensitivity was 78.8% and the specificity was 70.4%. When the cut-off point for Total IgE is 134.5; sensitivity was 75.8% and specificity was 74.1%. According to these results, 3 out of every 4 patients with positive allergy tests can be detected by ELR and total IgE values. Since allergy tests cannot be performed in every clinical center, it is extremely important to evaluate the success of more practical and accessible blood tests in predicting allergy test positivity. It may be beneficial for risky patients to take general allergen precautions against possible allergens until they have an allergy test. In light of our study results, large-sample and multicenter studies should be planned to evaluate the prediction of inflammatory markers for allergy test positivity in AR patients.

Declarations

The authors have no conflicts of interest to declare. The authors declared that this study has received no financial support.

This study was approved by the University of Health Sciences Turkey, Ümraniye Education and Research Hospital Ethics Committee (Date: 11/05/2023, Number: 140)

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