ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/intermed.2016-53939

Biomarkers of Inflammation in Allergic Rhinitis

Allerjik Rinitte İnflamasyonun Belirteçleri

Feridun GÜRLEK,[a]
Eyyüp TAŞDEMİR[b]

Clinics of
[a]Allergy and Immunology,
[b]Internal Medicine,
Bursa Training and Research Hospital
Bursa

Geliş Tarihi/*Received:* 18.11.2016
Kabul Tarihi/*Accepted:* 29.04.2017

Yazışma Adresi/*Correspondence:*
Feridun GÜRLEK
Bursa Training and Research Hospital,
Clinic of Allergy and Immunology,
Bursa,
TURKEY/TÜRKİYE
alergologfer@gmail.com

ABSTRACT Objective: Allergic rhinitis is one of the most common atopic diseases. The skin prick test and the allergen-specific IgE antibody test are used for its diagnosis. The aim of this study was to identify the presence of allergic inflammatory parameters with prognostic value, which are easily accessible, simple and inexpensive, to make them available for clinical use. **Material and Methods:** This study included people with and without allergic rhinitis between the ages of 18-55 years who were admitted to the Internal Medicine and Allergy and Clinical Immunology polyclinics. Those without a known disease were included in the healthy group. People who did not receive any immunotherapy, were identified as allergic by skin prick tests and had no other disease were included in the allergic rhinitis group. Data were obtained retrospectively by screening the patients' files, and hence patient approval was not required in this study. **Results:** The allergic rhinitis group comprised 114 (62.6%) females and 68 (37.4%) males, with a mean age of 31.37±9.89 years. The healthy group consisted of 50 (56.2%) males and 39 (43.8%) females, with a mean age of 31.93±10.87 years. In the allergic rhinitis group, while the eosinophil count (p=0.042), eosinophil-lymphocyte ratio (ELR) (p=0.007) and platelet-lymphocyte ratio (PLR) (p=0.007) were found to be significantly high, the median platelet volume (MPV) was found to be significantly low (p<0.001). MPV measurements were significantly lower in the allergic rhinitis group (p<0.001). For MPV, the sensitivity was 64.84%, the specificity was 65.17%, the positive predictive value (PPV) was 79.20% and the negative predictive value (NPV) was 47.50%. For PLR (p=0.005), the sensitivity was 61.54%, the specificity was 59.55%, the PPV was 75.70% and the NPV was 43.10%. For ELR (p=0.005), the sensitivity was 48.90%, the specificity was 74.16%, the PPV was 79.50% and the NPV was 41.50%. **Conclusion:** MPV, PLR and ELR do not directly indicate a single disease. We suggest that it is particularly important in primary health care to take a complete blood count in clinical practice to direct the patient to an allergy centre. Skin prick testing and allergen-specific IgE screening will be appropriate to confirm allergic rhinitis in suspected cases. We believe that a more extensive study is needed in this regard.

Keywords: Rhinitis, allergic, perennial; blood platelets; eosinophils

ÖZET Amaç: Allerjik rinit en sık rastlanılan atopik hastalıktır. Tanısında deri prick ve allerjen spesifik IgE testleri kullanılır. Çalışmanın amacı allerjik inflamasyonu gösteren ulaşılabilir, kolay, ucuz, prognostik olarak da değer taşıyan parametrelerin varlığını saptamak ve kullanıma sunulmasına katkıda bulunmaktır. **Gereç ve Yöntemler:** İç Hastalıkları ile Allerji ve Klinik İmmunoloji polikliniklerine başvuran 18-55 yaş arası, sağlıklı grupta bilinen bir hastalığı olmayan, allerjik rinit grubunda ise immunoterapi almamış deri prick testleri ile allerjik olduğu saptanmış ve başkaca bir hastalığı olmayan kişiler çalışmaya alındılar. Bilgiler retrospektif olarak hasta dosyaları taranarak elde edildi bundan dolayı hasta onamının alınmasına gerek duyulmadı. **Bulgular:** Allerjik rinit grubunun 114'ü kadın (%62,6), 68'i erkek (%37,4), yaş ortalaması 31,37±9,89 yıl, sağlıklı grupta 89 kişinin 50'si erkek (%56,2), 39'u kadın (%43,8), yaş ortalaması 31,93±10,87 yıl idi. Allerjik rinit grubunun eozinofil sayısı (p=0,042), eozinofil lenfosit oranı (ELR) (p=0,007), trombosit lenfosit oranı (PLR) (p=0,007) yüksek, median trombosit volüm (MPV) düşük bulunmuştur (p<0,001). Çalışmamızda MPV değeri allerjik rinit grubunda anlamlı idi (p<0,001). Sensitivitesi %64.84, spesifitesi %65,17, pozitif prediktif değer (PPV): %79,20, negatif prediktif değer (NPV) %47,50 bulundu. PLR için p=0,005, sensitivite %61.54, spesifite %59,55, PPV %75,70, NPV %43,10 idi. ELR için p=0,005, sensitivite %48,90, spesifite %74,16, PPV %79,50, NPV %41,50 idi. **Sonuç:** MPV, PLR ve ELR'nin hiçbiri tek bir hastalığı direkt olarak işaret etmez. Ancak yapılacak bir tam kan sayımı ile hastayı bir allerji merkezine yönlendirmenin birinci basamak sağlık hizmetlerinde önem taşıyacağını belirtmek isteriz. Her hastalıkta olduğu gibi hastanın öykü ve klinik bulguları gözardı edilmeksizin allerjik rinitten şüphelenilen durumlarda deri prick test, allerjen spesifik IgE bakılması uygun olacaktır. Bu konuda daha geniş kapsamlı çalışmalara gerek olduğu kanaatindeyiz.

Anahtar Kelimeler: Rinit, allerjik,yılboyu; kan trombositleri; eozinofiller

Allergic rhinitis is one of the most common chronic diseases. It is responsible for at least 2.5% of all visits to the doctor.[1] It is estimated that the incidence of allergic rhinitis in the community is between 10% and 25%. In Turkey, the frequency is reported between 11% and 17.6%.[2] Rhinitis is diagnosed by the presence of two of the nasal symptoms, including nasal obstruction, nasal itching, sneezing and a decrease in smell, for more than 1 h a day.[3,4] A study conducted by Yardımcı et al. on children in Bursa reported the frequency of allergic rhinitis to be 10.2%, while 9.5% of the siblings of the children with food allergies and 9.1% of the parents had the disease.[5]

Allergic rhinitis is one of the most common atopic diseases. Its prevalence shows regional differences, with ~25% of the general population having the disease. Allergic rhinitis can be categorised into seasonal and perennial. Seasonal allergic rhinitis occurs due to exposure to pollen of plants such as wind-pollinated trees, grasses and weeds, whereas perennial allergic rhinitis is caused by house dust mites, pet hairs, cockroaches and mould fungi. Allergic rhinitis is an IgE-mediated inflammatory disease of the nasal mucosa. Two components, including acute allergic reaction and late inflammatory events, play a role in its pathogenesis. Type I hypersensitivity reaction accounts for most of the acute clinical manifestations of allergic rhinitis. Macrophages, dendritic cells, CD4+ T cells, B cells and plasma cells play a role in the sensitisation phase. While mast cells play an important role in the early phase of inflammation, eosinophils, basophils, monocytes and lymphocytes play an important role in the late phase of inflammation. This period constitutes the clinical phase of the disease.[6]

Active eosinophil count increases in the blood and tissues due to various mechanisms. At one end of the process, there is increased eosinophil production, while migration of eosinophils to the tissue occurs at the other end along with an increase in life span. Eosinophil accumulation alone does not cause the pathology, activation and release of eosinophil-mediated mediators; the common mechanisms of these events include the involvement of transcription factors, cytokines, chemokines, adhesion molecules and survival regulatory pathways.[7] Interleukins (IL)-3, IL-5 and granulocyte macrophage colony-stimulating factor (GM-CSF) produced by T cells increase the production of eosinophils. Mediators such as eosinophil chemotactic factor, leukotriene B4, C5, C6, C7 and histamine, which increase eosinophil production during IgE-mediated events from mast cells and basophils, are released. Eosinophil production increases in skin diseases such as aspergillosis, brucellosis, chlamydiosis, coccidiomycosis, mycobacterial infections, psoriasis and pemphigus; in allergic and atopic diseases, in haematological malignancies such as leukaemia and lymphoma, carcinomas and sarcomas, vasculitis; in granulomatous connective tissue diseases and in adrenal hypofunction.[8] The purpose of this study was to determine the presence of allergic inflammatory parameters having prognostic value as well as being easily accessible, simple and inexpensive, to make them available for clinical use.

MATERIAL AND METHODS

In the Internal Medicine Polyclinic, between August 2014 and February 2016, 17.334 (10.400 females and 6.934 males) patient files were screened, and patients with the specified criteria among the patients who particularly received a healthy report were taken as the control group. A total of 15.500 (11.150 females and 4.350 males) patient files were screened from the Allergy Immunology Polyclinic between August 2014 and February 2016. Finally, a total of 271 patients, including 182 (67.1%) with allergic rhinitis and 89 (32.9%) as the control group, who were aged 18-55 years were included in the study. People without a known disease were included in the healthy group. Patients who did not receive any immunotherapy and were diagnosed as allergic by skin prick tests but had no other disease were included in the allergic rhinitis group. Between June 2015 and October 2015, allergic rhinitis patients were in the active phase of the disease, and the period of treatment was determined and complete blood counts were taken into consideration. People who did not have any systemic inflammatory disease, severe anaemia or

haema tologic disease, malignancy, chronic liver disease, heart or kidney disease, systemic corticosteroid use, anti-inflammatory or anticoagulant medication use were included in the study. Beckman Coulter device was used for analysis of haematologic data. The information was obtained retrospectively by screening patient files, and hence patients' approvals were not required. This study was approved by the ethics committee of Bursa High Specialization Training and Research Hospital.

STATISTICAL ANALYSIS

Descriptive statistics are presented as values of frequency, percentage, mean, standard deviation (SD), median and minimum (min) and maximum (max). The Pearson's chi-squared test was used for analysis of the relationships between categorical variables. The Kolmogorov-Smirnov test was used to assess the assumptions of normality in the analysis of the difference between the measured values of the two groups. The Mann-Whitney U test was used when the data did not fit a normal distribution. Independent samples t-test was used when the data fit a normal distribution. Receiver operating characteristic (ROC) analysis was performed to distinguish the patients with allergic rhinitis according to certain measurements and to determine the cut-off points. The area under the curve (AUC), cut-off point, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) values are presented for all biomarkers. The independent risk factors in allergic rhinitis were examined using logistic regression analysis by including those variables that were statistically significant in univariate analysis. The results are presented with Wald statistic, odds ratio (OR) and 95% confidence intervals (CIs). The level of statistical significance was considered at $p<0.05$. All analyses were performed using SPSS 22.0 software package.

RESULTS

The allergic rhinitis group was compared with the healthy group in terms of gender, age and specific hematogic measures (Table 1).

ROC analysis was performed to distinguish patients with allergic rhinitis from the healthy group

TABLE 1: Comparison between the allergic rhinitis and control group.

		Allergic Rhinitis Group			Control Group			p
Gender#	Female	114	62.6%		50	56.2%		0.307
	Male	68	37.4%		39	43.8%		
Age‡			31.37±9.89	31(17-55)		31.93±10.87	29(18-55)	0.858
Leukocyte‡			7.21±2.11	6.97(3.45-17.67)		7.53±2.19	7.07(3.42-17.41)	0.153
Lymphocyte‡			2.23±0.64	2.16(0.87-4.22)		2.4±0.76	2.29(0.66-5.42)	0.111
Platelet‡			251.86±64.48	241.5(105-519)		241.75±58.1	236(139-389)	0.23
Eosinophil‡			0.24±0.21	0.19(0-1.03)		0.17±0.11	0.14(0-0.49)	0.042*
Basophil‡			0.03±0.02	0.02(0-0.1)		0.03±0.02	0.03(0.01-0.08)	0.35
Mpv§			8.88±0.99	8.8(6.54-11.5)		9.62±1.1	9.5(7.6-12.2)	<0.001*
Neutrophil‡			4.11±1.85	3.88(1-15.95)		4.47±1.91	4.07(1.59-15.55)	0.054
ELR‡			0.1±0.09	0.08(0-0.45)		0.07±0.07	0.06(0-0.61)	0.007*
BLR‡			0.01±0.01	0.01(0-0.05)		0.01±0.01	0.01(0-0.04)	0.557
NLR‡			2.03±1.62	1.79(0.33-18.33)		2.19±2.55	1.79(0.48-23.56)	0.824
PLR‡			121.3±43.68	113.76(48-291)		110.98±54.05	102.51(42.14-474.24)	0.007*

PearsonChi-Square Test; ‡ IndependentSamples t Test; § Mann-Whitney U Test; *p<0.05

ELR; Eosinophil-lymphocyte ratio. **BLR;** Basophil-lymphocyte ratio. **NLR;** Neutrophil-lymphocyte ratio. **PLR:** Platelet-lymphocyte ratio. 271 people were included in the study, comprising 182 in the allergic rhinitis group and 89 in the healthy group. The allergic rhinitis group included 114 (62.6%) females and 68 (37.4%) males, with a mean age of 31.37±9.89 years. In the healthy group, there were 50 (56.2%) males and 39 (43.8%) females, with a mean age of 31.93±10.87 years. The allergic rhinitis group was compared with the healthy group in terms of gender, age and specific measures. In the allergic rhinitis group, while the eosinophil count (p=0.042), ELR (p=0.007) and PLR (p=0.007) were found to be high, the median platelet volume (MPV) was found to be low (p<0.001) (Table 1).

TABLE 2: ROC analysis for distinguishing patients with allergic rhinitis from the healthy group.

	Critical Value	AUC	Sensitivity%	Specificity%	PPV%	NPV%	PLR	NLR
MPV	≤ 9.1	0.687						
		p< 0.001	64.84	65.17	79.20	47.50	1.86	0.54
ELR	> 0.0885	0.600						
		p= 0.005	48.90	74.16	79.50	41.50	1.89	0.69
PLR	> 107.3	0.601						
		p= 0.005	61.54	59.55	75.70	43.10	1.52	0.65

ELR: Eosinophil-lymphocyte ratio; **PLR:** Platelet-lymphocyte ratio; **MPV;** Median platelet volume; **AUC:** Area under the curve; **PPV:** Positive predictiva value; **NPV:** Negative predictive value; **NLR:** Neutrophil lymphocyte ratio. ROC analysis was performed to distinguish patients with allergic rhinitis from the healthy group in terms of MPV, ELR and PLR measurements, which showed differences in the two groups. It was observed that for patients with MPV ≤9.1, the sensitivity was 64.84%, the specificity was 65.17% and the AUC was 0.687 (p<0.001; AUC=0.5). For patients with ELR>0.0885, the sensitivity was 48.9%, the specificity was 74.16% and the AUC was 0.600 (p=0.005; AUC=0.5). Regarding patients with PLR>107.3, the sensitivity was 61.54%, the specificity was 59.55% and the AUC was 0.601 (p=0.005; AUC=0.5) (Table 2).

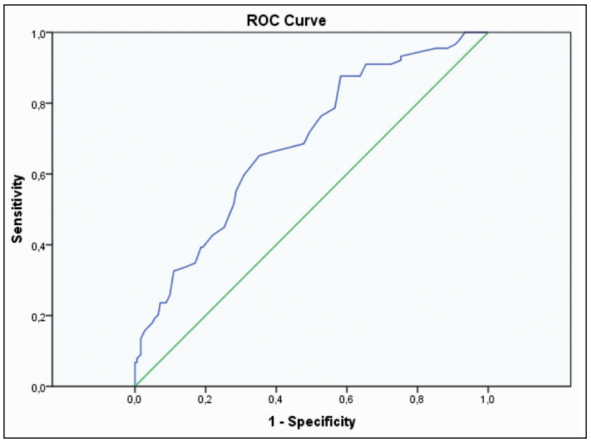

FIGURE 1: The ROC curves of MPV.
MPV; MPV measurements were significantly lower in the allergic rhinitis group (p<0.001). It was found that for MPV, the sensitivity was 64.84%, the specificity was 65.17%, the positive predictive value (PPV) was 79.20% and the negative predictive value (NPV) was 47.50%.MPV.

in terms of MPV, ELR and PLR measurements, which showed differences in the two groups (Table 2).

The ROC curves of median platelet volume (MPV), platelet lymphocyte ratio (PLR), and eosinophil lymphocyte ratio (ELR) are shown in Figures 1-3.

Logistic regression analysis was performed for determining the independent risk factors of allergic rhinitis in terms of MPV, ELR and PLR measurements, which showed differences in the two groups.

A one-unit decrease in MPV measurement increased the OR of allergic rhinitis by 2.062 times (p < 0.001). A one-unit decrease in ELR measurement increased the OR of allergic rhinitis by 1.147.54 times (p=0.002), which is a very high figure. This is because it forms multiple linear con-

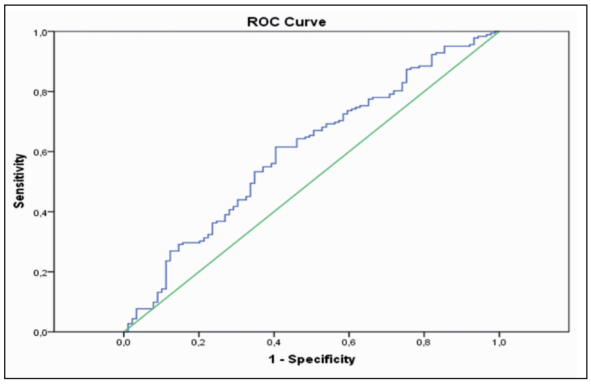

FIGURE 2: The ROC curves of PLR.
PLR; It was found that for PLR (p = 0.005), the sensitivity was 61.54%, the specificity was 59.55%, the PPV was 75.70% and the NPV was 43.10%.

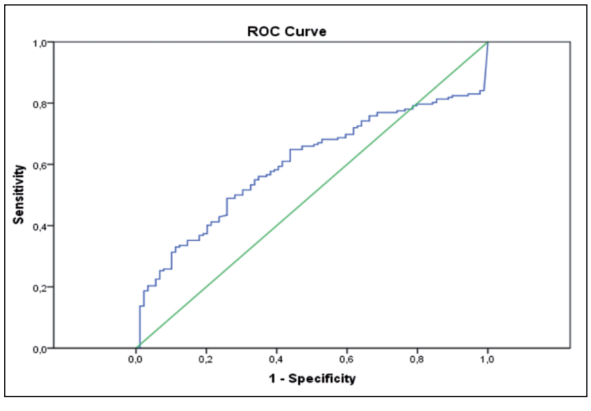

FIGURE 3: The ROC curves of ELR.
ELR; For ELR (p=0.005). the sensitivity was 48.90%, the specificity was 74.16%, the PPV was 79.50% and the NPV was 41.50%.

TABLE 3a: Logistic regression analysis for determining the independent risk factors of allergic rhinitis.

	Wald	p	OR	95% Lower Limit	95% Upper Limit
MPV	24.705	**<0.001***	0.485	0.364	0.645
ELR	9.563	**0.002***	1147.541	13.198	99777.853
PLR	0.165	0.684	1.001	0.995	1.008

MPV and ELR measurements were found to be effective risk factors for allergic rhinitis (* p<0.05).

TABLE 3b: Logistic regression analysis for determining the independent risk factors of allergic rhinitis for the variables separated by the cut-off points of MPV, ELR and PLR measurements.

	Wald	p	OR	95% Lower Limit	95% Upper Limit
MPV ($\leq$9.1| >9.1)	20.486	**<0.001***	3.748	2.115	6.64
ELR (>0.0885| $\leq$0.0885)	16.097	**<0.001***	3.452	1.885	6.323
PLR (>107.3| $\leq$107.3)	6.679	**0.01***	2.088	1.195	3.649

* p<0.05.

The OR of allergic rhinitis was 3.748 times higher in patients with MPV $\leq$9.1 compared to that in patients with MPV >9.1 (p<0.001; 95% CI: 2.115-6.64). The OR of allergic rhinitis was 3.452 times higher in patients with ELR >0.0885 compared to that in patients with ELR $\leq$0.0885 (p<0.001; 95% CI: 1.885-6.323). The OR of allergic rhinitis was 2.088 times higher in patients with PLR >107.3 compared to that in patients with PLR $\leq$107.3 (p<0.001; 95% CI: 1.195-3.649) (Table 3b).

nections due to the same denominator of the two variables in the model. To prevent this, the cut-off points and variables that we found and used in the ROC analysis were included in the model (Table 3a).

Logistic regression analysis was performed for determining the independent risk factors of allergic rhinitis for the variables separated by the cut-off points of MPV, ELR and PLR measurements, which showed differences in the two groups (Table 3b). All the three variables were found to be effective risk factors for allergic rhinitis.

DISCUSSION

NLR and PLR can be detected in haemogram analysis of peripheral blood. PLR was found to be high in various peripheral vascular diseases, coronary artery diseases and some gynaecological and hepatobiliary malignancies and it has also been associated with poor prognosis. NLR has been recommended to be used as a new biomarker to indicate systemic inflammation. NLR is increased in systemic inflammation, some gynaecological and gastrointestinal cancers and some cardiovascular diseases.[10-12] NLR and PLR can be easily calculated and are quite inexpensive.[10]

Dogru et al. also demonstrated NLR as an indicator of inflammation in children with allergic rhinitis. They found that NLR was higher in paediatric patients with moderate and severe allergic rhinitis compared to that in paediatric patients with mild allergic rhinitis. The mean NLR was higher in the allergic rhinitis group compared to that in the control group. There has not yet been a study on this subject in adult population.[13] In our study on adult subjects, there was no significant difference in NLR between the allergic rhinitis group and the healthy group. PLR was significantly higher in the allergic rhinitis group.

It is known that the baseline values of leukocyte count in the paediatric age group are higher than those in the adult age group. Therefore, in our study, neutrophil-lymphocyte ratios in the adult population may not be significant and have not been reliably detected as a biomarker in our study. It is also possible that severe allergic rhinitis is present in the case of secondary infection. Dogru et al. included patients with asthma and/or eczema, unlike our study.

Qin et al. suggested that NLR and PLR can be used as useful markers in systemic lupus erythe-

matosus (SLE) activity score. Kim et al. also suggested that these ratios can be used as a useful marker in psoriatic arthritis activity index.[14,15] Boztepe et al. reported that in patients with chronic sinusitis who underwent endoscopic sinus surgery, the sensitivity was 39.4% and the specificity was 88.9% for PLR.[16] Zhang et al. reported a sensitivity of 76.9% and a specificity of 41.6% for NLR in patients with neutrophilic asthma.[17]

In addition, several researchers have investigated these parameters as activation criteria for Behcet's disease, obstructive sleep apnoea syndrome (OSAS), chronic obstructive pulmonary disease (COPD), infective endocarditis and hypertension.[18-22]

Blood platelets primarily play a role in thrombosis and haemostasis. When they are active, the mediators such as chemokines and cytokines are synthesised and MPV is increased. Increased MPV can be used as a biomarker of inflammatory diseases characterised by chronic systemic inflammation. In various studies, MPV and platelet count were examined in cardiovascular diseases, chronic rhinosinusitis, otitis media and nasal polyps.[23-27]

Yılmaz et al. showed that high NLR and PLR values may be useful as an indicator of inflammation in patients with chronic rhinosinusitis regardless of the presence of absence of a polyp. Moreover, they suggested that its clinical use could be increased in evaluating treatment eligibility and prognosis in the future.[28] In our study, MPV measurements were significantly lower in the allergic rhinitis group ($p<0.001$). It was found that for MPV, the sensitivity was 64.84%, the specificity was 65.17%, the PPV was 79.20% and the NPV was 47.50%. For PLR ($p=0.005$), the sensitivity was 61.54%, the specificity was 59.55%, the PPV was 75.70% and the NPV was 43.10%.

Concurrent elevation of NLR and PLR always may be suggestive of the presence of another inflammation, especially infection, except for allergic inflammation. However, the elevation of NLR, independent of PLR and concomitant MPV may be more significant in terms of establishing the relationship between platelets and allergic inflammation.

Yenigün et al. found that ELR was significantly higher in both symptomatic and asymptomatic paediatric patients with allergic rhinitis compared to that in the control group. Moreover, they found that it can be used in combination with skin prick test.[29] In our study, the eosinophil count ($p=0.042$) and ELR ($p=0.007$) were found to be significantly high in the allergic rhinitis group. For ELR ($p=0.005$), the sensitivity was 48.90%, the specificity was 74.16%, the PPV was 79.50% and the NPV was 41.50%. Increase in the number of eosinophils is a known phenomenon in allergic inflammation. We studied ELRs in the present study and found that the results were similar to those of Yenigün et al., but were different in terms of age groups.

While basophils circulate in the peripheral blood under homeostatic conditions, they are generally accumulated in the affected tissues in allergic disorders, including asthma, atopic dermatitis and allergic rhinitis. They are involved in the onset of allergic inflammation and also contribute to the migration of other proinflammatory cells such as neutrophils and eosinophils. They are considered to be precursors of mast cells in immune response. It has been found that basophils play a role in IgE-mediated, delayed-onset allergic inflammation in the skin along with neutrophils and eosinophils.[30] Brescia et al. performed a study on patients with chronic rhinosinusitis and nasal polyps and identified that basophil lymphocyte ratio (BLR) had a heterogeneous prognostic role in the formation of polyps.[31] In our study, there was no significant difference between the allergic rhinitis and control groups in terms of BLR. But the patient group of Brescia et al. was different from ours. They were investigating BLR in patients with or without recurrent polyps who underwent chronic rhinosinusitis and nasal polyp operation.

CONCLUSION

The use of MPV, ELR and PLR, together with specific history, allergen-specific IgE and skin prick tests is useful in the diagnosis of inflammation in patients with allergic rhinitis. In our study, MPV, ELR and PLR values were predominantly found as risk factors for allergic rhinitis inflammation. The MPV value was found to be increased in systemic and allergic inflammation, whereas it was decreased in patients with allergic rhinitis, although it was in the normal limit. Our patients had no other allergic disease other than symptomatic rhinitis. There is a need for larger studies to establish the relationship between platelet counts and mean platelet volumes and allergic rhinitis.

Although these parameters are used by several researchers in various studies. None of them point out directly to a single disease. However, we would like to mention that it is particularly important in primary health care to take a complete blood count in clinical practice to direct the patients to an allergy centre. Of course, skin prick testing and allergen-specific IgE screening will be appropriate to confirm allergic rhinitis in suspected cases in the absence of the patient's history and clinical findings being missed, as in any disease. We believe that a more extensive study is needed in this regard.

Conflict of Interest

Authors declared no conflict of interest or financial support.

Authorship Contributions

Writing, discussing, finding sources: *Feridun Gürlek, Eyyüp Taşdemir;* ***Idea, design, analysis, writing:*** *Feridun Gürlek;* ***Critical review:*** *Feridun Gürlek, Eyyüp Taşdemir.*

REFERENCES

1. Spector SL, Bernstein IL, Li JT, Berger WE, Kaliner MA, Schuller DE, et al. Parameters for the diagnosis and management of sinusitis. J Allergy Clin Immunol 1998;102(6 Pt 2):S107-44.
2. Küçüködük S, Aydin M, Cetinkaya F, Dinç H, Gürses N, Saraçlar Y. The prevalence of asthma and other allergic diseases in a provinve of Turkey. Turk J Pediatr 1996;38(2):149-53.
3. Lund V. Allergic rhinitis--making the correct diagnosis. Clin Exp Allergy 1998;28 Suppl 6:25-8.
4. Bachert C. Persistent rhinitis - allergic or non-allergic? Allergy 2004;59 Suppl 76:11-5.
5. Yardimci G, Canitez Y, Sapan N, Ragbetli C. [Prevalence of food allergy and allergic diseases at 6-14 age group children and their family in a city centre]. KÜ Tıp Fak Derg 2015;17(2):21-8.
6. Patel NJ. Seasonal and acute allergic reactions. In: Auerbach PS, ed. Wilderness Medicine: Expert Consult Premium Edition-Enhanced Online Features and Print, 6e (Auerbach, Wilderness Medicine). 6th ed. Philadelphia: Mosby; 2012. p.1224-31. Available from: https://www.amazon.com/dp/1437716784/ref=rdr_ext_tmb
7. Ackerman SJ, Bochner BS. Mechanisms of eosinophilia in the pathogenesis of hypereosinophilic disorders. Immunol Allergy Clin North Am 2007;27(3):357-75.
8. Poster RS, Kaplan JL. The Merck Manual of Diagnosis and Therapy. 19th ed. USA; Merck Sharp & Dohme Corp; 2011. p.987-93.
9. Romagnani S. The role of lymphocytes in allergic disease. J Allergy Clin Immunol 2000; 105(3):399-408.
10. Bhat T, Teli S, Rijal J, Bhat H, Raza M, Khoueiry G, et al. Neutrophil to lymphocyte ratio and cardiovascular diseases: a review. Expert Rev Cardiovasc Ther 2013;11(1):55-9.
11. Proctor MJ, McMillan DC, Morrison DS, Fletcher CD, Horgan PG, Clarke SJ. A derived neutrophil to lymphocyte ratio predicts survival in patients with cancer. Br J Cancer 2012;107 (4):695-9.
12. Wang D, Yang JX, Cao DY, Wan XR, Feng FZ, Huang HF, et al. Preoperative neutrophil-lymphocyte and platelet-lymphocyte ratios as independent predictors of cervical stromal involvement in surgically treated endometrioid adenocarcinoma. Onco Targets Ther 2013;6: 211-6.
13. Dogru M, Evcimik MF, Cirik AA. Is neutrophil-lymphocyte ratio associated with the severity of rhinitis in children. Eur Arch Otorhinolaryngol 2016;273(10):3175-8.
14. Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, et al. Neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. 2016;26(3):372-6.
15. Kim DS, Shin D, Lee MS, Kim HJ, Kim DY, Kim SM, et al. Assessments of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in Korean patients with psoriasis vulgaris and psoriatic arthritis. J Dermatol 2016;43(3): 305-10.
16. Boztepe OF, Gün T, Demir M, Gür ÖE, Ozel D, Doğru H. A novel predictive marker for the recurrence of nasal polyposis following endoscopic sinus surgery. Eur Arch Otorhinolaryngol 2016;273(6):1439-44.
17. Zhang XY, Simpson JL, Powell H, Yang IA, Upham JW, Reynolds PN, et al. Full blood count parameters for the detection of asthma inflammatory phenotypes. Clin Exp Allergy 2014;44(9): 1137-45.
18. Alan S, Tuna S, Türkoğlu EB. The relation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume with the presence and severity of Behçet's syndrome. Kaohsiung J Med Sci 2015;31(12): 626-31.

19. Kurtipek E, Bekci TT, Kesli R, Sami SS, Terzi Y. The role of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in exacerbation of chronic obstructive pulmonary disease. J Pak Med Assoc 2015;65(12):1283-7.
20. Sunbul M, Gerin F, Durmus E, Kivrak T, Sari I, Tigen K, et al. Neutrophil to lymphocyte and platelet to lymphocyte ratios in patients with dipper versus non-dipper hypertension. Clin Exp Hypertens 2014;36(4):217-21.
21. Koseoglu S, Ozcan KM, Ikinciogullari A, Cetin MA, Yildirim E, Dere H. Relationship Between Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio and Obstructive Sleep Apnea Syndrome. Adv Clin Exp Med 2015; 24(4):623-7.
22. Zencir C, Akpek M, Senol S, Selvi M, Onay S, Cetin M, et al. Association between hematologic parameters and in-hospital mortality in patients with infective endocarditis. Kaohsiung J Med Sci 2015;31(12):632-8.
23. Somuk BT, Soyalıç H, Koc S, Gürbüzler L, Doğru S, Eyibilen A. Mean platelet volume as an inflammatory marker of chronic otitis media with effusion. Int J Pediatr Otorhinolaryngol 2014;78(11): 1958-60.
24. Vizioli L, Muscari S, Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract 2009;63(10):1509-15.
25. Aktas G, Sit M, Tekce H, Alcelik A, Savli H, Simsek T, et al. Mean platelet volume in nasal polyps. West Indian Med J 2013;62(6):515-8.
26. Sagit M, Cetinkaya S, Dogan M, Bayram A, Vurdem UE, Somdas MA. Mean platelet volume in patients with nasal polyposis. B-ENT 2012;8(4): 269-72.
27. Koc S, Eyibilen A, Erdogan AS. Mean platelet volume as an inflammatory marker in chronic sinusitis. Eur J Gen Med 2011;8(4):314-7.
28. Yilmaz B, Ozgur A, Sereflican M, Uysal IO, Sengul E, Ozbay M, et al. New predictive hematologic parameters in chronic rhinosinusitis: a multicenter study. Acta Med Anatol 2016;4(4):137-40.
29. Yenigun A, Sezen S, Calim OF, Ozturan O. Evaluation of the eosinophil-to-lymphocyte ratio in pediatric patients with allergic rhinitis. Am J Rhinol Allergy 2016;30(2): e21-5.
30. Karasuyama H, Obata K, Wada T, Tsujimura Y, Mukai K. Newly appreciated roles for basophils in allergy and protective immunity. Allergy 2011;66(9):1133-41.
31. Brescia G, Pedruzzi B, Barion U, Cinetto F, Giacomelli L, Martini A, et al. Are neutrophil-, eosinophil-, and basophil-to-lymphocyte ratios useful markers for pinpointing patients at higher risk of recurrent sinonasal polyps? Am J Otolaryngol 2016;37(4):339-45.