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RHINOLOGY

The association of allergic rhinitis severity with neutrophil–lymphocyte and platelet–lymphocyte ratio in adults

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Abstract

Objective To investigate the association of allergic rhinitis (AR) severity with neutrophil–lymphocyte and platelet–lymphocyte ratios in adult patients.

Methods The study design was prospective observational study and the study included 209 AR patients and 243 healthy individuals. The patient group comprised 38.2% males with a mean age of 31.8 years. All patients who were diagnosed with persistent AR were included. The healthy control group comprised 52.7% males with a mean age of 32.3 years. The blood examination results of patients and healthy individuals were compared in terms of neutrophil–lymphocyte and platelet–lymphocyte ratios. The values were further compared within the patient group, according to AR severity.

Results The neutrophil–lymphocyte ratio was 1.70 ± 0.65 in the healthy group and 2.02 ± 1.24 in the patient group. The platelet–lymphocyte ratio result was 100.85 ± 25.33 in the healthy group and 120.67 ± 40.59 in the patient group. When we compared the neutrophil–lymphocyte and platelet–lymphocyte ratios between the groups, we found statistically significant differences in both ratios ($p = 0.003$, $p = 0.000$, respectively). Both the neutrophil–lymphocyte and the platelet–lymphocyte ratios were higher in patients with moderate–severe AR.

Conclusion Both neutrophil–lymphocyte and platelet–lymphocyte ratios are useful markers for diagnosis of persistent AR. Specialists may benefit from these markers to assess the severity of the disease at the beginning of the diagnostic process.

Keywords Allergic rhinitis · Neutrophil–lymphocyte ratio · Platelet–lymphocyte ratio

Introduction

Allergic rhinitis (AR) is a disease that affects approximately 15–25% of the world population [1]. While AR is not a life-threatening disease, it can affect daily life negatively, decrease quality of life, cause sleep disturbances, and lead to loss of daily activity and working days. Generally, diagnosis is based on clinical findings and patient history. Laboratory tests that can be used in the diagnosis and clinical course of AR are still limited and should be improved. For example, in-vitro allergen-specific IgE tests are expensive. Total IgE measurement is cheaper, but it has the disadvantage of yielding a false positive result in patients with high serum values and variable sensitivity.

AR is an allergic and inflammatory disease of the nose characterized by itching, sneezing, and nasal and/or postnasal drip. AR is associated with an IgE-mediated immune response to allergens, and there is systemic inflammation in patients in addition to nasal inflammation [2]. Studies have shown a relationship between systemic inflammation and AR [3]. In addition, the neutrophil–lymphocyte ratio (NLR) and the platelet–lymphocyte ratio (PLR) have been investigated in recent years as an important parameter of systemic inflammation, and there are studies reporting that NLR and PLR have prognostic significance in many diseases, including cardiovascular diseases and cancer [4–6].

We aimed to investigate whether NLR and PLR, which are indicators of systemic inflammation, would be useful in diagnosis and monitoring the severity of disease in adult AR

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patients. To the best of our knowledge, present paper is the first study to examine the relationship between NLR–PLR and AR in adult patients.

Methods

A total of 209 patients with persistent AR, who were diagnosed and followed-up at the Health Sciences University, Okmeydani Training and Research Hospital, were included in our study. Institutional review board approval was obtained from the Okmeydani Training and Research Hospital Ethical Committee. Written informed consent was obtained from the patients.

The control group included 243 healthy individuals aged from 18 to 50 years. Pregnant women and patients with systemic or chronic disease, anemia, polycythemia, leukocytosis/leukopenia, thrombocytopenia/thrombocytosis, and acute–chronic infections were excluded from the study. Our study included persistent AR patients with allergic complaints of more than 4 days per week and more than 4 weeks consecutively. Patients who had used any medication for AR in the past and patients with intermittent AR were excluded. The patients were divided into two groups, "mild" and "moderate to severe", according to AR severity. The diagnosis and severity of AR disease were determined according to the "Allergic Rhinitis and its Impact on Asthma" (ARIA) guidelines [7]. The mild severity group included 76 patients and 133 patients were defined as moderate–severe. A prick test was performed to determine the allergens to which the patients were sensitive. The age, gender, weight in kilograms (kg), height (cm) and educational status (college degree and above: CD/high-school degree and below: HSD) of the individuals in each group were recorded. The hemoglobin (Hb), platelet (PLT), white blood cell (WBC), neutrophil, lymphocyte, and monocyte counts were recorded. The number of neutrophils was divided by the number of lymphocytes to obtain the NLR and the number of platelet was divided by the number of lymphocytes to obtain the PLR. The Hb, PLT, WBC, neutrophil, lymphocyte, and monocyte counts were studied with the Mindray BC-6800 (Mindray, Shenzhen, China). The same measurement device and analysis were used for the parameters we examined in our study.

Skin prick test

A skin prick test was performed with the same antigens on the forearm of all patients. Histamine (10 mg/mL) and physiological saline were taken as positive and negative. Skin reaction was evaluated at 20 min; skin reactions of 3 mm or more were considered positive while lower values were considered negative. No complications were observed during or after the tests.

Statistical analysis

The SPSS 17 (SPSS Inc., Chicago, Illinois, USA) program was used for statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed in percentages. The appropriateness of the variables to normal distribution was determined using the Kolmogorov–Smirnov test. The student's *t* test was used for normal distribution of continuous variables, and the Mann–Whitney *U* test was used for non-normal distributions. The Chi-square test was used for categorical variables. The Spearman correlation was used to evaluate the relationships between statistical analyses. A value of $p < 0.05$ was considered significant.

Results

The study included 452 participants, 208 (46%) male and 244 (54%) female, aged between 18 and 50 years. The mean age of the patients was 32.1 ± 8.3 years. There was no statistically significant difference in the mean ages of the AR and the control groups ($p = 0.526$; $p > 0.05$) (Table 1). Weight and height were measured in both groups. There was no difference in weight, while those in the patient group were significantly taller than in the control group (Table 1). The female gender ratio was higher in the patient group than in the control group ($p = 0.002$) (Table 1). The level of higher

Table 1 Demographic data

	Control group ($n = 243$) Mean ± SD	Patient group ($n = 209$) Mean ± SD	*p*
Age (year)	32.35 ± 8.17	31.86 ± 8.47	0.526
Weight (kg)	75.65 ± 11.62	76.84 ± 9.70	0.234
Length (cm)	169.51 ± 7.86	172.09 ± 9.57	0.002
Gender (*n*) male/female	128/115	80/129	0.002
Education Status (n) (CD/HSD)	84/159	98/111	0.008

CD college degree and above level, *HSD* high-school degree or below

Table 2 Blood analysis of participants

	Control group ($n=243$) Mean ± SD	Patient group ($n=209$) Mean ± SD	p
Hemoglobin(g/dL)	14.39 ± 1.36	13.52 ± 1.56	0.000
WBC (10^3/uL)	7.52 ± 1.82	7.50 ± 2.14	0.483
Neutrophil (10^3/uL)	4.19 ± 1.38	4.33 ± 1.74	0.632
Lymphocyte (10^3/uL)	2.55 ± 0.61	2.35 ± 0.76	0.000
Monocyte(10^3/uL)	0.52 ± 0.14	0.49 ± 0.16	0.009
PLT (10^3/uL)	247.61 ± 47.17	266.75 ± 70.08	0.003
NLR	1.70 ± 0.65	2.02 ± 1.24	0.003
PLR	100.85 ± 25.33	120.67 ± 40.59	0.000

SD standard deviation, *NLR* neutrophil–lymphocyte, *PLR* platelet–lymphocyte ratio, *PLT* platelet, *WBC* white blood cell

Table 3 Mean and standard deviation values with whole blood analysis according to disease severity

	Mild ($n=76$) Mean ± SD	Moderate–severe ($n=133$) Mean ± SD	p
Age	38.42 ± 13.1	31.17 ± 10.17	< 0.05
Gender (n) male/female	30/46	50/83	> 0.05
NLR	1.62 ± 0.59	2.25 ± 1.45	0.000
PLR	99.76 ± 27.64	132.62 ± 42.04	0.000

SD standard deviation, *NLR* neutrophil–lymphocyte ratio, *PLR* platelet–lymphocyte ratio

education in the patient group was higher than the control group at a statistically significant level ($p=0.008$) (Table 1).

The hemoglobin, lymphocyte, monocyte, platelet, NLR, and PLR values were significantly higher in AR patients compared to the control group ($p<0.001$; $p<0.001$; $p<0.01$; $p<0.01$; $p<0.01$; $p<0.001$, respectively) (Table 2). When the prick test sensitivity in the patient group was examined, 92% ($n=192$) were found to be sensitive to house mites.

The mildly severe AR patient group included 76 patients and 133 patients were in the moderate–severe AR group. The NLR and PLR values were significantly higher in the moderate–severe AR group of patients compared to the mild AR group ($p<0.05$) (Table 3) (Figs. 1, 2).

Discussion

Our study has two important findings. First, NLR and PLR values were higher in adult AR patients than in the control group. NLR and PLR are important parameters that are easily available and cost-effective as tests in the follow-up of systemic inflammation. The presence of systemic inflammation in addition to local nasal inflammation in AR was

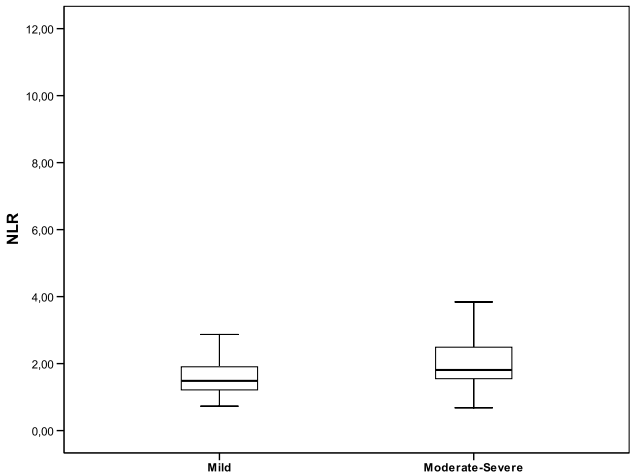

Fig. 1 Correlation between NLR value and severity of allergic rhinitis can be seen in figure (*NLR* neutrophil–to-lymphocyte ratio)

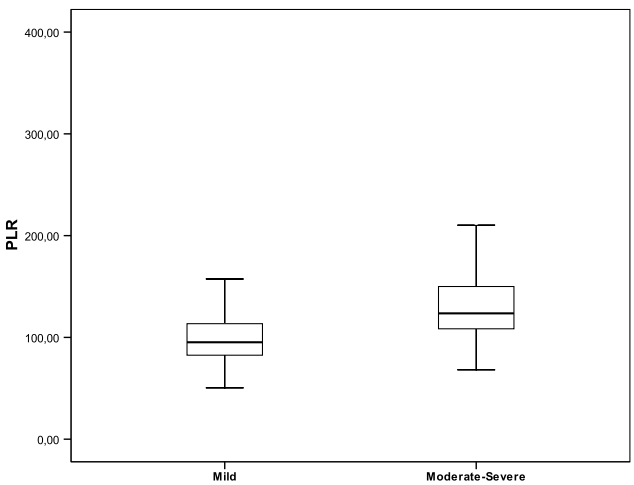

Fig. 2 Correlation between PLR value and severity of allergic rhinitis can be seen in figure (*PLR* platelet-to-lymphocyte ratio)

the source of our idea to investigate NLR and PLR values in AR. The relationship of NLR with some diseases, such as cardiac disease, chronic disease and mediterranean fever, is shown in the literature [8–10].

A study by Dogru et al. in pediatric AR patients found high NLR values in the AR group compared to the control group, and NLR was shown to be significant in follow-up of the disease severity [11]. The relationship between asthma and NLR was investigated in children by Dogru et al., and higher NLR values were obtained in children with asthma than in the normal population [12]. Similarly, in this study, we found that NLR values were related to disease and severity in adult AR patients.

We suggest that increased NLR is caused by neutrophils that migrate to the nasal mucosa and by an increase in bone marrow production in AR patients. Increased neutrophils in the nasal cytology of AR patients confirm this [13, 14]. A negative skin prick test and persistent rhinitis symptoms indicate non-allergic rhinitis (NAR). Non-allergic rhinitis with mast cells (NARMA), where mast cells are involved, includes subtypes such as non-allergic rhinitis with neutrophils (NARNE) that are mediated by neutrophils [15]. We thought that neutrophils could increase not only in AR but also in NAR forms such as NARNE. We found that the high NLR value in our study was not caused by NAR, due to prick test positivity.

Another important result of our study is that NLR and PLR values are effective in determining AR severity. In the moderate–severe severity disease group, NLR and PLR were significantly higher compared to the mild group. In a study of 64 patients with grass pollen-sensitive AR, the patients with mild and moderate–severe AR were cytologically compared, and eosinophil, mast cells, or plasma cells were significantly higher in patients with moderate–severe AR compared to the mild AR group [13]. In contrast, Gelardi et al. reported neutrophil predominance in nasal cytology in patients with AR sensitive to house dust mites [16]. Similarly, in our study, the high NLR value can be explained due to neutrophils' dominance, because the home dust mite sensitivity in the patient group was seen in 92% of patients in the prick test. In light of this information, due to the neutrophils' dominance, patients with more severe AR had higher NLR levels.

There are some studies showing the correlation between NLR values and disease severity. Bell's Palsy is characterized by varying degrees of facial nerve paralysis as a result of inflammation that develops on the basis of a possible viral infection. In a study, it was shown that NLR values increased with increasing Bell's palsy grade [17]. Behcet disease, which is a systemic inflammatory vascular disease, has shown that NLR is higher than healthy group [18]. In the study of patients with IgA nephropathy, it was reported that high NLR values reflect more severe renal inflammation and that patients' response to corticosteroid treatment will be weaker [19]. There are two conclusions from these studies; first, inflammatory diseases lead to higher NLR values compared to healthy group and second, higher NLR values correlated with the severity of inflammatory disease. The involvement of neutrophils in the inflammation process, the release of inflammatory cytokines and the mediation of various immune reactions by lymphocytes are reflected as higher NLR values in severe inflammation [19]. This situation supports the correlation of disease severity with NLR, which is the most important result of our study.

The other parameter in our study was PLR. This is the first study showing the relationship between AR and PLR. In the patient group, PLR was higher than the healthy group. The positive correlation with the severity of the disease was also an important result. In a study by Uslu et al., a relationship between PLR level and rheumatoid arthritis activity level was shown [20]. In systemic lupus erythematosus patients, Wu et al. showed that PLR and NLR are two useful inflammatory markers in activity monitoring [21]. Zhou et al. showed that there was a significant difference between NLR and PLR values among the mild–moderate/severe pancreatitis patient groups, and the importance of NLR and PLR in the severity of the disease and prognosis were highlighted [22]. In patients with atopic dermatitis, a positive correlation was found between disease severity and NLR–PLR, and these two markers were found useful in atopic dermatitis [23].

Some studies have shown that factors such as age and smoking may affect NLR rates [24]. Controversially, in other study, they found that NLR was not affected by age [17]. It's still unclear. Therefore, in our study, no significant difference was found between the healthy group and AR patient group in terms of age. When the mean age of the patients was evaluated according to the severity of the disease in the patient group, the mean age in the mild severe AR group was significantly higher than the moderate–severe group. In this respect, we think that it may have the potential to very minimal effect on results due to large population. As smoking status was not found for all patients in patient files, we could not report possible impacts of smoking on NLR.

Some methods used in objective severity measurement in AR are indicated in the ARIA guideline; these include the visual analog score (VAS), acoustic rhinometry, nitric oxide (NO) measurement, and nasal cytology [2]. We suggest that both NLR and PLR may be used as objective markers in patients with AR.

The study had several limitations. The NLR–PLR correlation was not examined with other techniques such as nasal cytology or NO. Second, the control of the severity of the disease during the treatment process was not taken into account, the change in the NLR–PLR values was not studied. Nevertheless, we do not know exactly whether this

is a useful parameter to use in the follow-up of the disease severity, it needs further studies. The strength of our study was the large sample.

Conclusion

A positive correlation was found between patients with AR and the healthy control group with higher NLR–PLR values found in patients with AR compared to the control group. NLR–PLR values were compared and positive correlation was obtained between higher NLR–PLR values and AR severity. To the best of our knowledge, this is the first study in the literature showing the relationship between AR and NLR–PLR in the adult age group. In patients with persistent AR, NLR and PLR values can be used in the diagnosis and determination of AR severity. As NLR–PLR is a very easy and fast test, these results are very beneficial for AR patients. Our study should be supported by additional studies that include other inflammatory markers such as NO in a prospective study of a large patient population.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent The study design was prospective observational study and this research was performed with human participants. All patients were signed written informed consent.

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