



## Evaluation of neutrophil-to-lymphocyte ratio in patients with symptomatic rhinitis

Engin Başer<sup>1</sup> , Papatya Bayrak Degirmenci<sup>2</sup> , İlker Burak Arslan<sup>1</sup> , İbrahim Çukurova<sup>1</sup> 

<sup>1</sup>Department of Otorhinolaryngology, Izmir Tepecik Training and Research Hospital, Izmir, Turkey

<sup>2</sup>Department of Allergy and Immunology, Manisa Celal Bayar University, Manisa, Turkey

### ABSTRACT

**Objectives:** In this study, we aimed to measure the diagnostic value of neutrophil-to-lymphocyte ratio (NLR) in both perennial allergic rhinitis (AR) and non-allergic rhinitis (NAR) patients during their period of active symptoms.

**Patients and Methods:** A total of 161 patients (101 males, 60 females; mean age 34.0±11.1 years; range, 18 to 56 years) consisting of 70 persistent allergic rhinitis (PAR) and 39 NAR patients diagnosed between March 2018 and March 2019 in the adult allergy outpatient clinic, having a Total Nasal Symptom Score (TNSS) of ≥8, and recent complete blood count results available before undergoing any medical treatment and 52 control patients (28 males, 24 females; mean age 31.7±7.8 years; range, 18 to 44 years). The NLR was calculated by dividing the number of neutrophils by the number of lymphocytes.

**Results:** There was no statistically significant difference in the age or gender between the groups ( $p>0.05$ ). There was no statistically significant difference in the neutrophil, lymphocyte, and NLR between the groups ( $p>0.05$ ).

**Conclusion:** Our study shows that NLR is not a useful tool in the diagnosis and management of treatment in PAR and NAR in adults.

**Keywords:** Allergic rhinitis, inflammation, neutrophil-to-lymphocyte ratio, non-allergic rhinitis.

The term rhinitis is defined as inflammation of the nasal mucosa characterized by nasal discharge, sneezing, nasal obstruction, and itchy nose and/or eyes. Allergic rhinitis (AR) is the most common form of non-infectious rhinitis and is associated with immunoglobulin E (IgE)-mediated immune response against allergens. Allergic rhinitis is a global health problem which significantly affects the quality of life of individuals. In addition to nasal inflammation in AR, systemic inflammation also occurs.<sup>[1,2]</sup> Non-allergic rhinitis (NAR) consists of a heterogenous patient group with rhinitis complaints, without

signs of clinical infection and systemic allergic inflammation (allergen-specific IgE in blood and/or positive prick test results). This patient group is often defined as NAR which can be classified into various subgroups such as drug-induced rhinitis, senile rhinitis, pregnancy rhinitis, occupational rhinitis, gustatory rhinitis, hormonal rhinitis, and idiopathic rhinitis.<sup>[3]</sup>

The diagnosis of AR is made based on symptoms induced by exposure to the allergen, skin prick test positivity, and allergen-specific IgE in blood.<sup>[4]</sup> The diagnosis of NAR is based

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Correspondence: Engin Başer, MD. İzmir Tepecik Eğitim ve Araştırma Hastanesi Kulak Burun Boğaz Kliniği, 35020 Konak İzmir, Türkiye.

e-mail: dr.enginbaser@hotmail.com

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on detailed medical history, lack of sensitivity to allergens, and ruling out rhinosinusitis symptoms.<sup>[5]</sup>

In the literature, there is a limited number of studies evaluating systemic inflammation in AR and NAR.<sup>[1,6]</sup> The neutrophil-to-lymphocyte ratio (NLR) is a frequently used, inexpensive test which can be easily calculated in complete blood count (CBC) analysis of peripheral blood, and is an important indicator of systemic inflammation.<sup>[7,8]</sup> In addition, many studies have shown the utility and prognostic significance of NLR as an indicator of chronic inflammation in cardiovascular diseases, hypertension, diabetes, familial Mediterranean fever, hepatic cirrhosis, and malignancies.<sup>[1,9-11]</sup> Systemic inflammation is present in AR and studies on patients of the pediatric age group have demonstrated its relationship with NLR.<sup>[1,12]</sup> However, there is no study conducted in adult patients with NLR. In NAR, there is heavy inflammation of the nasal mucosa and it has not been established whether this is a systemic response.

In the present study, we aimed to measure the diagnostic value of NLR in both AR and NAR patients during their period of active symptoms and to investigate any systemic effect of nasal inflammation with NLR and NLR value as a parameter for AR and/or NAR.

## PATIENTS AND METHODS

A total of 161 patients (101 males, 60 females; mean age 34.0±11.1 years; range, 18 to 56 years) consisting of 70 persistent allergic rhinitis (PAR) and 39 NAR patients diagnosed between

March 2018 and March 2019 in the adult allergy outpatient clinic, having a Total Nasal Symptom Score (TNSS) of ≥8, and recent CBC results available before undergoing any medical treatment and 52 control patients (28 males, 24 females; mean age 31.7±7.8 years; range, 18 to 44 years) were included in the study. The PAR group consisted of patients with positive skin prick test. The NAR group consisted of patients with rhinitis complaints without signs of clinical infection and systemic allergic inflammation (allergen-specific IgE in blood and/or positive prick test results). The control group consisted of patients between 18 and 44 years of age without nasal symptoms undergoing septoplasty and with CBC results from preoperative workup. All patients were selected among those with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) within normal ranges, and no additional systemic or local inflammatory diseases in their medical history or physical exam. Patients in whom ≥8 TNSS and blood samples were obtained immediately after examination or within five days at most were included in the study. Venous blood samples were collected from all patients and analyzed within 10 min using the same blood analyzer.

The TNSS is used as a subjective test in many studies to evaluate AR before and after treatment.<sup>[13-16]</sup> The TNSS test assesses the severity of symptoms of nasal congestion, nasal itching, sneezing, and rhinorrhea experienced by patients in the past week. The patients are asked to score each symptom from 0 to 3 (0: no complaints; 1: mild; 2: moderate; 3: severe). With maximum score of 12, this subjective tool is quick, easily applied, well-tolerated, and used to

**Table 1.** Demographic characteristics of patient and control groups

	n	%	Mean±SD	Median	Min-Max
Age (year)			34.0±11.1	33	18-56
Gender					
Male	101	62.7			
Female	60	37.3			
Groups					
Allergic rhinitis	70	43.5			
Non-allergic rhinitis	39	24.2			
Control group	52	32.3			

SD: Standard deviation; Min: Minimum; Max: Maximum.

evaluate symptoms and treatment outcomes of patients. The same method may be used to track changes that occur throughout the treatment.<sup>[17]</sup>

The diagnosis of AR was made based on medical history, physical examination, and laboratory findings. The patients who presented to the tertiary hospital adult allergy-immunology outpatient clinic with the preliminary diagnosis of AR based on medical history and physical examination were administered the skin prick test to demonstrate allergic sensitization. The skin prick tests were performed according to the European Academy of Allergy and Clinical Immunology (EAACI) guidelines for the most common inhalant allergens in Turkey, including house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), fungi (*Aspergillus fumigatus*, *Alternaria alternata*, *Cladosporium herbarum*, and *Penicillium notatum*), grasses (*Lolium perenne*, *Festuca pratensis*, *Phleum pratense*, *Poa pratensis*, and *Dactylis glomerata*), weeds (*Plantago lanceolata*, *Artemisia vulgaris*, *Rumex acetosa*, *Taraxacum vulgare*, and *Parietaria officinalis*), and trees (*Sambucus nigra*, *Populus alba*, *Ulmus scabra*, *Salix caprea*, *Fagus sylvatica*, *Carpinus betulus*, *Quercus robur*, *Fraxinus excelsior*, and *Olea europaea*) with histamine and diluent control (Allergopharma Ltd, Reinbek, Germany).<sup>[18]</sup>

The patients with negative skin prick test results were evaluated for mite and pollen sensitivity with allergen-specific IgE in the blood. Those with negative results were considered NAR.

The NLR was calculated by dividing the number of neutrophils by the number of lymphocytes.

A written informed consent was obtained from each participant. The study protocol was approved by the University of Health Sciences, Izmir Tepecik Training and Research Hospital Ethics Committee (No: 2019/12-23, Date: 25.07.2019). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Statistical analysis**

Statistical analysis was performed using the Number Cruncher Statistical System (NCSS)

**Table 2.** Comparison of demographic characteristics according to groups

	Allergic (n=70)			Non-allergic (n=39)			Control (n=52)			p	
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median		Min-Max
Age (year)	48	68.6	34.2±12.6	35	19-55	26	65.0	37.3±11.5	38	18-56	0.082*
Gender	22	31.4				24	46.2				0.246†
Male											
Female											

SD: Standard deviation; Min: Minimum; Max: Maximum; \* One-way ANOVA test; † Pearson chi-square test.

**Table 3.** Neutrophil count, lymphocyte count, and NLR according to groups

	Allergic (n=70)			Non-allergic (n=39)			Control (n=52)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Neutrophil count	55.9±6.2	55	46-70	57.1±6.4	59	41-66	57.1±8.1	57	44-77	0.579*
Lymphocyte count	32.9±6.6	34	17-43	30.1±6.3	28	21-48	31.9±7.4	31	15-45	0.122*
NLR	1.8±0.7	1.7	1.1-4	2.0±0.6	2.1	0.85-3	2.0±0.9	1.8	1-5.1	0.082†

NLR: Neutrophil-to-lymphocyte ratio; SD: Standard deviation; Min: Minimum; Max: Maximum; \* One-way ANOVA test; † Kruskal-Wallis test.

version 2007 software (NCSS LLC, Kaysville, UT, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max), or number and frequency. The normality of quantitative data was tested by the Kolmogorov-Smirnov, Shapiro-Wilk test, and graphical evaluations. One-way analysis of variance (ANOVA) test was used for comparison of three or more groups and Bonferroni test for two-way comparison of groups with normal distribution. The Kruskal-Wallis test was used for the comparison of three or more groups without normal distribution. The Pearson chi-square test was used to compare qualitative data. A *p* value of <0.05 was considered statistically significant.

## RESULTS

There were 70 (43.5%) PAR patients and 39 (24.2%) patients in the study group and 52 (32.3%) individuals in the control group. Demographic characteristics of the patient and control groups are presented in Table 1.

Table 2 shows demographic characteristics of all participants according to groups. There was no statistically significant difference in the age and sex between the groups (*p*>0.05). Mean neutrophil count of allergic rhinitis, non-allergic rhinitis and control group were 55.9±6.2, 57.1±6.4 and 57.1±8.1, respectively. Mean lymphocyte count of allergic rhinitis, non-allergic rhinitis and control group were 32.9±6.6, 30.1±6.3 and 31.9±7.4, respectively. Neutrophil-to-lymphocyte ratio was same in allergic rhinitis and control group but slightly higher in non-allergic rhinitis group. There was no statistically significant difference in the neutrophil, lymphocyte, and NLR between the groups (*p*>0.05) (Table 3).

## DISCUSSION

Rhinitis is a worldwide problem characterized by congestion, rhinorrhea, sneezing, nasal itching, and nasal obstruction. It is mainly classified as AR and NAR. Allergic rhinitis is caused by an allergen which induces nasal symptoms. Nasal obstruction and rhinorrhea in NAR is caused by non-allergic, non-infectious triggers such as climate change, tobacco smoke, caustic odors, and barometric pressure differences.<sup>[19]</sup>

Neutrophils and lymphocytes are blood elements which play an important role in the inflammation process.<sup>[20]</sup> Previous studies have shown that lymphopenia and neutrophilia in the peripheral blood is associated with systemic inflammation response.<sup>[21]</sup> The NLR is calculated using neutrophil and lymphocyte counts in CBC and is an indicator of increasing popularity. The NLR is usually accepted as an indicator of subclinical inflammation.<sup>[22]</sup> There are many studies in the literature on NLR associated with various diseases. The NLR has been associated with mortality rates in community-acquired pneumonia.<sup>[23]</sup> It has also been shown to be helpful in determining short and long-term mortality in acute coronary syndrome, and increased NLR is associated with a higher mortality risk.<sup>[24,25]</sup> Elevated NLR has been shown in various peripheral vascular diseases, coronary artery diseases, and some gynecological and hepatobiliary malignancies and associated with poor prognosis.<sup>[25]</sup> In addition to clinical evaluation, the NLR is a useful parameter in the diagnosis of acute appendicitis and differentiation of complicated appendicitis.<sup>[26]</sup> Intiaz et al.<sup>[9]</sup> investigated the NLR in chronic diseases such as hypertension, diabetes mellitus, asthma, and arthritis in adults

and found no significant relationship between the NLR and allergic asthma. Some authors reported elevation of NLR in sudden hearing loss and emphasized its importance as an indicator of poor prognosis.<sup>[25,27]</sup> Similarly, Aydogdu<sup>[20]</sup> reported elevated NLR in nasal polyposis and described its prognostic value for the evaluation of recurrence.

The use of NLR as a prognostic marker of inflammation is still debated in the literature.<sup>[12]</sup> However, Dogru et al.<sup>[1]</sup> reported NLR was associated with AR severity and could be a useful indicator of inflammation in pediatric AR. Another study including children also showed that AR could be a helpful indicator of AR severity and could be used as an objective measurement.<sup>[12]</sup> Goker et al.<sup>[28]</sup> found relatively higher NLR in adult AR patients, compared to healthy population. The authors also suggested that NLR increased, when the severity of AR increased. However, in our study in adults, there was no significant difference between the groups in terms of the neutrophil count, lymphocyte count, and NLR.

Review of the literature reveals several studies showing the correlation between NLR and disease severity. In a study, the NLR increased with increasing Bell's palsy grade.<sup>[29]</sup> In Behçet disease, which is a systemic inflammatory vascular disease, the NLR was also reported higher than healthy individuals.<sup>[30]</sup> However, despite high TNSS, we found no significant correlation between the NLR and disease severity in our study.

Furthermore, a previous study showed that nasal inflammation was more intense during the symptomatic period and in severe AR.<sup>[31]</sup> The fact that all of the patients in our study had a TNSS of  $\geq 8$  and that NLR was evaluated during the period of intense nasal inflammation is important in which these findings are from, when the patients were actively sick. This is because NLR is a continuously changing parameter. However, according to our results, local nasal inflammation had no systemic effect, or at least it did not affect the NLR.

The main limitations of our study include its retrospective design, the lack of classification of the patients with AR according to the allergen

type, and the lack of discrimination of the subgroup of NAR.

In conclusion, our study shows that NLR is not a useful tool in the diagnosis and management of treatment in PAR and NAR in adults.

#### Declaration of conflicting interests

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