The correlation between asthma disease and neutrophil to lymphocyte ratio.

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Abstract

Purpose: It is shown that neutrophil to lymphocyte ratio (NLR) ((NLR; an indicator of inflammation)) measured in peripheral blood has a contribution in the determination of diagnosis and prognosis in numerous diseases. The purpose of this study was to investigate the correlation between asthma control status and NLR in asthmatic patients, which is a chronic inflammatory disease.

Material and method: 142 patients, who were followed up due to the diagnosis of asthma and had no acute asthma attack, and 104 healthy subjects were included in the study. Respiratory function tests (RFT) was applied to the patients who were followed up due to the diagnosis of asthma. Annual number of attacks, onset age of thedisease, and disease duration were examined. Disease control status was assessed with the asthma control test (ACT). It was categorized as ACT ≥ 20 and ACT<20. The difference between patient and control groups in terms of NLR was examined.

Results: Mean NLR was 2.2 ± 1.2 in the patient group and 1.83 ± 1.02 in the control group. The difference was statistically significant (p=0.005). Also, a significant correlation was found between ACT ≥ 20 and ACT<20 and NLR (p=0.002). There was no statistically significant difference between NLR and RFT values (p>0.05).

Conclusion: Mean NLR was higher in patients with asthma compared to control group. Also as the asthma control status worsened, NLR increased. We think that NLR can be guiding in asthmatic patients together with ACT especially in the assessment of asthma control status.

Keywords: Neutrophil to lymphocyte ratio, Asthma, Asthma control test.

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Introduction

Asthma is a chronic inflammatory airway disease that has airway hypersensitivity causing coughing attacks, recurrent wheezing, and dyspnea and that is diagnosed based on anamnesis, spirometric examination, and physiological and pathological characteristics. It is found that its prevalence rate varies based on the countries and between 1% and 18% [1,2].

Management of asthma, as stated by international guidelines, is based on the assessment of disease control [3,4]. A useful numerical method to evaluate the level of disease control is the asthma control test (ACT), which includes questions regarding symptoms, medication use, and self-assessed disease control [5]. Pathology of asthma is explained by the fact that numerous inflammatory cells and mediators affect all the airways. Even though inflammation affects all the airways, its physiological effects are the most significant on medium-sized bronchi [6-10]. In addition to airway inflammation, systemic inflammation is also present in asthmatic patients. The increased circulating pro-inflammatory cytokines such as interleukin (IL)-6 and Tumor necrosis factor- α (TNF-α) play a role in this inflammation. These proinflammatory cytokines in asthmatic patients increase in immune cells such as neutrophils and natural killer cells and stimulate hepatic production of acute- phase proteins such as C-reactive protein (CRP) [11,12].

More recently, an elevation in the neutrophil to lymphocyte ratio (NLR), an indicator of inflammation, has been associated with disease severity, hospitalization, malnutrition, and mortality in various chronic diseases such as cardiovascular, chronic obstructıve pulmonary disease (COPD) and kidney diseases [13-16].

There is also a chronic inflammation in asthma. Cytokines in the pathogenesis of asthma cause an increase in neutrophils [12]. This situation makes us think that NLR can elevate in asthmatic patients. Even though there is a limited number of related studies, the results were contradictory [17,18].

The purpose of this study is to assess the correlation between asthma disease, which is known to have inflammation in its pathogenesis, and asthma control status and NLR, which is a new indicator of inflammation.

Method

142 patients who were diagnosed with asthma according to Global Initiative for Asthma criteria at Sakarya University Training and Research Hospital, (Sakarya, Turkey), between 2014 and 2015, and 104 healthy volunteers, having similar characteristics in terms of age, gender and educational level were included in the study. Approval of the ethics committee and patient consents were taken. Hemogram, white blood cells (WBC), neutrophil count, lymphocyte count, CRP and NLR values of asthma and control groups were recorded and their results were compared. The patients having diabetes, hypertension, hyperlipidemia, coronary artery disease, cancer, liver diseases, taking systemic steroids, being smokers and experiencing acute asthma attacks were not included in the study because such diseases may affect the hemogram parameters. Because the infections may affect the neutrophil

level, the patients with fever, cough and sputum complaints were excluded from the study. Physical examinations of all the asthmatic patients and control group were performed in order to exclude infections. The individuals with findings of infection were excluded from the study.

Demographic data, onset age of the disease, disease duration, triggers, laboratory examinations, respiratory function tests (RFT) and ACT values of the patients were recorded. The disease control status of all participants in the asthma group was determined by the same pulmonologist using the Asthma Control Test™ (ACT).

Asthma control test™ (ACT)

The asthma group completed a 5-item questionnaire assessed with their asthma symptoms, use of rescue medications, and the impact of asthma on their daily life. Scores range from [5–25] (higher is better): a total score of 25 is considered to be complete control, a score of between [20–24] is considered as partial control and a score of 19 and below is considered to be uncontrolled disease [5]. In statistical analysis, participants achieving a score higher than 20 were assessed as a single group (partial control and complete control), and participants obtaining a score of lower than 19 were evaluated as a separate group (uncontrolled disease). The validity and reliability of this questionnaire was previously established in Turkish adults with asthma [19].

Laboratory tests

Blood samples were collected in a hematologic sample tube containing anticoagulant, and the following hematology parameters were investigated using Cell-Dyn 3700 SL hematology analyzer (Abbott Laboratories, North Chicago, IL, USA): neutrophils and lymphocytes. The NLR was calculated by using neutrophils / lymphocytes.

Statistical analysis

Statistical Package for the Social Sciences (version 21) software was used to analyze the data. While normally distributed continuous variables were evaluated using the t-test, nonparametric variables were analyzed by using the Mann–Whitney U test, and categorical variables were compared using the Chi square test. The General Linear Model was used for the adjustment of age and gender. A value of $p<0.05$ was accepted as statistically significant.

Results

142 patients with asthma and 104 healthy individuals as a control group were included in the study. Table 1 shows demographic and clinical characteristics, laboratory parameters and respiratory function findings of all the participants. There was no significant correlation between the groups in terms of gender, age, WBC, lymphocyte, CRP and haemoglobin. There was a significant correlation between the groups in terms of neutrophil and NLR (Table 1).

Objective effect

There were 9 PR cases, 15 SD cases and 4 PD cases in treatment group. Besides, there were 7 PR cases, 14 SD cases and 7 SD cases in control group. The PR is 32.1% (9/28) and 25.0% (7/28), respectively.

Table 1.Demographic and clinical characteristics, laboratory parameters and respiratory function findings of all the participants. NLR: Neutrophil-lymphocyte Ratio; ACT: Asthma Control Test™; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 second; PEF: Peak Expiratory Flow; IgE: Immunoglobulin E For DCR in the two groups, the value is 85.7% (24/28) and 75.0% (21/28), respectively. Though the curative effect was higher in treatment group, P>0.05 showed no significantly difference as shown in Table 1. A statistically significant correlation was determined between ACT ≥ 20 and ACT<20 in terms of Neutrophil-lymphocyte ratio (Table 2).

Gender (F/M)	Asthma (n:142)	Controls (n: 104)	P value
	(93 /49)	(70/34)	0.437
	Mean ± sd	Mean ± sd	
Age (years)	48.4 ± 11.4	51.8 ± 13.1	0.163
Hemoglobin(gr/dl)	13.3 ± 1.3	13.4 ± 1.3	0.469
Neutrophil (K/uL)	4.5 ± 1.5	3.6 ± 1.17	0.001
Lymphocyte (K/uL)	2.2 ± 0.6	2.1 ± 0.5	0.32
NLR	2.2 ± 1.2	1.83 ± 1.02	0.005
CRP (mg/L)	4.7 ± 2.8	4.6 ± 3.7	0.237
WBC	6.8 ± 2.5	6.3 ± 1.8	0.113
IGE (IU/ml)	201.7 ± 286.02	-	
Onset age (year)	40.2 ± 12.2	-	
Disease duration (years)	7.15 ± 7.4	-	
Number of attacks (year)	2.3 ± 1.54	-	
ACT	18.3 ± 5.1	-	
FVC(%)	86.6 ± 18.2	-	
FEV1(%)	78.2 ± 19.5	-	
FEV1/FVC	77.2 ± 8.3	-	
PEF(%)	78.2 ± 21.8	-	

Table 2. The correlation between NLR and ACT

Asthma Test™	Control	ACT ≥ 20	ACT<20	p value
		n=73	n=69	

NLR	2.0+1.1	2.51+1.33	0.002

While no significant correlation was observed between NLR and FVC, FEV1, FEV1/FVC, PEF, IgE, number of attacks, disease duration, a significant correlation was determined between NLR and ACT and CRP values (Table 3).

Table 3. The correlation between NLR and clinical characteristics, laboratory parameters and respiratory function in asthmatic patients. NLR: Neutrophil-Lymphocyte Ratio; FVC; Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 second; PEF: Peak Expiratory Flow; IgE: Immunoglobulin E; ACT: Asthma Control Test™.

		FVC	FEV1	FEV1/FVC	PEF	IGE	Attack	Disease duration	ACT	CRP
NLR	R	0.109	0.146	0.101	0.062	0.063	0.11	0.187	0.206	0.458
	P	0.113	0.084	0.230	0.466	0.459	0.561	0.072	0.014	0.001

Discussion

In this study, NLR that is used as an inflammatory indicator and that is shown especially in an inflammatory marker in numerous studies in recent years was examined in asthma patients. Also the effect of NLR on the control status of the disease was assessed in asthmatic patients. Our data confirm that NLR in patients with asthma was higher compared to controls. Also as asthma becomes uncontrolled, NLR increases. No correlation was observed between NLR and annual number of attacks, disease duration, and respiratory function test results.

It is reported that NLR can be guiding in the prognosis of diseases in the studies conducted on NLR, which is an inflammatory marker and which is shown to be prone to atherosclerotic base in some chronic diseases [13-16,21-24]. Based on these studies, we assessed NLR in asthma disease.

In the management of asthma, simple and accessible biomarkers are required; however there is no specific consensus in the literature [18].

Inflammatory markers have an important place in the pathogenesis of asthma disease. The correlation between cytokines and asthma is reported in some studies. Cytokines in the pathogenesis of asthma cause an increase in neutrophils [12]. Among the studies reporting the correlation between NLR and asthma; Imtiaz et al. stated that there is no correlation; Zhang et al. and Dogru et al. reported data highlighting that they have a correlation [17,18,20]. In the study of Imtiaz et al., NLR was not compared with control group. It was not a study conducted only with asthmatic patients but a study examining the prevalence of NLR in chronic diseases [17]. The study of Dogru et al. was a study comparing the children with asthma and the healthy ones [20]. In the present study, NLRs of healthy controls and patients with asthma were compared and NLR was found to be higher in patients with asthma compared to the control group. We are of the opinion that asthma disease is not only an airway disease but also a systemic inflammatory disease.

Viral infections can frequently cause acute asthma attacks and asthma attack may lead to neutrophil infiltration in the airway mucosa. In a study in the literature, heterogeneous airway inflammation containing eosinophil, neutrophil and mast cells was determined in an acute asthma attack [25]. In the present study, the patients with infection findings and acute asthma attacks were excluded.

In a study assessing the correlation of NLR in COPD patients; NLR and CRP showed a positive correlation [16]. In the present study, CRP and NLR showed a positive correlation.

Pro-inflammatory cytokines such as (IL)-6 and TNF- α increase in asthmatic patients with asthma and these increase in immune cells such as neutrophils and natural killer cells and stimulate hepatic production of acute- phase proteins such as CRP in asthmatic patients [11,12]. This hypothesis can be thought as the result of the correlation of CRP and NLR in asthmatic patients.

In asthma patients; no correlation was found between NLR and SFT values, IgE values, number of attacks and disease duration, but the significant correlation determined between NLR and ACT scores made us think that NLR can be guiding in the control of asthma disease.

There are some limitations in this study. Firstly, the population size was relatively small. Secondly, we did not set a specific blood sampling time although circadian variations in circulating neutrophil and lymphocyte counts were reported. The strengths of this study are that the patients who are exactly diagnosed by asthma according to the anamnesis, spirometric examination and physiological characteristics were included in the study and also there was no comorbid chronic disease and infection which could affect NLR.

In conclusion, mean NLR is higher in patients with asthma compared to the control group. Also as asthma becomes uncontrolled, NLR increases. We think that NLR could be used to evaluate systemic inflammation in asthmatic patients. Also in the outpatient clinic controls of the asthma patients, we think that NLR can be assessed in addition to the asthma control test because it is a simple, easy, and cheap method. However, since previous data reporting the correlation between asthma and NLR are contradictory with each other, we are of the opinion that further studies are required with larger patient groups.

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