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Is there a relationship between systemic immune-inflammatory indices and asthma?

Systemic immune inflammatory indices in patients with asthma

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Abstract

Aim: Immune inflammatory response plays an important role in patients with asthma. The goal of the current study is to determine whether pan-immune inflammation value (PIV) and systemic inflammatory response index (SIRI) are effective in predicting asthma.

Material and Methods: This retrospective study included 55 patients and 55 healthy controls followed in the Allergy and Immunology Clinics of Ordu University Training and Research Hospital.

Results: Neutrophil, Monocyte, MPV and PDW were statistically significant between the groups ($p<0.05$). A statistically significant difference was found between SIRI, PIV and dNLR, indices between the groups ($p<0.05$). No statistically significant difference was detected between SII, NLR, PLR and LMR compared to the controls ($p>0.05$).

Discussion: We concluded that SIRI and PIV could be novel and cost-effective inflammatory indices in patients with asthma.

Keywords

Asthma, Inflammation, Systemic Inflammatory Response Index, Pan-Immune-Inflammation Value

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Introduction

Asthma is a common chronic inflammatory disease with a heterogeneous spectrum that can cause shortness of breath, cough, wheezing and chest tightness [1]. Asthma affects 1-20% of the population in different countries and 300 million people worldwide [2]. In Turkey, it has been reported that the prevalence of asthma in adults ranges from 1.2 to 9.4% [3]. The main features of asthma are reversible bronchial obstruction and airway hyperresponsiveness caused by chronic airway inflammation, and systemic inflammation is part of this condition. Inflammation is a response of the immune system in many diseases [4-6]. In asthma, an inflammatory response occurs as a result of the immune response occurring more than normal to stimuli in the airway.

Oxidative stress (OS) plays a crucial role in the pathogenesis of many diseases and has not been fully elucidated [7-11]. OS occurs as a result of the deterioration of the balance between free radicals and antioxidants and plays a significant role in the pathogenesis of many diseases, including asthma [12]. It is known that there is a link between increased oxidative stress and asthma severity.

Systemic inflammatory mast cell activation occurs in patients with asthma, which is mediated by a variety of cell cytokines (e.g., eosinophilic neutrophils, macrophages, platelets, etc.) and a variety of mediators, which have been considered crucial in the development of clinical asthma [13]. For asthma, biomarkers that are easy to measure are needed to distinguish between phenotypes, determine treatment option, and predict response to treatment. In recent years, cell counts in the peripheral blood sample and combinations such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLO) have been accepted as indicators of systemic and ocular inflammatory conditions. There are many studies showing the systemic immune-inflammatory index such as pregnancy loss [14], sepsis [15], chronic urticaria [16] and breast cancer [17]. SIRI and PIV are new immune biomarker indices that are important in terms of immune response and systemic inflammation.

Systemic inflammation index (SII), which is a new parameter calculated by the formula of neutrophil x platelets/lymphocytes; compared to PLO and NLR, it is a much more important marker in showing inflammation and immune response. As a new inflammatory biomarker, SII has been proposed as a prognostic indicator in many different clinical settings, including asthma and autoimmune disorders [14]. Recently, Erdogan et al. found that patients with an SII value ≥895.6 had a probability of having NERD with a sensitivity of 30.56%, whereas those with a lower SII had a probability of having asthma with a sensitivity of 92.65% [18]. Peripheral blood biomarkers have been the focus of research lately, as they are inexpensive, available, and common measurements. Limited data are available on SII and asthma. In our study, while inflammation has such an important place in the pathogenesis of asthma, we aimed to determine hemogram parameters and new inflammation indices compared with the control group.

Material and Methods

This retrospective study was conducted at the Ordu University, Education and Research Hospital, Department of Immunology and Allergic Diseases Outpatient Clinic from June 2022- to March 2023. A total of 55 patients diagnosed with asthma were included in the present study. The control group consisted of age- gender matched healthy individuals. There was no significant difference between the groups in terms of age and gender. The data of the study groups were obtained from the hospital automation system. The current study was approved by the ethics committee of Ordu University (Date:31.03.2023 / No: 2023/87). The study was conducted in accordance with the Helsinki Declaration rules.

The hemogram parameters and serum C-reactive protein (CRP) levels were assessed. Neutrophil, lymphocyte, platelet and monocyte levels of groups were used in the complete blood parameters. The NLR, PLR, LMR, SII, SIRI PIV and dNLR respectively, were calculated as follows: the ratio of neutrophils to lymphocytes, platelets to lymphocytes, lymphocytes to monocytes, that of platelets x (neutrophils / lymphocytes), (neutrophils x monocytes) / lymphocytes and (neutrophils x platelets x monocytes) / lymphocytes. The neutrophil count is divided by the result of the WBC count minus the neutrophil count.

Diagnosis of asthma

The diagnosis of asthma was made using clinical history and by demonstrating objective measures of reversible airway obstruction [forced expiratory volume in one second (FEV1)< 80% and FEV1/forced vital capacity (FVC)< 70% with an improvement in FEV1 12% and 200 mL after 400 mcg of salbutamol or average daily diurnal PEF variability> 10% over two weeks) [3].

Exclusion criteria

The study exclusion criteria were as follows: exacerbation of asthma in the last month, active neoplastic processes, diagnosed active viral or bacterial infection, chronic kidney disease and elevated serum CRP/ erythrocyte sedimentation rate.

Statistical analysis

SPPS 22 was used to carry out all data analysis. Data were reported as means ± min-max. Whether the data were normally distributed or not was determined with the Kolmogorov-Smirnov test. Variables that did not show normal distribution were compared with the Mann-Whitney U test. Categorical variables were compared with the chi-square test. Statistical significance was accepted as <0.05.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The present study consisted of 55 asthma patients with an average age of 41.8 ± 15.2 years and 55 healthy controls with an average age of 41.5± 12.5 years. There was no statistically significant difference between the groups in terms of age and gender (Table1).

Median (min-max) outcomes of the hemogram parameters and indexes between the groups are shown in Table 2.

Neutrophil, Monocyte, MPV and PDW were statistically significant between the groups (p<0.05, Table 2). However, there was no statistically significant difference between other hemogram parameters. In addition, inflammatory indices were

calculated for the study groups. A statistically significant difference was found between SIRI and PIV and dNLR indices between the groups (p<0.05). Table 2). However, there was no significant difference between SII, NLR, PLR and LMR groups (p>0.05, Table 2).

Table 1. Demographic information of the study groups.

Parameters		Asthma (n=55) mean ± SD	Control (n=55) mean ± SD	p
Gender	Male	22 (40%)	28 (50.9%)	0.58*
	Female	33 (60%)	27 (49.1%)	
Age (year)		41.8 ± 15.2	41.5 ± 12.5	0.93¥

*Chi-Square test ¥ Student t -test

Table 2. Comparison of blood parameters of the study and control groups.

Parameters	Asthma (n=55) median (min-max)	Control (n=55) median (min-max)	p*
White Blood Cell (10^3/L)	7.7 (4.3-11.9)	7.4 (4.4-10.3)	0.580
Neutrophil (10^3/L)	4.5 (1.6 -8.3)	3.7 (2.4-6.9)	0.020
Lymphocyte (10^3/L)	2.4 (1.2- 4.3)	2.25 (1.2-3.9)	0.204
Monocyte (10^3/L)	0.6 (0.3-1.5)	0.48 (0.26-0.75)	0.045
Hemoglobin (g/dL)	13.6 (9.9-17.1)	13.3 (10.4-16.6)	0.237
Platelet (10^3/L)	268 (152- 402)	263 (162-458)	0.526
MPV (fL)	10.2 (8.4-12.1)	9.3 (5.9-12.1)	<0.001
PDW	11.8 (8.6-17.9)	9.7 (5.6-16.1)	<0.001
PCT	0.28 (0.14-0.37)	0.31 (0.17-0.56)	0.067
CRP (mg/L)	4.5 (0.4-10.5)	1.8 (0.2 -5.0)	0.574
SII	515.5 (146.8 -1094)	460.3 (208- 1036)	0.148
SIRI	1.09 (0.24- 3.9)	0.84 (0.36- 1.8)	0.023
PIV	295.2 (58.7- 1121.6)	220.3 (85.6 -580.3)	0.045
NLR	1.93 (0.6-4.1)	1.76 (0.9-3.4)	0.228
PLR	118.5 (61.4-271)	123.1 (60.6-205)	0.243
LMR	4.67 (1.85 – 9.75)	4.96 (2.2 -10.2)	0.401
dNLR	1.4 (0.3-2.4)	1.36 (0.3-2.3)	0.020

*Mann-Whitney U test NLR: Neutrophil-to-Lymphocyte Ratio, CRP: C-reactive protein, MPV: Mean Platelet Volume, PCT: Procalcitonin, PDW: Platelet distribution width, PLR: Platelet-to-Lymphocyte ratio, dNLR: Derived NLR ratio (neutrophil count divided by the result of WBC count minus neutrophil count), SII: Systemic inflammatory index (neutrophil x platelet / lymphocyte count), SIRI: Systemic inflammatory response index (neutrophil × monocyte / lymphocyte count) and PIV: Pan-immune inflammation value (neutrophil × platelet x monocyte /lymphocyte count).

Discussion

Asthma is a complex inflammatory disorder that occurs with a chronic inflammatory deterioration in the respiratory tract and its incidence is increasing, especially with urbanization [19]. Airway inflammation seen in asthma patients is continuous and the relationship between asthma severity and inflammation has not been fully clarified yet. Therefore, the evaluation of the inflammatory process in asthma and the effective management of the process are clinically very important.

In the present study, for the first time, we demonstrated NLR, PLR, LMR, SII, SIRI, and PIV indices together in patients with asthma. This study was to examine whether systemic inflammatory indices play a role in predicting the prognosis of patients with asthma. In this retrospective study, we demonstrated that SIRI, PIV and dNLR levels were higher and statistically significant in patients with asthma compared to the control group (p<0.05). Although SII and NLR levels were higher in asthma patients compared to the control group, they were not statistically significant (p>0.05). However, we indicated that PLR and LMR levels were found to be lower in the patient group compared to the control group, and there was no statistical difference between the groups. Moreover, we examined hemogram parameters and neutrophil, lymphocyte, PDW, and PCT values were found to be higher and statistically significant in the patient group compared to control subjects (p<0.05). However, WBC lymphocyte hemoglobin, CRP and platelet levels were high but not statistically significant in the patient group than in healthy subjects.

In Erdogan's study examining systemic immune inflammation in asthma patients, he reported the probability of having nonsteroidal antiinflammatory drug (NSAID)-exacerbated respiratory disease (NERD) in patients with an SII value of ≥895.6, and a sensitivity of 92.65% in patients with a low SII value of 30.56%. In addition, N/L ratio was found as a risk factor for NERD that is affecting SII. [18]. Erdogan indicates that the presence of SII below the threshold has shown that it can be used to exclude the diagnosis of NERD. Another study conducted by Sagmen et al. showed that PLR levels were higher in asthma patients compared to the control group [20]. However, they reported that they found the NLR levels to be the same in both groups. They concluded that PLR could be valuable in asthma control and they stated that further clinical studies should be done. In a study by Thasen et al. they indicated that NLR and PLR levels were high in asthma patients with respect to the non-asthmatic healthy controls [21]. They concluded that at high inflammation, NLR and PLR are indicative of strong interdependence.

A study by Lin et al. on breast cancer patients found PIV levels to be significant [22]. They concluded that PIV was an independent predictor of breast cancer. They thought that it helps the clinicians implement targeted and individualized treatment strategies. In our study, SIRI and PIV levels we found to be significant between the study and healthy subjects. Similar studies have shown that patients with high levels of NLR, PLR and SII have a poor prognosis [23, 24]. The results obtained were different from those of our study. In the present study, NLR, PLR and SII levels were not statistically significant among the groups.

A study by Ceran et al. on Hypoxic Ischemic Encephalopathy (HIE) patients demonstrated that NLR, SII and PIV values were found statistically significant compared to the healthy subjects [25]. They hypothesized that systemic inflammatory indices may be reliable and readily available predictors of HIE risk. They also concluded that NLR was an independent factor in distinguishing between moderate and severe HIE. Similar to the studies, we found the PIV and SIRI values to be significant.

Conclusion

In conclusion, we indicated that SIRI and PIV is a new and practical inflammatory index that can be used in the evaluation of asthma patients. These indices can be an inexpensive, practical and safe indicator of the inflammatory state in patients with asthma. However, a larger patient population is needed to obtain stronger results.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
The authors declare no conflict of interest.

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