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Monocyte eosinophil ratio and red blood cell distribution width in the diagnosis of asthma

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Abstract

Objective: Bronchial asthma is often associated with chronic airway inflammation and airway hyperresponsiveness in which many cells and mediators are involved. Pulmonary function tests (PFTs) are used in the diagnosis of the disease. Yet PFTs are not available in every healthcare institution or some of the patients cannot cooperate with the procedure. The aim of this study was to determine whether mean platelet volume (MPV), platelet distribution width (PDW), monocyte lymphocyte ratio (MLR), monocyte eosinophil ratio (MER), and platelet lymphocyte ratio (PLR) can be used in the diagnosis of bronchial asthma.
Method: Two hundred and twelve patients who were diagnosed with bronchial asthma according to the Global Initiative for Asthma (GINA) criteria and 187 patients who were deemed not to have asthma were included in the study. Two patient groups were compared by examining the hemogram parameters at the time of diagnosis or exclusion of asthma.
Results: The levels of MPV, neutrophil-lymphocyte ratio (NLR), and PLR were significantly lower in the Asthma group ($p < 0.001$, 0.005, and 0.002 respectively) while the lymphocyte, eosinophil, monocyte, basophil, PDW, MLR, and MER levels were higher in the same group. On ROC analysis areas under the curve (AUC) for RDW, MER, and PDW were found as 0.81, 0.93, and 0.76 respectively.
Conclusion: In conclusion, higher lymphocyte, eosinophil, PDW, MLR, and MER whereas lower levels of MPV, NLR and PLR support the diagnosis of asthma.

Keywords: Asthma, Red Cell Distribution Width, Monocyte, Eosinophil

INTRODUCTION

Asthma is one of the most common chronic respiratory diseases that affects 1-20 % of the population in different countries and an estimated 300 million people around the World (1). The disease is often associated with chronic airway inflammation and airway hyperresponsiveness in which many cells and mediators are involved. It can be triggered by factors such as exercise and may improve with treatment or spontaneously. Asthma can be seen at any age, creates an obstacle in daily life, negatively affects the quality of life, and therefore becomes a global public health problem (2). Asthma; constitutes a significant social and economic burden and morbidity for patients, their families, and the health system (3). Asthma is a serious cause of labor loss and disability worldwide. Anamnesis, physical examination findings, and pulmonary function tests (PFTs) are used to diagnose the disease. Yet PFTs are not available in every healthcare institution, some patients cannot cooperate with the procedure, or due to their health conditions, PFTs cannot be performed. There is a need for objective tests without the need for the patient's effort to help doctors during the diagnosis. Hemogram parameters such as white blood cell (WBC) count, red blood cell distribution width (RDW), mean platelet volume (MPV), platelet distribution width (PDW), neutrophil-lymphocyte ratio (NLR), and platelet lymphocyte ratio (PLR) have been investigated as diagnostic parameters in some diseases (4, 5). In the COVID-19 pandemic, recent studies reported an association between high levels of PDW and COVID-19 mortality

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(6). All parameters mentioned above are studied by routine complete blood count tests that clinicians might overlook. This study aimed to determine whether MPV, PDW, monocyte lymphocyte ratio (MLR), monocyte eosinophil ratio (MER), and PLR can be used in diagnosing bronchial asthma.

METHOD

Files of patients admitted to Pulmonary Medicine Clinic in Bursa City Hospital/Bursa Turkey between January 2020, and October 2021 were investigated. Two hundred and twelve patients who presented with complaints such as shortness of breath and chest tightness underwent a complete blood count blood analysis and were newly diagnosed with asthma bronchiale according to the Global Initiative for Asthma (GINA) criteria as a result of the evaluation, and 187 patients who were deemed not to have asthma were included in the study. Pregnants, patients with chronic obstructive pulmonary disease (COPD), asthma attack, renal and cardiac failure, and respiratory insufficiency were excluded. All patients' demographic information and clinical data were recorded (Table 1). Two patient groups were compared by examining the hemogram parameters (Neutrophil, lymphocyte, monocyte, eosinophil, platelets, and PDW) at the time of diagnosis or exclusion of asthma. Leukocytes were measured using fluorescent flow cytometry; erythrocytes and platelets were measured using the impedance method. NLR, PLR, and monocyte lymphocyte ratio (MLR) values were calculated by dividing neutrophil, platelet, and monocyte levels to lymphocyte count. MER, neutrophil eosinophil ratio (NER), and lymphocyte eosinophil ratio (LER) were obtained by dividing monocyte, neutrophil, and lymphocyte levels to eosinophil, respectively. The ethics committee approval was obtained from Bursa City Hospital Clinical Research Ethics Committee (Ethics Committee Approval No:2021-22/4) in accordance with Helsinki Declaration. Statistical analyses were performed using SPSS 25.0 software. The normality of the sample data was evaluated with the Kolmogorov-Smirnow test, and the continuous variables were defined by the mean ± standard deviation, median (interquartile range 25-75 %), categorical variables were expressed as frequency and percent. A Student's t-test or a Mann-Whitney U test was used to compare the independent groups. The ROC analysis was performed for optimal cut-off values to predict asthma, and a p-value less than 0.05 was set as the statistical significance level.

RESULTS

The mean age was determined to be 29.5 (18-80) in the No-Asthma group and 30 (18-71) in the Asthma group (Table 1), with the Asthma group having a significantly greater median age ($p < 0.001$). The gender distribution in the No-Asthma group was 45.5% (85) women and 54.5% (102) men, while it was 59.9 % (127) women and 40.1% (85) men in the Asthma group.

Table 1. Demographic Data and Laboratory Findings of Patients with Asthma and Controls

Variable		No-Asthma		Asthma		p-value
		n=187		n=212		
		n	%	n	%	
Gender	Female	85	45.5	127	59.9	0.004
	Male	102	54.5	85	40.1	
Age (years)		29.5 (18-80)		30 (18-71)		0.001
WBC $10^3/\mu L$		7.1 (3.9-14)		7.3 (2.6-18.6)		0.09
Neutrophil $10^3/\mu L$		4.38 (1.02-13.6)		4.06 (1.06-13.83)		0.2
Lymphocyte $10^3/\mu L$		1.96 (0.49-3.85)		2.21 (0.6-5)		0.02
Eosinophil $10^3/\mu L$		0.17 (0.02-0.92)		0.22 (0.03-1.6)		0.05
Monocyte $10^3/\mu L$		0.4 (0.14-1.1)		0.51 (0.09-1.14)		0.001
Platelets $10^3/\mu L$		247 (132-454)		241 (130-556)		0.8
Basophil $10^3/\mu L$		0.04 (0.01-0.24)		0.05 (0.01-0.17)		0.001
RDW fL		12 (10.9-31.9)		13.9 (12-29)		0.05
MPV fL		8 (6.3-10.7)		7.8 (5.9-10)		0.001
PDW fL		16 (15-18)		16.7 (14.9-20.9)		0.001
NLR		2.06 (0.3-27.2)		1.8 (0.33-13)		0.005
PLR		122 (57-363)		107 (54-251)		0.002
MLR		0.18 (0.05-0.69)		0.22 (0.03-0.68)		0.004
MER		2.29 (0.33-16.5)		10 (1.3-161)		0.04
LER		11.9 (1.7-67)		10(1.36-161)		0.2
NER		24.5 (0.3-68)		18.6 (0.71-46)		0.04

RDW: Red blood cell distribution width, MPV: mean platelet volume, PDW, platelet distribution width, NLR: neutrophil-lymphocyte ratio, PLR: platelet lymphocyte ratio, MLR: monocyte lymphocyte ratio, MER: monocyte eosinophil ratio, LER: lymphocyte eosinophil ratio NER: neutrophil eosinophil ratio. Categorical variables were compared by the Chi-square test. Independent groups were compared by the Mann-Whitney U test. Bold values denote statistical significance at $p < 0.05$.

The levels of MPV, NLR, PLR, and NER were significantly lower in the Asthma group ($p < 0.001$, 0.005, 0.002, and 0.04, respectively). In contrast, the red blood cell distribution width (RDW), lymphocyte, eosinophil, monocyte, basophil, PDW, MLR, and MER levels were higher in the same group. The Roc analysis with ROC curves was performed for optimal cut-off values to predict Bronchial Asthma (Figure 1). Youden Index was exploited to identify the optimal cut-off values. In addition, a p-value less than 0.05 was set as the statistical significance level. Areas under the curve for comparison of the No-Asthma group to the Asthma group were calculated. Areas under the curve (AUC) for eosinophil, RDW, MLR, MER, and PDW were found as 0.57, 0.81, 0.57, 0.93 and 0.76 respectively (Table 2).

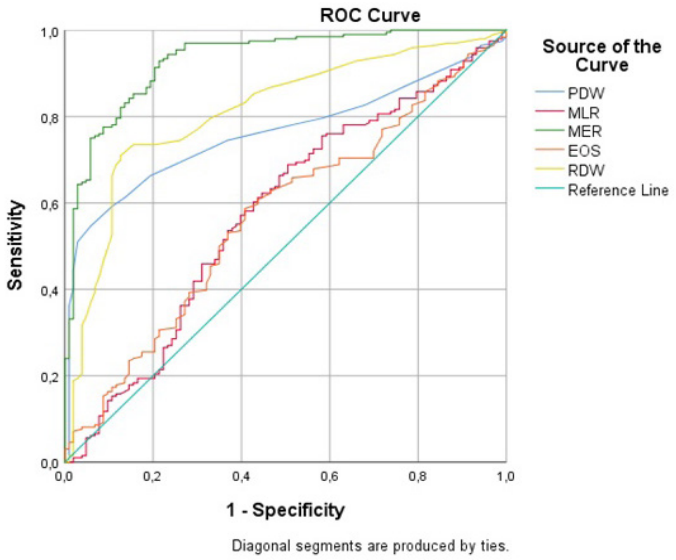

Figure 1. The ROC Curve of platelet distribution width (PDW), monocyte lymphocyte ratio (MLR), monocyte eosinophil ratio (MER), eosinophils (EOS), and red blood cell distribution width (RDW).

Table 2. ROC Analysis of patients with asthma and controls.

Variable	AUC (95%CI)	Cut-off	Sensitivity %	Specificity %	p
EOS	0.572	≥0.19	58	59	0.04
RDW	0.81	≥12.7	74	73	0.001
MLR	0.577	≥0.2	59	57	0.02
MER	0.930	≥4.83	84	83	0.001
PDW	0.76	≥16.1	70	72	0.001

EOS: Eosinophil, RDW: Red Blood Cell Distribution Width, MLR: monocyte lymphocyte ratio, MER: monocyte eosinophil ratio, PDW: platelet distribution width. Bold values denote statistical significance at the p <0.05

DISCUSSION

Lymphocytes play an essential role in the maintenance of immune system function. After a viral infection, changes in total lymphocyte numbers vary with different virus types. Asthma is a heterogeneous disease that may activate the immune system (7). In the present study Asthma group had significantly higher lymphocyte levels (p=0.02). Eosinophils are circulating and tissue-resident leukocytes that can potentially produce proinflammatory effects in some diseases. Eosinophils also have been shown to have various other functions like immunoregulation and antiviral activity. In severe eosinophilic asthma, high blood eosinophil levels have been associated with worse disease control and bad prognosis (8). The present study aimed to determine if eosinophil levels can help diagnose asthmatic subjects. In the present study, eosinophil levels of Asthmatic subjects were significantly higher.

Mean platelet volume is easily measured in the complete blood count analysis and reflects the functional and activity of platelets and their production rate from megakaryocytes. Some previous studies reported elevated levels of MPV in cerebrovascular diseases. (9), whereas other studies reported reduced MPV levels in rheumatoid arthritis (10). In the present study, MPV levels remained lower in the Asthma group. Similar to the present study, Sun et al. reported that patients with stable asthma had a lower MPV than controls. They included asthmatic subjects with exacerbation and found that asthmatic patients with exacerbations had lower MPV than stable asthmatic subjects (11). In light of these findings, investigating the mechanisms that cause the decrease in MPV values may be a method for treating and preventing the disease.

Red blood cell distribution width measures the variation of red blood cell volume. In a study, Gunbatar et al. reported a positive correlation between the apnea-hypopnea index of patients with obstructive sleep apnea syndrome and RDW (12). In this study, there were higher levels of RDW in patients with asthma compared to controls. High RDW values might be due to ongoing or recurrent inflammatory conditions. Previous studies reported low levels of PDW in COPD compared to healthy controls and smokers (13). In the present study, PDW levels were higher in the Asthma group. In a study, Ulucan et al. reported that major adverse cardiovascular events were more frequent in patients with a high PDW value (14). In infectious diseases, parameters such as C-reactive protein, erythrocyte sedimentation rate, and neutrophil levels are elevated, while some parameters, such as albumin, decrease. Today it's known that systemic inflammation observed in asthma has effects beyond the respiratory system (15). In light of this study and the studies mentioned above, systemic inflammation observed during asthma may be associated with a decrease in MPV. In contrast, an increase in RDW and PDW was observed in some other inflammatory conditions.

Recent studies suggest a preponderant role for monocyte-macrophage activation in the development of immunopathology and bad prognosis of COVID-19 patients (16, 17). In a study, macrophages were higher in asthmatic subjects' blood (18). In the present study, monocyte levels in the Asthma group were significantly higher. The present study hypothesized that the ratio of the values of these cells, which have an essential role in the inflammatory response, to the values of other inflammatory cells might guide the diagnosis of asthma. MLR and MER were both found to be higher in the asthmatic subjects whereas. In light of the obtained results and previous studies, higher levels of monocyte, MLR, and MER might indicate asthma. MER had an AUC of 93 (sensitivity 84 % and specificity 83 %).

In recent years, NLR and PLR have been in use by researchers in the diagnosis and prognosis of many inflammatory conditions. High levels of NLR were reported in patients with COVID-19 (19). In a study regarding patients with systemic lupus erythematosus, high NLR and PLR levels reflected inflammatory response and disease activity (20). In the present study, NLR, PLR, and NER were lower in the Asthma group. In a study, Yenigun et al. reported a high eosinophil-lymphocyte ratio and eosinophil counts in pediatric patients with allergic rhinitis (21). The present study aimed to investigate the usefulness of the LER in the diagnosis of asthma, yet no differences were found between groups.

Limitations of the Study

This study has limitations; besides its retrospective design, even though all parameters studied belong to the period before the treatment of asthma, information on unregistered diseases or therapies couldn't be obtained might have affected the parameters. The study results can guide the diagnosis stage but do not help the disease follow-up.

CONCLUSION

In conclusion, higher lymphocyte, eosinophil, monocyte, basophil, PDW, MLR, and MER, whereas lower levels of MPV, NLR, NER, and PLR support the diagnosis of asthma in patients who present to the clinic of the pulmonary disease with dyspnea in whom PFTs cannot be performed or who cannot cooperate with PFTs.

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Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Ethical Declaration

The ethics committee approval was obtained from Bursa City Hospital Clinical Research Ethics Committee (Ethics Committee Approval No:2021-22/4) in accordance with Helsinki Declaration.

Authorship Contributions

Concept:İK, Design: İK, SD, Supervising: İK, Financing and equipment: İK, SD, Data collection and entry: İK, Analysis and interpretation İK, SD, Literature search: İK, SD, Writing: İK, SD.

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