

Evaluation of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio and mean platelet volume according to the disease activity index in patients of ankylosing spondylitis

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ABSTRACT

Objective: To determine the relationship between neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and mean platelet volume (MPV) with acute phase reactants in patients with ankylosing spondylitis (AS) and to show the usability of these parameters in the activation periods and follow-up of the disease.

Material and Method: The demographic data (age, gender) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of 70 patients who had been followed regularly for at least 1 year and whose diagnosis of AS was definite were recorded. The control group consists of 70 people who do not have any disease. Among the laboratory parameters, neutrophil, platelet, lymphocyte count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), NLR, PLR and MPV values were retrospectively checked and recorded.

Results: In our study, a statistically significant difference was found between the AS patients and the control group in MPV, NLR and PLR values. In addition, these values were found to be statistically significantly different between the groups with low disease activity and high disease activity in the AS patient group. There was a weak negative correlation between MPV value and BASDAI, ESR and CRP values. There was no statistically significant correlation between NLR value and ESR and CRP. There was no correlation between PLR value and ESR and CRP.

Conclusion: As a result of our study, NLR, PLR and MPV values are seen as simple, easy and inexpensive markers that can be used to determine disease activity in AS patients.

Keywords: Ankylosing spondylitis, NLR, PLR

INTRODUCTION

Ankylosing spondylitis (AS) is the most common subtype of the Spondyloarthritis (SpA) group that causes inflammatory back pain. It is a common inflammatory disease that causes structural and functional disability (1). AS is an autoimmune disease which is manifested by a variety of genetic and environmental factors influence (2). Axial skeleton and especially sacroiliac joint involvement is prominent in AS (3). The most important complaint is inflammatory back pain. Entesal and peripheral joint involvement is usually present. The most common extraarticular involvement is uveitis (4).

There is no specific laboratory finding to diagnose patients with AS. Acute phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)

may be normal in patients with AS, but are frequently used in the diagnosis and treatment of the disease. Rheumatoid factor (RF) and antinuclear antibodies (ANA) are negative (5). Imaging methods are important in the diagnosis and classification of AS (6).

Because AS progresses with periods of exacerbation and remission, some scales are used in disease activation and evaluation of response to treatment.; It evaluates disease-specific symptoms such as fatigue, spinal and peripheral joint pain, swelling, and morning stiffness.

It is evaluated on scores ranging from 0-10. An increase in the score indicates an increase in disease activity. It is a reliable and change-sensitive scale developed to evaluate disease activity and progression (7).

Recently, it has been found that neutrophil, lymphocyte and platelet values, which are a part of the immune system and obtained from the routine complete blood count in the follow-up of rheumatological diseases, are associated with autoimmune diseases, malignancies, inflammatory diseases and chronic diseases. In addition, it has been shown that neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) are associated with ESR, CRP, interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) values (8).

Mean platelet volume (MPV) is obtained directly from the hemogram parameter. It decreases in the activation of rheumatological diseases and shows a negative correlation with ESR, CRP. This may indicate that MPV can be used as a negative acute phase reactant. There are differences in studies on NLR and PLR in rheumatological patients.

The aim of our study is to determine the relationship between NLR, PLR, MPV values of our AS patients who are followed up in our outpatient clinic with acute phase reactants according to the disease activation level and to show the usability of these parameters during the activation periods and follow-up of the disease.

MATERIAL AND METHOD

This study was approved by the university/local human research ethics committee, and all procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee, the 1964 Declaration of Helsinki and subsequent amendments or comparable ethical standards. Ethics committee approval was obtained from Hitit University Clinical Researchs Ethics Committee for the study (Date: 05.02.2020, Decision No: 169). In our study, the files of AS patients registered in Hitit University Erol Olçok Training and Research Hospital Physical Therapy and Rehabilitation Department between 2018-2019 were retrospectively scanned. Demographic data (age, gender) and BASDAI score of 70 patients who had been followed up regularly for at least 1 year and whose diagnosis of AS was definite were recorded. The control group consists of 70 people who do not have any disease. The exclusion criteria of the patient group were acute infection, diabetes, cancer or chronic diseases. Laboratory results of the patient and control groups were examined. CRP (mg/L), ESR (mm/h) values were obtained from biochemical analysis. Neutrophil ($10^9/L$), lymphocyte ($10^9/L$), platelet ($10^9/L$) counts and MPV (fL) values were obtained from the hemogram analysis. The NLR value was determined by dividing the neutrophil count by the lymphocyte count and the PLR value by dividing the platelet count by the lymphocyte count. Clinical evaluation and laboratory data of only one examination data of a patient were included in the study. The patient group

was divided into two groups with BASDAI score below 4 as low activity and 4 and above high activity. CRP, ESR, platelet, MPV, NLR and PLR values obtained from routine hemogram analysis were compared with the disease and control groups. In addition, these values were compared in the patient group according to the BASDAI score.

Statistical Analysis

Statistical analyzes were performed using a package program called SPSS (IBM SPSS Statistics 24). Frequency tables and descriptive statistics were used in the interpretation of the findings. Parametric methods were used for measurement values suitable for normal distribution. In accordance with parametric methods, "IndependentSample-t" test (t-table value) method was used to compare the measurement values of two independent groups. Nonparametric methods were used for measurement values that are not suitable for normal distribution. In accordance with non-parametric methods, "Mann-Whitney U" test (Z-table value) method was used to compare the measurement values of two independent groups. The expected Pearson- χ^2 and continuity correction cross tables were used to examine the relationships between two qualitative variables. "Pearson" correlation coefficient in examining the relationship of two quantitative data with normal distribution; "Spearman" correlation coefficient was used to examine the relationship of two quantitative data that do not have normal distribution. Binary Logistic Regression: Backward LR model was used to determine the factors affecting high disease activity.

RESULTS

There is no statistically significant relationship between the groups and gender ($p>0.05$). Groups are gender-neutral and homogeneous. A statistically significant relationship was found between the BASDAI classes of the patients and their gender ($\chi^2=6.121$; $p=0.013$). It was found that 23 (82.1%) of the women were in the low disease activity class and 21 (50.0%) of the men were in the high disease activity class. It was determined that those with low disease activity level were predominantly female, and those with high disease activity level were predominantly male (Table 1).

Variable	Gender				Statistical analysis* Possibility
	Female	Male	n	%	
Group					
Ankylosing spondylitis	28	50.0	42	50.0	$\chi^2=0.000$
Control	28	50.0	42	50.0	$p=1.000$
Patient BASDAI class					
Low activity (<4)	23	82.1	21	50.0	$\chi^2=6.121$
High activity (≥ 4)	5	17.9	21	50.0	$p=0.013$

* Continuity correction or "Pearson- χ^2 " cross tables were used to examine the relationships of two qualitative variables.

A statistically significant difference was found between the groups in terms of CRP, MPV, NLR, Platelet and PLR values ($p < 0.05$). The CRP, NLR, Platelet and PLR values of those in the ankylosing spondylitis group were found to be statistically significantly higher than those in the control group, and the MPV value was significantly lower (Table 2).

Variable	Group	Ankylosing spondylitis (n=70)	Control (n=70)	p value
		X \pm SS	X \pm SS	
Age (years)		41.08 \pm 10.25	42.54 \pm 10.45	0.052
Disease Duration (years)		6.25 \pm 2.4	-	
CRP(mg/L)		10.74 \pm 14.22	4.60 \pm 3.37	0.020
ESR (mm/h)		14.95 \pm 13.87	12.70 \pm 10.14	0.622
Neutrophil (10 ⁹ /L)		4.33 \pm 1.35	4.07 \pm 1.30	0.245
Lymphocyte (10 ⁹ /L)		2.29 \pm 0.79	2.46 \pm 0.64	0.055
NLR		2.06 \pm 0.89	1.75 \pm 0.71	0.010
Platelet(10 ⁹ /L)		272.07 \pm 64.60	250.71 \pm 60.92	0.022
MPV(fL)		9.75 \pm 1.35	10.47 \pm 0.93	0.004
PLR		132.40 \pm 55.05	110.21 \pm 51.27	0.010

* IndependentSample-t test was used for comparing the measurement values of two independent groups in the data with normal distribution, and the "Mann-Whitney U" test statistics were used to compare the measurement values of two independent groups in the data without normal distribution.

While there was no statistically significant difference in age according to the BASDAI classes of the patients ($p > 0.05$), a statistically significant difference was found in terms of CRP, ESR, platelet, NLR, MPV, PLR values ($p < 0.05$). CRP, ESR, platelet, NLR, and PLR values of those in the high disease activity group were significantly higher, while MPV was significantly higher in the low disease activity group (Table 3).

There was a positive correlation between BASDAI score and CRP, ESR and a weak negative correlation with MPV. There was a weak correlation between CRP values and ESR in the positive direction and a negative correlation with MPV. In the correlation analysis of ESR values, negative weak correlation with MPV was obtained.

Variable	BASDAI class	Low disease [<4] (n=44)	High disease [≥ 4] (n=26)	Statistical analysis
		X \pm SS	X \pm SS	
Age(years)		40.80 \pm 10.55	41.58 \pm 9.90	t=-0.306 p=0.760
CRP		4.42 \pm 2.90	21.43 \pm 18.82	p=0.000
ESR		11.41 \pm 9.59	20.92 \pm 17.72	p=0.018
NLR		1.95 \pm 0.84	2.26 \pm 0.94	p=0.047
Platelet		276.05 \pm 55.40	365.35 \pm 78.52	P <0.001
MPV		10.24 \pm 0.88	9.90 \pm 1.92	p=0.003
PLR		131.76 \pm 53.69	133.46 \pm 58.35	p=0.008

"Independent Sample-t" test (t-table value) for comparing the measurement values of two independent groups in the data with normal distribution; "Mann-Whitney U" test statistics were used to compare the measurement values of two independent groups in the data that did not have a normal distribution.

There was a weak positive correlation between NLR and PLR value, and a weak negative correlation between MPV and its value (Table 4).

Correlation* (n=70) Variable		BASDAI score	CRP	ESR	NLR	PLR	MPV
BASDAI score	r	1.000	0.705	0.298	0.195	0.238	-0.305
	p	-	0.000	0.012	0.006	0.034	0.020
CRP	r		1.000	0.467	0.225	0.068	-0.285
	p		-	0.000	0.061	0.577	0.033
ESR	r			1.000	0.160	0.226	-0.301
	p			-	0.184	0.060	0.023
NLR	r				1.000	0.421	-0.299
	p				-	0.000	0.049
PLR	r					1.000	-0.044
	p					-	0.113

*"Pearson" correlation coefficient was used to examine the relationship of two quantitative data with normal distribution, and "Spearman" correlation coefficient was used to examine the relationship of two quantitative data with no normal distribution.

DISCUSSION

Ankylosing spondylitis (AS) is a common rheumatic disease that predominantly affects the axial skeleton, with structural and functional disability causing inflammatory low back pain. More than 80% of patients usually start to show their first symptoms before the age of 30. Men are significantly more affected by the disease than women. In our study, a statistically significant relationship was found between BASDAI classes and gender. It was determined that those with low disease activity level were predominantly female, and those with high disease activity level were predominantly male.

MPV shows the average circulating platelet size obtained from a complete blood count. Its normal value is 7.5-11.5 fl. It is a parameter indicative of platelet function and activity, and it decreases with the pressure of pro-inflammatory cytokines and acute phase markers on the bone marrow in inflammation and shows a negative correlation in the inflammatory process (9,10). In studies conducted with RA patients, MPV levels were found to be lower in the patient group compared to the control group, and an inverse correlation was found with disease activity scores (11).

Negative correlations were found with BASDAI in AS patients, with CRP in psoriatic arthritis patients, and with ESR in SLE patients (12,13). Although many studies have suggested that MPV decreases in inflammatory diseases and it can be studied as a negative marker, some studies have found that MPV value is similar between AS patients and the control group and does not correlate with CRP (14). In our study, a statistically significant difference was found in MPV value between AS patients and the control group. MPV level was found to be significantly lower in AS patients. In addition, MPV value was found

to be statistically significantly higher in AS patients, in the group with low disease activity. There was a weak negative correlation between MPV value and BASDAI, ESR and CRP values.

It suggested that the increase in the number of neutrophils and platelets in the systemic circulation in the presence of inflammation, and the decrease in the number of lymphocytes, NLR and PLR parameters can be used as a marker in rheumatic diseases and in the activation periods of these diseases. The NLR value is an easy, cheap and simple parameter obtained by dividing the number of neutrophils obtained from the complete blood count by the number of lymphocytes and the PLR value by the number of lymphocytes (15). In recent studies, there are many studies showing the usability of NLR and PLR as inflammatory and activity markers in inflammatory rheumatic diseases. In some studies, it was reported that the NLR value was higher in the active disease group than in the inactive disease group according to the BASDAI score and there was a positive correlation between the BASDAI score and the NLR value. Contrary to these studies, there are also studies that could not find a correlation between BASDAI and NLR (10,16,17). It is included in studies in which a significant positive correlation was found between NLR values and ESR and CRP levels (17). In our study, the NLR values were found to be statistically significantly different between the AS patients and the control group, and the AS group with high disease index and the AS group with low disease index. In our study, no statistically significant correlation was observed between NLR value and ESR and CRP.

PLR has been found as an inflammatory marker and a valuable prognostic factor in some malignancies and patients diagnosed with heart failure (17,18). In a study conducted with AS patients, a significant statistical difference was found between the patient group and the control group in PLR value (17). In a meta-analysis study, PLR values did not differ significantly between the patient and control groups (14). In some correlation studies, a positive correlation was found between PLR and ESR and CRP (16,19). In our study, the PLR value was found to be statistically significantly different in both the patient group and patients with AS with high activity index. There was no correlation between PLR value and ESR and CRP.

CONCLUSION

As a result of our study, NLR, PLR and MPV values are seen as simple, easy and inexpensive markers that can be used to determine disease activity in AS patients. The limitation of our study is that it is retrospective. These parameters may also guide new indices to be investigated in future studies for AS diseases, and we believe that they will contribute to the literature.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval was obtained from Hitit University Clinical Researchs Ethics Committee (Date: 05.02.2020, Decision No: 169).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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