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DIAGNOSTIC IMPORTANCE OF MEAN PLATELET VOLUME IN ANKYLOSING SPONDYLITIS AS A DISEASE ACTIVITY PREDICTOR

Dr Ramsha Mehmood[1], Dr Aisha Abrar[2], Dr Ahmed Naeem[3]

[1] DHQ Hospital Bhakkar

[2] Sargodha Medical College

[3] THQ Hospital Samundri, District Faisalabad

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Abstract:

Introduction: *Ankylosing spondylitis (AS) is a chronic progressive inflammatory rheumatic disease that leads to a significant reduction in quality of life. Average platelet volume (MPV) is part of a complete blood test (CBC) and is associated with platelet function and activation.*

Aim: *To evaluate the diagnostic value of MPV in patients with AS and to assess its relationships with disease activity index.*

Place and Duration: *In the Rheumatology department of Allied Hospital Faisalabad for one year duration from April 2019 to March 2020.*

Patients and methods: *A total of 100 patients with AS (78 men: 22 women) were diagnosed according to modified New York classification criteria for AS, and 146 (99 men: 47 women) healthy subjects were selected for age and gender as controls. Demographic data, disease activity scores were measured using ankylosing spondylitis activity index (BASDAI), history, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and MPV.*

Results: *The mean age of patients was 38.0 ± 9.0 years and controls 35.8 ± 8.3 years. Men constituted 78% of patients and 67.8% of controls. The mean BMI was 28.3 ± 5.5 kg / m2 in patients and 28.6 ± 3.8 kg / m2 in the control group. There were no statistically significant differences in age, sex and BMI between patients and the control group (p> 0.05). MPV was significantly higher in patients with AS compared to healthy controls (9.215 ± 1.57 vs. 7.753 ± 0.86). MPV had a good ability to distinguish between active AS and inactive patients with AS. The optimal cut-off point was less than 9.9. MPV had the highest accuracy (79%) with a high specificity of 86.8%, the positive predictive value (PPV) in the 50% initial test was 84.9%, and in the 90% preliminary test was 98.1% with a sensitivity of 74.2% and the negative predictive value (NPV) at the 10% initial test was 96.8%. MPV had a significant positive correlation with disease activity. Increased MPV will increase disease activity.*

Conclusion: *MPV was significantly higher in patients with AS than in the control group and was directly correlated with ESR, CRP and BASDAI.*

Key words: *mean platelet volume, ankylosing spondylitis, disease activity, BASDAI*

Corresponding author:

Dr. Ramsha Mehmood,

DHQ Hospital Bhakkar

QR code

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INTRODUCTION:

Ankylosing Spondylitis (AS) is a chronic systemic inflammatory disease that primarily affects the axial skeleton. The estimated prevalence of AS in Pakistan is 0.13%, where 84% are HLA-B27 positive, and 2.1% of healthy populations have a positive HLA-B27 level[1-2]. The collective effect of AS has a significant impact on the quality of life of patients, over 75% of patients can remain employed and enjoy a good quality of life[3]. Laboratory indicators, including the erythrocyte sedimentation rate (ESR) and C-reactive protein level (PCR), include the most commonly used methods for assessing Alzheimer's disease[4-5]. However, these markers have several limitations, such as reflecting short-term inflammatory activity and low ability to distinguish with other overlapping inflammations. MPV is a machine-calculated measure of average platelet size[6]. It reflects platelet size and platelet production in the bone marrow, and can be used as an indicator of platelet activation and inflammation. Previous research has shown a link between AS and MPV levels. Increased platelet size as a result of platelet activation has been shown to be associated with numerous inflammatory diseases[7]. As far as we know, there is no prior research on the relationship between MPV and disease activity in AS patients in Pakistan. This study designed to evaluate the diagnostic value of blood MPV in patients with AS and to assess its relationship with acute phase reactants (ESR and CRP) and disease activity index.

PATIENTS AND METHODS:

Study design

This case-control study was conducted at the Rheumatology department of Allied Hospital Faisalabad for one year duration from April 2019 to March 2020.

A total of 100 consecutive patients diagnosed with AS according to modified New York criteria were enrolled in the study and compared with 146 healthy controls of the same age and sex. The informed consent was obtained from each participant covered by this study. Ethical approval was obtained from the Ethical Committee. Patients were excluded if they had one of the following symptoms: other autoimmune diseases such as Sjogren's syndrome, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease and psoriasis, acute or chronic infection, cancer, end-stage renal disease, liver disease, hepatitis and liver cirrhosis such as haematological disorder or blood transfusion in the last 4 months, acute myocardial infarction, cerebrovascular disease and 6 months of pregnancy or postpartum.

Data collection and input

Patient data and controls were entered through interviews and questionnaires using a paper-based clinical trial (CRF) form. All patients were asked for age, gender, illness and smoking time, height in centimeters and weight in kilograms. Body mass index (BMI) was measured according to BMI = weight / height2, disease activity and functional class, and drugs were recorded. All controls were asked for age, gender, cigarette, height, weight and BMI.

Data monitoring and methods

Blood samples were taken in both groups for measuring complete blood count (CBC), erythrocyte sedimentation rate (ESR), C. reactive protein (CRP), red cell distribution width (RDW) and mean platelet volume (MPV). Disease activity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the functional class was evaluated using the Bath Ankylosing Spondylitis functional index (BASFI)

Statistics analysis

The Kolmogorov-Smirnov test was carried out to assess the normal distribution of continuous variables. If they were normally distributed, the mean ± standard deviation was used. Categorical variables are represented by numbers and percentages. The chi-square test was used to analyze the categorical variable. The Student's t-test was used to analyze the mean difference between the two groups. The receiver's operational curve was used to assess validity. MPV to differentiate patients with AS from control, i.e. if AUC $\geq$ 0.9 indicates an excellent test, 0.8-0.89: good test, 0.7-0.79: honest test, otherwise unacceptable). Logistic regression analysis was performed to assess the relationship between patient baseline and disease activity. SPSS version 20.0, Graph Pad Prism software package version 7.0 was used to perform statistical analysis $p < 0.05$ was considered significant.

RESULTS:

The study involved 100 patients with AS and 146 people from the control group. The mean age of patients was 38.0 ± 9.0 years and controls 35.8 ± 8.3 years. 78% of these men were patients and 67.8% were controls. The mean BMI was 28.3 ± 5.5 kg / m2 in patients and 28.6 ± 3.8 kg / m2 in the control group. There was no statistically significant difference between patients and the control group in terms of age, sex and BMI ($p > 0.05$). Other clinical features are presented in Table 1.

Table 1 Baseline characteristics of ankylosing spondylitis patients and controls

Variables	Patients=100	Controls=146	p-value
Age (mean ± SD), years	38.0 ± 9.0	35.8 ± 8.3	0.057
Sex n (%)			0.081
Female	22 (22.0%)	47 (32.2%)	
Male	78 (78.0%)	99 (67.8%)	
BMI	28.3 ± 5.5	28.6 ± 3.8	0.596
Smoking n (%)	41 (41.0%)	45 (30.8%)	0.1
Disease duration	9.0 (5.0-13.8)	-	-
BASDAI	4.2 ± 1.6	-	-
BASFI	4.1 ± 1.6	-	-
Biologics n (%)	89 (89%)	-	-
DMARDs n (%)	17 (17%)	-	-
NSAIDs n (%)	68 (68%)	-	-
Steroids n (%)	5 (5%)	-	-
ESR median(IQR)	34 (18-50.8)	-	-
CRP median(IQR)	9 (5-15.2)	-	-

SD: standard deviation; BMI: body mass index; BASDAI: Bath ankylosing spondylitis disease activity Index; BASFI: Bath ankylosing spondylitis functional index; DMARDs: Disease-modifying anti-rheumatic drugs; NSAIDs: Non-steroidal antiinflammatory drugs; ESR: Erythrocytes sedimentation rates; CRP: C-reactive protein

MPV was significantly higher in patients with AS compared to healthy controls (9.215 ± 1.57 and 7.753 ± 0.86) as shown in Figure 1.

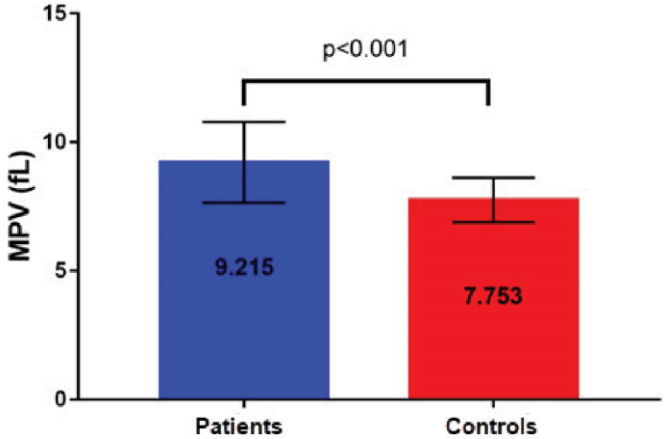

Figure 1 Error bars of mean platelet volume in patients and controls

MPV has the ability to distinguish between patients with active and inactive AS. At the optimal cut-off point below 9.9 MPV had the highest sensitivity (79%) with 86.8% high specificity, with positive predictive value (PPV) 84% in the previous 50% test, 98.1% with 74.2% accuracy, and 9% and 90% in the previous test. In the previous test, the 10% negative predictive value (NPV) was 96.8% as in Figure 2.

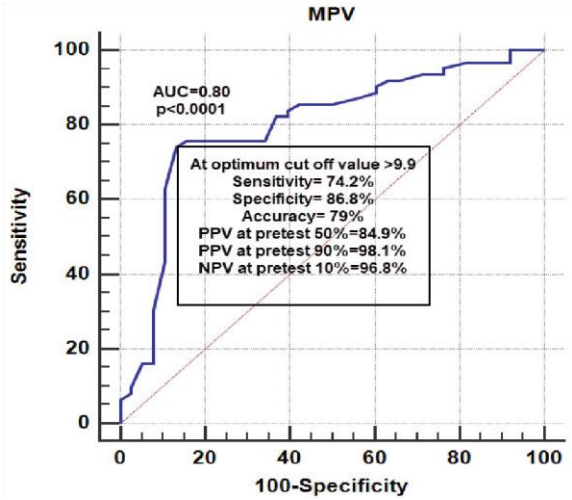

Figure 2 ROC curve to differentiate between active AS and inactive AS. MPV: mean platelets volume; AUC: area under curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; AS: ankylosing spondylitis

Logistic regression analysis to determine the impact of demographic and clinical features on MPV showed that only MPV has a significant positive correlation with disease activity. Increasing MPV will increase disease activity about 11 times, as in Table 2.

Table 2 Logistic regression analysis to show a correlation of AS disease activity with MPV and other demographic and clinical characteristics

Variables	OR	95% C.I. for OR		p-value
		Lower	Upper	
Age	0.933	0.705	1.234	0.628
Males	152.556	0.481	48427.067	0.087
BMI	0.789	0.503	1.239	0.303
Disease duration	0.847	0.597	1.203	0.355
BASFI	1.869	0.534	6.544	0.328
ESR	1.037	0.931	1.156	0.505
CRP	5.057	1.196	21.377	0.028
MPV	11.405	1.341	97.011	0.026
Methotrexate users	79678.521	0	-	0.996
Sulfasalazine users	185.97	0	$9X10^{14}$	0.726
Infliximab users	5.989	0.003	10818.191	0.64
Etanercept users	0.067	0	434.819	0.547
Adalimumab users	0.02	0	-	0.997
Steroid users	0	0	-	0.998
NSAID users	194.147	0.322	117127.25	0.107
Analgesia users	0	0	3.883	0.086

Overall accuracy of the model 94%, P of the model <0.001; BMI: Body mass index, BASDAI: Bath ankylosing spondylitis disease activity index, BASFI: Bath ankylosing spondylitis functional index; MVP: Mean platelet volume

DISCUSSION:

This study looked at the relationship between blood MPV and disease activity in AD patients. It showed that MPV was significantly higher in patients than in the control group and was significantly associated with disease activity. MPV was an important measure that distinguished an active substance from an inactive disease. This is clinically important in the prediction and early diagnosis of disease activity and early treatment. MPV had good ability to distinguish active AS from patients with inactive AS[8-9]. At the optimal breakpoint> 9.9 MPV had the highest precision with high specificity, high precision, high positive predictive value and high

negative predictive value. Another notable observation was the significant direct correlation between MPV and ESR and RP and BASDI. This indicates that the increase in MPV is associated with inflammatory markers that suggest disease activity and, consequently, high disease activity. Sezgin et al. It was found that the optimal MPV cutoff value in patients with AD was higher than in healthy controls of 10.4, sensitivity 35.9%, specificity 85.0% and AUC 0.58 and p = 0.016. However, MPV negatively correlated with ESR and CRP and did not correlate with BASDAI. The difference between the current and previous survey may be related to the study plan, sample size, and differences in geographical factors[10-11].

Ustun et al. It has been reported that MPV levels in AS patients were higher than in healthy controls, but there was no significant difference between active and inactive AS patients compared to MPV[12-13]. Previous studies have rated MPV, and its relationship to disease activity has conflicting results. A possible explanation may be associated with an increase in pro-inflammatory cytokines and acute phase reagents that can suppress platelet size and reduce MPV by affecting mega-karyopoiesis and affecting platelet release from bone marrow. On the other hand, larger platelets are known to be inflammatory and thrombotic agents and are more reactive[14-15]. This can be attributed to time-dependent changes in MPV during various phases of inflammation. In acute inflammation, excessive production and release of platelets from the bone marrow can lead to smaller platelets, while in chronic inflammation platelets with higher chromogenic and proinflammatory cytokines can dominate and cause an increase in MPV.

In a previous study involving 30 active AS patients, MPV and BASDAI results were not initially correlated. After treatment, MPV values increased, BASDAI scores decreased, and a statistically significant negative correlation. However, this study included more patients with AS and control than previous ones.

CONCLUSION:

MPV was significantly higher in AS patients than in controls. The MPV was a good test to differentiate AS from controls. There was a direct correlation between MPV with ESR, CRP, and BASDAI. This suggests that The MPV can be used in diagnosis and prediction of AS disease activity. Larger sample size and longer duration study to further validate the findings of this study.

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