Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2018, 7(8): 40-45

Diagnostic Value of Mean Platelets Volume in Ankylosing Spondylitis as a Predictor of Disease Activity

Faiq I. Gorial*

Rheumatology Unit, Department of Medicine, College of Medicine, University of Baghdad, Baghdad, Iraq

**Corresponding e-mail: faiqig@gmail.com*

ABSTRACT

Background: *Ankylosing spondylitis (AS) is a chronic progressive inflammatory rheumatic disease that leads to significant decrease in the quality of life. Mean platelet volume (MPV) is a part of the complete blood count (CBC) test and correlates with the platelets function and activation.* ***Objective:*** *To evaluate the diagnostic value of MPV in patients with AS and to assess its relationships with disease activity index.* ***Patients and Methods:*** *A total of 100 patients with AS (78 males: 22 females) were diagnosed according to the modified New York classification criteria for AS and 146 (99male: 47 female) healthy individuals were matched in age and sex as controls. Demographic data, disease activity scores using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), medical history, C-reactive protein (CRP), erythrocytes sedimentation rate (ESR), and MPV were measured.* ***Results:*** *Mean age of patients was 38.0 ± 9.0 years and controls were 35.8 ± 8.3 years. Males were 78% in patients and 67.8% in controls. The mean BMI was 28.3 ± 5.5 kg/m^2 in patients and 28.6 ± 3.8 kg/m^2 in controls. There were no statistically significant differences in age, sex, and BMI between patients and controls ($p>0.05$). 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 differentiate between active AS and inactive AS patients. Optimum cut off point was less than 9.9. MPV had the highest accuracy (79%) with high specificity 86.8 %, positive predictive value (PPV) at pretest 50% was 84.9%, and at pretest, 90% was 98.1% with sensitivity 74.2% and negative predictive value (NPV) at pretest 10% was 96.8%. MPV had a significant positive correlation with disease activity. Increased MPV will increase disease activity.* ***Conclusion:*** *MPV was significantly higher in AS patients than in controls and directly correlated with ESR, CRP, and BASDAI.*

Keywords: Mean platelet volume, Ankylosing spondylitis, Disease activity, BASDAI

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic, systemic, inflammatory disorder that primarily affects the axial skeleton [1]. In Iraq, the estimated prevalence rate of AS is 0.13%, in which 84% are HLA-B27 positive, while 2.1% of healthy populations are HLA-B27 positive [2,3]. The collective impact of AS has a substantial influence on patients' quality of life over 75% of patients are able to remain in employment and enjoy a good quality of life [4]. Laboratory indicators, including the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level comprise the most widely used methods to assess AS disease [5]. However, these markers have several limitations, such as the reflection of short-term inflammatory activity and low discrimination ability with other superimposed inflammatory conditions [6-8].

The MPV is a machine-calculated measurement of the average size of platelets. It reflects the platelet size and the rate of platelet production in bone marrow, and it may be used as an indicator of platelet activation and severity of inflammation [9].

An association between AS and MPV levels has been demonstrated in a previous study [10]. It has been shown that increased platelet size, as a result of platelet activation, is associated with numerous inflammatory diseases [11-14].

Up to the best of our knowledge, there is no previous study on MPV in Iraqi patients with AS and relationship with disease activity. 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 Unit of Baghdad Teaching Hospital in Medical City and Basra centre for biological therapy in Al-Basra General Hospital from August 2016 to March 2017.

Sample Selection

A total of 100 consecutive patients diagnosed to have AS according to the modified New York criteria were included in the study and compared with another 146 healthy controls matched in age and sex [15]. Informed consent was obtained from each participant included in this study according to the declaration of Helsinki. Ethical approval was obtained from the Ethics Committee in Medical Department, College of Medicine, Baghdad University, Iraq.

Patients were excluded from the study if they had one of the following: Other autoimmune diseases such as Sjogren Syndrome, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel diseases and psoriasis, acute or chronic infection, malignant diseases, end-stage renal disease, liver disease such as hepatitis and liver cirrhosis, hematological disorders or received blood transfusion during the past 4 months, acute myocardial infarction, cerebrovascular disease, and pregnancy or postpartum 6 months.

Data Collection and Entry

Data entry of patients and controls were done using paper clinical research (CRF) form through interview and questionnaires. All patients were asked for age, sex, disease duration, and smoking status, height in centimeter and weight in kilogram. Body mass index (BMI) was measured according to the equation BMI=weight/height^2, disease activity and functional class, and medications were recorded. All controls were asked for age, sex, smoking status, height, weight, and BMI.

Methods and Data Monitoring

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) [16,17].

Statistical Analysis

Kolmogorov-Smirnov test was done to assess the normal distribution of continuous variables. If they were normally distributed then mean ± standard deviation was used. Categorical variables were presented using numbers and percentages. Chi-square test was used to analyze the categorical variable. Student t-test was used to analyze the difference in means between two groups. Receiver operating curve was used to assess the validity. MPV to differentiate AS patients from controls i.e. if AUC $\geq$ 0.9 indicates excellent test, 0.8-0.89: good test, 0.7-0.79: fair test otherwise unacceptable). Logistic regression analysis was performed to assess the relationship between baseline patient's characteristics with disease activity. SPSS version 20.0, Graph Pad Prism version 7.0 software package were used to do the statistical analysis $p<0.05$ was considered significant.

RESULTS

A total of 100 AS patients and 146 controls were involved in the study. The mean age of patients was 38.0 ± 9.0 years and controls 35.8 ± 8.3 years. Of those males were 78% in patients and 67.8% in controls. The mean BMI was 28.3 ± 5.5 kg/m^2 in patients and 28.6 ± 3.8 kg/m^2 in controls. There were no statistically significant differences in age, sex, and BMI between patients and controls ($p>0.05$). Other clinical features were shown 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 anti-inflammatory 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 vs. 7.753 ± 0.86) as illustrated in Figure 1.

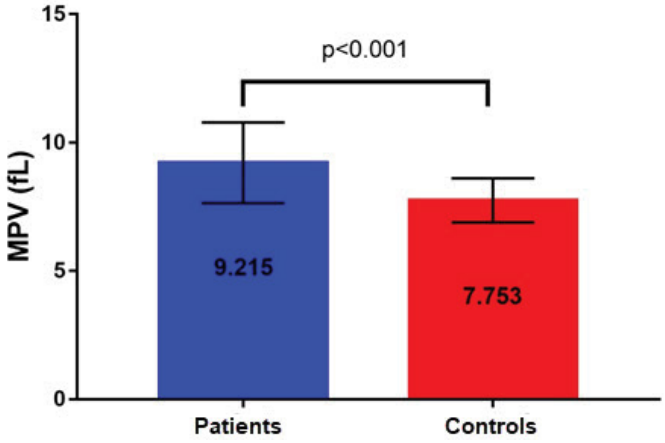

Figure 1 Error bars of mean platelet volume in patients and controls

MPV had a good ability to differentiate between active AS and inactive AS patients. At optimum cut off point less than 9.9, MPV had the highest accuracy (79%) with high specificity 86.8%, positive predictive value (PPV) at pretest 50% was 84.9%, and at pretest 90% was 98.1% with sensitivity of 74.2% and negative predictive value (NPV) at pretest 10% was 96.8% as in Figure 2.

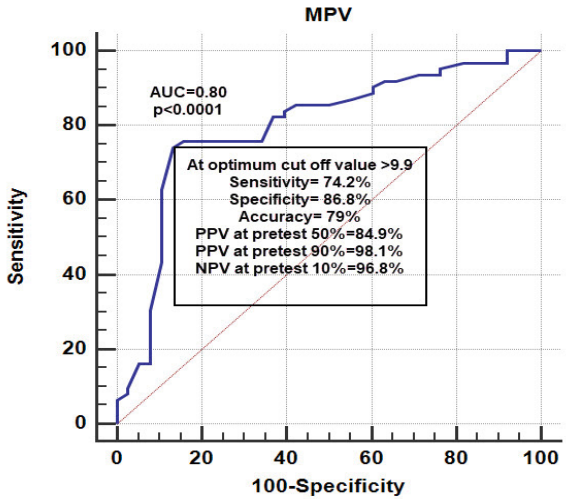

Figure 2 ROC curve to differentiate between active AS and inactive AS. MPV: mean platelets volume; AUC: area under curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; AS: ankylosing spondylitis

Logistic regression analysis to find the effect of demographic and clinical characteristics on MPV showed only disease MPV had a significant positive correlation with disease activity. Increased MPV will increase disease activity by about 11 folds 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 evaluated blood MPV in AS patients and its relationship with diseases activity. It showed that MPV was significantly higher in patients compared with controls and significantly associated with disease activity. MPV was a valid measure to differentiate active disease from inactive. This is clinically important to predict and early diagnose disease activity and early treatment.

MPV had a good ability to differentiate active AS from inactive AS patients. At the optimum cut off point >9.9, MPV had the highest accuracy with high specificity, high positive predictive value with good sensitivity and high negative predictive value.

Another observation of note was a significant direct correlation between MPV with ESR and RP and with BASDI. This indicates that increased MPV is associated with inflammatory markers suggestive of disease activity and in consequence high disease activity.

Sezgin, et al., found that MPV was higher in AS patients than in healthy controls with optimum cut-off value equals to 10.4, sensitivity 35.9%, specificity 85.0%, and AUC 0.58 and p=0.016 [18]. However, MPV was negatively correlated with ESR and CRP and not correlated with BASDAI. The difference between the current study from the previous study may be related to the differences in the study design, sample size, and geographical factors.

Ustun, et al., reported that MPV level in AS patients were higher than healthy controls but there was no significant difference between active and inactive AS patients according to MPV [19]. The previous studies evaluated MPV and its relation with disease activity has conflicting results. A possible explanation may be related to increasing pro-inflammatory cytokines and acute phase reactants that can suppress platelet size and decrease MPV by affecting megakaryopoiesis and platelet release from bone marrow [20]. On the other hand, larger platelets are known to include pro-inflammatory and thrombotic agents and more reactive [21,22]. This may be attributed to the time-dependent changes of MPV during different inflammation phases. In acute inflammation, the over-production and release of platelets from bone marrow may lead to smaller sized platelets while in chronic inflammation period platelets containing chromogenic and pro-inflammatory cytokines with a larger size may predominate causing increased MPV.

In a previous study including 30 active AS patients, MPV and BASDAI scores were found to have no correlation initially. After treatment, MPV values increased and BASDAI scores decreased and they had a statistically significant negative correlation [23]. Nevertheless, the current study included a larger number of AS patients and controls compared to the previous one.

LIMITATIONS

Limitations of the present study include short duration of the study, the financial barrier to do the tests for every AS patients even when clinically not required plus the healthy control individuals tests. Many AS patients who are residents of cities that face war circumstances and even those who reside quite cities but distant from the study centers made these AS patient not involved in the study and all these have affected not only the sample size but also the geographical distribution and coverage. However, this is the first study in Iraq that evaluated MPV as a parameter in patients with AS and its correlation with disease activity. It is a cheap and easy test to be performed as it is a common component of the complete blood count (CBC) test that is nowadays widely distributed in nearly every healthcare facility and by an automated machine.

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.

DECLARATIONS

Acknowledgment

I thank all the participants in the study and Dr. Ali Makki for helping in the data collection. This work was supported by Baghdad teaching Hospital and Baghdad College of Medicine, University of Baghdad. There was no specific grant or any funding.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Zochling, Jane, and Emma UR Smith. "Seronegative spondyloarthritis." *Best Practice and Research Clinical Rheumatology,* Vol. 24, No. 6, 2010, pp. 747-56.

[2] Abdelrahman, M. H., et al. "Prevalence of HLA-B27 in patients with ankylosing spondylitis in Qatar." *International Journal of Rheumatology,* Vol. 8, No. 6, 2012, pp. 213-16.

[3] Mustafa, Khader N., Mohammed Hammoudeh, and Muhammad Asim Khan. "HLA-B27 prevalence in Arab populations and among patients with ankylosing spondylitis." *The Journal of Rheumatology,* Vol. 39, No. 8, 2012, pp. 1675-77.

[4] Doward, Lynda C., et al. "Translation and validation of non-English versions of the Ankylosing Spondylitis Quality of Life (ASQOL) questionnaire." *Health and Quality of Life Outcomes,* Vol. 5, No. 1, 2007, p. 7.

[5] Ruof, J., and G. Stucki. "Validity aspects of erythrocyte sedimentation rate and C-reactive protein in ankylosing spondylitis: a literature review." *The Journal of Rheumatology,* Vol. 26, No. 4, 1999, pp. 966-70.

[6] Colglazier, Christopher Lee, and Paul George Sutej. "Laboratory testing in the rheumatic diseases: a practical review." *South Medical Journal,* Vol. 98, No. 2, 2005, pp. 185-91.

[7] Kavanaugh, Arthur. "The role of the laboratory in the evaluation of rheumatic diseases." *Clinical Cornerstone,* Vol. 2, No. 2, 1999, pp. 11-25.

[8] Mercan, Ridvan, et al. "The association between neutrophil/lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis." *Journal of Clinical Laboratory Analysis,* Vol. 30, No. 5, 2016, pp. 597-601.

[9] Yuri Gasparyan, Armen, et al. "Mean platelet volume: a link between thrombosis and inflammation?." *Current Pharmaceutical Design,* Vol. 17, No. 1, 2011, pp. 47-58.

[10] Kisacik, Bunyamin, et al. "Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis." *Joint Bone Spine,* Vol. 75, No. 3, 2008, pp. 291-94.

[11] Sakallı, Hale, and Öznur Kal. "Mean platelet volume as a potential predictor of proteinuria and amyloidosis in familial Mediterranean fever." *Clinical Rheumatology,* Vol. 32, No. 8, 2013, 1185-90.

[12] Yavuz, Sevgi, and Aydin Ece. "Mean platelet volume as an indicator of disease activity in juvenile SLE." *Clinical Rheumatology,* Vol. 33, No. 5, 2014, pp. 637-41.

[13] Soydinc, Serdar, et al. "Mean platelet volume seems to be a valuable marker in patients with systemic sclerosis." *Inflammation,* Vol. 37, No. 1, 2014, pp. 100-06.

[14] Öztürk, Z. A., et al. "Could platelet indices be new biomarkers for inflammatory bowel diseases." *European Review for Medical and Pharmacological Sciences,* Vol. 17, No. 3, 2013, pp. 334-41.

[15] Van Der Linden, Sjef, Hans A. Valkenburg, and Arnold Cats. "Evaluation of diagnostic criteria for ankylosing spondylitis." *Arthritis and Rheumatism,* Vol. 27, No. 4, 1984, pp. 361-68.

[16] Sieper, J., et al. "The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis." *Annals of the Rheumatic Diseases,* Vol. 68, No. 2, 2009, pp. 1-44.

[17] Calin, A., et al. "Outcome variables in ankylosing spondylitis: evaluation of their relevance and discriminant capacity." *The Journal of Rheumatology,* Vol. 26, No. 4, 1999, pp. 975-79.

[18] Sezgin, Melek, et al. "Serum RDW and MPV in Ankylosing Spondylitis: Can they show the disease activity?." *Clinical Hemorheology and Microcirculation,* Vol. 65, No. 1, 2017, pp. 1-10.

[19] Ustun, Nilgun, et al. "Mean Platelet Volume Level in Patients with Ankylosing Spondylitis and its Relationship with Disease Activity and Presence of Cardiovascular Risk Factors." *European Journal of General Medicine,* Vol. 11, No. 4, 2014, pp. 239-43.

[20] Bath, Philip, et al. "Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease." *Stroke,* Vol. 35, No. 3, 2004, pp. 622-26.

[21] Pereg, David, Tatiana Berlin, and Morris Mosseri. "Mean platelet volume on admission correlates with impaired response to thrombolysis in patients with ST-elevation myocardial infarction." *Platelets,* Vol. 21, No. 2, 2010, pp. 117-21.

[22] Chu, S. G., et al. "Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta□ analysis." *Journal of Thrombosis and Haemostasis*, Vol. 8, No. 1, 2010, pp. 148-56.

[23] Kisacik, Bunyamin, et al. "Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis." *Joint Bone Spine,* Vol. 75, No. 3, 2008, pp. 291-94.