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Research Article

Can the mean platelet volume be a predictor of disease activity in primary Sjogren syndrome?

Ahmet Omma[1]*, Orhan Kucuksahin[2], Sevinc Can Sandikci[1], Bahar Ozdemir[3], Sukran Erten[2], Yasar Karaaslan[1]

[1]Department of Rheumatology, Ankara Numune Training and Research Hospital, Ankara, Turkey
[2]Department of Rheumatology, Yildirim Beyazit University, Internal Medicine, Ankara, Turkey
[3]Yildirim Beyazit University, Internal Medicine, Ankara, Turkey

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***Correspondence:**
Dr. Ahmet Omma,
E-mail: ahmetomma@hotmail.com

ABSTRACT

Background: Disease activity in primary Sjogren syndrome (PSS) is measured by the EULAR Sjogren's syndrome disease activity index (ESSDAI) and patient reported index (ESSPRI). Studies investigating the association between ESSDAI and ESSPRI and previously reported indicators of systemic inflammation are few in the literature. The aim of this study was to determine the clinical utility of the mean platelet volume (MPV) in predicting disease activity in PSS patients.
Methods: A total of 190 subjects including ninety-five PSS patients and ninety-five healthy controls were enrolled. Associations between MPV and other known indicators of systemic inflammation (red cell distribution width (RDW), neutrophil to lymphocyte ratio (NLR) and patient clinical characteristic, ESSDAI and ESSPRI were investigated by using spearman correlation and linear regression analysis.
Results: MPV levels were found to be significantly higher in the PSS group than the control group (10.5±1.2 versus 9.0±1; P<0.001 respectively). Correlation and regression analysis showed a positive correlation between MPV levels and ESSDAI scores (r=0.24, p=0.01). There was a negative correlation between ESSPRI and MPV levels (r=-0.32, p=0.001). NLR and RDW did not show any significant correlation with either ESSDAI or ESSPRI scores.
Conclusions: MPV levels are significantly elevated in PSS patients compared to their control peers, positively correlate with ESSDAI but negatively with ESSPRI scores. MPV might be a useful inflammatory marker to measure disease activity in PSS.

Keywords: Primary Sjögren syndrome, Mean platelet volume, Neutrophil/lymphocyte ratio, Disease activity

INTRODUCTION

Primary Sjogren syndrome (PSS) is a progressive autoimmune condition characterized by lymphocytic infiltrates and destruction of salivary and lacrimal glands. As the disease progresses, other organs such as the kidney, lungs, vessels and muscles may be involved as well.[1] Extra-glandular manifestation in PSS has been associated with the degree of auto-immune dysregulation that occurs, and the presence or amount of auto-antibodies is regarded as the hallmark for disease severity.[2] The sporadic nature of PSS manifestation triggered the EULAR Sjogren task force to propose the EULAR Sjögren's syndrome disease activity (ESSDAI) index score to assess disease severity in 2010.[3] This clinical index score assesses PSS in a standardized manner and scores disease severity within 12 organ domains. Another simple index designed to measure patient's symptoms in PSS is the EULAR Sjögren's syndrome patient reported index (ESSPRI).[4] Both clinical

indices have good construct validity and have been widely accepted for to use in daily clinical practice and clinical trials. Although promising, both ESSDAI and ESSPRI do not include the conventional acute phase reactants that are usually used to evaluate disease relapse or remission.

Similar to other auto-immune diseases, high titers of auto-antibodies and inflammatory markers in PSS have been associated with disease severity. However; their exact correlation with the recently introduced ESSDI scores hasn't been proven yet. Previous studies have associated several inflammatory and hematologic markers including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), neutrophil/lymphocyte ratio (NLR), mean platelet volume (MPV) with disease activity in rheumatoid arthritis, ankylosing spondylitis, Behçet's disease and Familal Mediterranean fever. Among these inflammatory markers, MPV and NLR have recently gained wide interest for their role in predicting disease severity.[5-9] Elevated levels of MPV and NLR have been linked with inflammation and disease severity in several rheumatologic diseases and both markers are easily attainable at low cost from traditional hematologic parameters.[8-9] Considering PSS as a systemic auto-immune disease, we hypothesized that MPV, NLR and other hematologic parameters may be useful predictors of disease severity in PSS. The present study aimed to determine the correlation between these markers and ESSDAI and ESSPRI scores in PSS patients.

METHODS

Patients and controls

This study is a prospective cross-sectional study of 95 consecutive Primary Sjogren syndrome patients who presented to the Yildirim Beyazit University, Internal Medicine, Division departments of Rheumatology (Ankara, Turkey). Primary Sjogren syndrome (PSS) was defined according to the 2002 American European consensus group (AECG) criteria for diagnosing PSS.[10] All PSS patients did not have any history of auto-inflammatory disease, malignancy, diabetes, infection, end-stage renal disease or hematological disorder.

An age-sex matched group of 95 healthy individuals who visited for routine physical examinations were used as controls. Healthy participants did not have any history of underlying auto-immune condition, malignancy, hematological disorder or recent infection.

Prospective data on clinical and laboratory characteristics of all subjects were recorded and entered into an institutional review board approved database. Disease activity was calculated according to the EULAR Sjögren's syndrome disease activity (ESSDAI) and patient reported index (ESSPRI).[3-4] A well written informed consent was received from all study participants and the study was approved by the institutional review and ethical committee.

Biochemical and hematological measurements

Venous blood samples were taken by the puncture of antecubital vein of patients after overnight fasting. All laboratory tests (CRP, serum glucose level, liver and kidney function tests) were analyzed at the central laboratory of the hospital. Complete blood parameters (neutrophils, lymphocytes, monocytes, eosinophils, basophils and platelet) were determined from EDTA anticoagulated tubes using an automated coulter counter. The NLR was calculated as the absolute neutrophil measurement divided by the absolute lymphocyte measurement. Westergren method was used for ESR. CRP was determined with turbidimetric method. All blood samples were analysed within two hours.

Statistical analysis

All data was analysed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) 15.0 program for Windows. Continuous variables are expressed as mean±SD and categorical variables as numbers and percentages. The students t-test was used in comparing the means of continuous variables and the Chi-square test was used to evaluate the differences in proportions. Disease activity scores (ESSDAI and ESSPRI) were compared by using one-way analysis of variance (ANOVA). Spearman rank correlation analysis was performed to determine the relationship between ESSDAI and ESSPRI scores, hematological and demographic parameters. Statistical significance was accepted at p-values less than 0.05.

RESULTS

The demographic and clinical characteristics of PSS patients are given in Table 1. The mean age of all 95 patients was 47.7±10.6 years and 88 (92.6%) of them were females. Sixty patients had a positive salivary gland biopsy with a focus score >1.

Shown in Table 2 is a comparison of demographic features and hematologic parameters in both patients and control groups. Both groups were similar in terms of age and gender. Hemoglobin levels were lower and MPV levels were found to be significantly higher in the PSS group than the control group (10.5±1.2 versus 9.0±1; P<0.001 respectively).

Correlation and regression analysis showed a positive correlation between MPV levels and ESSDAI but a negative correlation with and ESSPRI scores (r=0.24, p=0.01 and r=-0.32, p=0.001; respectively). ESR positively correlated with MPV levels but not CRP (Table 3).

Table 1: Characteristics of primary Sjögren's syndrome patients.

	PSS patients (n=95)
Age (years)	47.7±10.6
Gender (female)	88 (92.6%)
Age at the time of diagnosis (years)	44.7±10.2
Disease duration (years)	2.0±1.8
Positive salivary gland biopsy (focusscore ≥1), n (%)	60/79 (75.9%)
Antinuclearantibody (ANA) positivity, n (%)	81/92 (88%)
Autoantibodies to antiRo or antiLa, n (%)	56/91 (61.5%)
Anti-Ro positivity	53/91 (58.2%)
Anti-La positivity	21/91 (23.1%)
CRP (mg/L)	5.4±10.2
ESR (mm/h)	28±16
WBC (x10^9/L)	6.85±2.03
Neutrophil (x10^9/L)	4.03±1.52
Lymphocyte (x10^9/L)	2.12±0.75
NLR (%)	2.05±0.95
Hb (g/dL)	13.1±1.3
PLT (x10^9/L)	255±64
MPV (fL)	10.5±1.2
RDW (%)	13.8±1.4
ESSDAI	6.1±4.0
ESSPRI (0-10)	3.5±1.9

Results are expressed as mean±SD or number (%), where appropriate. ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; EULAR, European League Against Rheumatism; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; NLR, neutrophil to lymphocyte ratio; WBC, White blood cell count; PLT, platelet; MPV, mean platelet volüme; RDW, red cell distribution width.

Table 2: Demographic and laboratory characteristics of PSS patients and controls.

	PSS (n=95)	Control (n=95)	P values
Age (years)	47.7±10.6	47.2±7.7	0.55
Gender (F/M)	88/7	82/13	0.15
WBC (x10^9/L)	6.85±2.03	7.37±1.57	0.05
Neutrophil (x10^9/L)	4.03±1.52	4.38±1.24	0.08
Lymphocyte (x10^9/L)	2.12±0.95	2.31±0.67	0.06
NLR (%)	2.05±0.95	2.04±0.92	0.96
Hb (g/dL)	13.1±1.3	13.9±1.2	<0.001
PLT (x10^9/L)	255±64	266±61	0.20
MPV (fL)	10.5±1.2	9.0±1.1	<0.001
RDW (%)	13.8±1.4	13.6±1.0	0.32
ESR (mm/h)	28±16	10±6	<0.001
CRP (mg/L)	5.4±10.2	2.9±1.6	0.02

Results are expressed as mean±SD. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; NLR, neutrophil to lymphocyte ratio; WBC, White blood cell count; PLT, platelet; MPV, mean platelet volüme; RDW, red cell distribution width.

Table 3: Regression analysis showing correlations between ESR, CRP, ESSDAI and ESSPRI and patient demographic or laboratory parameters.

	ESR	CRP	ESSDAI	ESSPRI
Age (years)	r= 0.24 P=0.001	NS	NS	NS
Disease duration (years)	NS	NS	NS	NS
WBC (x10^9/L)	NS	r= 0.20 P=0.004	NS	NS
Neutrophil (x10^9/L	NS	r= 0.26 P<0.001	NS	NS
Lymphocyte (x10^9/L)	NS	NS	NS	NS
NLR (%)	NS	r= 0.25 P<0.001	NS	NS
Hb (g/dL)	r= - 0.31 P<0.001	NS	NS	NS
PLT (x10^9/L)	NS	NS	NS	NS
MPV (fL)	r= 0.38 P<0.001	NS	r= 0.24 P=0.01	r= - 0.32 P=0.001
RDW (%)	r= 0.22 P=0.002	NS	NS	NS
ESR (mm/h)	-	r= 0.28 P<0.001	NS	NS
CRP (mg/L)	r= 0.28 P<0.001	-	NS	NS

NS, nonsignificant; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; NLR, neutrophil to lymphocyte ratio; WBC, White blood cell count; PLT, platelet; MPV, mean platelet volüme; RDW, red cell distribution width.

DISCUSSION

With an estimated prevalence of 0.9-6 per 1000 individuals, PSS is regarded as the second most common systemic auto-immune disease after rheumatoid arthritis.[1-2] The systemic nature of the disease is characterized by its involvement in other organs including the kidneys, lungs and muscles.[1] Disease severity is therefore determined by how extensive the underlying inflammation has affected other organ systems. Since their development, the ESSDAI and ESSPRI scores have been accepted as gold standards to measure disease activity in primary Sjogren Syndrome. In this study, we aimed to investigate the association between MPV, NLR and RDW levels and ESSDAI and ESSPRI scores in PSS patients.

Recently, the utility of MPV as an inflammatory marker in auto-inflammatory disorders has been extensively investigated. Several authors have attempted to determine the association between MPV and auto-immune diseases like rheumatoid arthritis, ankylosing spondylitis, Behcet's disease and familial Mediterranean fever. A retrospective study by Kisacik, et al investigated the correlation

between MPV and the clinical indices of both RA and AS. The study found MPV levels to be significantly lower in RA and AS patients compared to control peers. A significant increase in MPV levels was recorded in both patient groups after treatment. AS disease activity scores negatively correlated with MPV levels after treatment.[6] A similar study that evaluated the possible relationship between systemic sclerosis (SS) and MPV levels reported a negative correlation between MPV levels and disease severity. Conversely, MPV levels in SS patients were found to be higher than that of a group of healthy controls.[11] Our study identified correlations between MPV levels and two different disease activity indices currently used in measuring disease severity in PSS. MPV levels positively correlated with ESSDAI scores but negatively with ESSPRI scores. In addition, we recorded significantly elevated levels of MPV than healthy controls. These findings are similar to that reported by Tezcan, et al in their study of 42 PSS patients who were compared with 32 healthy controls. The authors found higher MPV levels in PSS patients than controls but could not identify a correlation between MPV levels and disease severity.[12]

The mean platelet volume is a hematologic parameter that indicates the average size of blood platelets. MPV is higher when there is destruction of platelets and may be seen in several inflammatory conditions such as immune thrombocytopenic purpura (ITP), myeloproliferative diseases or platelet related disorders. Elevated MPV levels can be a sign of rapid platelet turnover. In PSS patients, levels of B-cell activator factor (BAFF) are elevated and this can contribute to immune-mediated platelet lysis. The absence of concomitant thrombocytopenia in the presence of elevated MPV levels in our patients may be a reason for supports the idea of thrombolysis.

We used the ESSDAI and ESSPRI to evaluate disease severity in PSS patients because of its recent wide use in clinical practice. In an extensive review of the use of ESSDAI by Seror, et al the authors confirmed the validility of ESSDAI in most clinical studies and on-going clinical trials.[13] Risselada, et al in their analysis of 195 PSS patients critically appraised the value of the ESSDAI in clinical practice for the first time. ESSDAI scores were found to be low and stable in the general population and were commended for their ability to capture disease activity in patients in whom individual changes may be present.[14] Our patient population closely matches the epidemiological and demographic characteristics that have been described for PSS. Nine out of 10 subjects recruited for this study were women with a mean age of 47 years. With a mean disease-duration of 2 years, positive salivary gland biopsy was seen in 76% of the patients.

In addition to the elevated MPV levels that were encountered in this study, Hb levels were significantly low in the PSS patient group. The presence of underlying chronic condition can serve as an explanation for low Hb levels. Conversely, as reported in previous studies for other auto-immune diseases, the current study couldn't identify any significant relationship between hematologic parameters like RDW and NLR and disease activity scores.[15-17]

Findings from the current study are promising however they may be limited by very few factors. Firstly, the cross-sectional nature of the study may not allow an appropriate evaluation of disease activity in PSS patients. Also, the timing of measuring laboratory parameters in PSS patients was not standardized and correlated with disease symptoms. Most of the patients enrolled in the study were consecutive patients who visited the outpatient clinic for periodic check-up and evaluation. The presence or absence of symptoms and their severity at presentation was not taken into consideration before measuring MPV levels.

CONCLUSION

In conclusion, we describe for the first time in the medical literature a positive correlation between an easy to measure and cheap hematological parameter (MPV) and disease severity in patients with primary Sjogren Syndrome. MPV levels were elevated in PSS patients compared to their control counterparts. Prospective studies enrolling a larger number of patients would be needed to determine the validity and utility of MPV in predicting disease severity in PSS patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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