Association between mean platelet volume levels and inflammation in SLE patients presented with arthritis

Sahin Safak[1], Ali Ugur Uslu[2] , Korkmaz Serdal[2], Tasliyurt Turker[1], Senel Soner[3], Akyol Lutfi[4]

1. Gaziosmanpasa University, Faculty of Medicine, Department of Internal Medicine, Tokat, Turkey
2. Cumhuriyet University, Faculty of Medicine, Department of Internal Medicine, Sivas, Turkey
3. Erciyes University, Faculty of Medicine, Department of Rheumatology, Kayseri, Turkey
4.Bozok University, Faculty of Medicine, Department of Internal Medicine, Yozgat, Turkey

Abstract

Background: Systemic lupus erythematosus (SLE) may be characterized by periods of remissions and chronic or acute relapses. The complexity of clinical presentation of the SLE patients leads to incorrect evaluation of disease activity. Mean platelet volume (MPV) has been studied as a simple inflammatory marker in several diseases. There is no study in the literature about MPV levels in adult SLE patients with arthritis.

Objectives: We aimed to investigate the MPV levels in the SLE population with arthritis during and between activations.

Methods: The study consisted of 44 SLE patients with arthritis in activation period (Group 1), the same 44 SLE patients with arthritis in remission period (Group 2) and 44 healthy controls (Group 3). Erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), white blood cell count, platelet count, and mean platelet volume (MPV) levels were retrospectively recorded from patient files.

Results: The mean ages of the SLE subjects were 42 ± 16 years, while the mean ages of controls was 41 ± 17 years. MPV was significantly lower in Group 1(7.66±0.89fL) than in Group 2 (8.61±1.06 fL) and Group 3(8.62±1.11fL) ($p<0.0001$). The differences between groups reached statistical significance.

Conclusions: We suggest that MPV levels decrease in patients with arthritis of SLE activation when compared to the same patients in remission and healthy controls.

Key words: Systemic lupus erythematosus, Arthritis, Mean platelet volume

DOI: http://dx.doi.org/10.4314/ahs.v14i4.21

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown cause that may affect any organ of the body. Arthritis lupus is typically non-erosive, non-deforming, and frequently appears before other manifestations of SLE. It affects predominantly women, especially in their 20s and 30s. The clinical course of SLE is characterized by periods of remissions and relapses[1]. The correct evaluation of disease activity is of great importance because of the the complexity of the disease. Common methods including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are not completely in accordance with evaluating activation of SLE with arthritis[2,3]. Anti-double stranded DNA antibody and complement are used to certain clinical manifestations of the disease, especially nephritis, rather than the activity of the disease itself and arthritis[4]. Currently, disease activity in SLE can be assessed using composite disease activity indices, such as the SLE Disease Activity Index (SLEDAI) and British Isles Lupus Assessment Group (BILAG) [5]. However, they could be complex for use in routine clinical practice. Therefore, there is a great amount of interest in the identification of biomarkers that can quantify disease activity, although a single biomarker is unlikely to replace clinical evaluation because of the heterogeneity of SLE[6].

Corresponding author
Sahin Safak,
Gaziosmanpasa University,
School of Medicine
Department of Internal Medicine, Tokat, Turkey
Phone: +90 507 3404452
Email: drsafaksahin@gmail.com
Fax : +90 356 2129500

Mean platelet volume (MPV) is a parameter detected during routine blood count and to which clinicians do not usually pay much attention. Platelet volume is known to be a marker determined from megakaryocytes during platelet production, which is associated with platelet function and activation. Under normal circumstances, there is an inverse relationship between platelet size and number[7,8]. MPV has been studied as a simple inflammatory marker in several diseases. Some studies have reported that MPV increases

in myocardial infarction and cerebrovascular disease; while in contrast, it decreases in active rheumatologic diseases including rheumatoid arthritis (RA), ankylosing spondylitis and ulcerative colitis[9-12]. To our knowledge, there is not a study in the literature about MPV levels in adult SLE patients with arthritis. The present study aimed to investigate the MPV levels in an adult SLE population.

Patients and Methods

The data used in the present study were obtained retrospectively from patients who had SLE diagnosis with arthritis complaints based on ACR criteria in August 2011-December 2012 period in Rheumatology Clinic of the School of Medicine of the Cumhuriyet University (Sivas, Turkey). Ethical approval for the study was obtained from the local ethics committee. The study consisted of 44 SLE patients with arthritis in activation period (Group 1), the same 44 SLE patients with arthritis in remission period (Group 2) and 44 healthy controls (Group 3). The age of SLE patients and healthy controls ranged in 18 to 79 years. Participants with a history of smoking, acute or chronic infectious diseases, hemoglobin >16.5 g/dl, thrombocytopenia, anemia, hypertension, angina pectoris, myocardial infarction, diabetes mellitus, anti-phospholipid syndromes, recurrent miscarriage, amyloidosis, thrombosis or chronic renal insufficiency were excluded from the study. ESR, CRP, White Blood Cell (WBC) count, platelet count, and MPV levels were retrospectively recorded from patient files. All blood samples were studied within less than one hour after the sampling. The complete blood count have been performed in the same analyzer, Mindray BC-6800, which is routinely checked every month in the central laboratory of our institution.

Statistical analyses

Data were evaluated using the Statistical Package for Social Sciences 12.0 program for windows and by analyzing descriptive statistics (means and standard deviation), comparing the means of quantitative data for more than two groups with Kruskal–Wallis test and by comparing dual groups using the Student's t-test. P value of 0.05 was considered significant. Correlations between parameters were computed through Pearson's correlation analysis. Variables found to be statistically significant in univariate analyses were entered into multivariate logistic regression analysis. Multivariate logistic regression models were created to identify independent predictors of activation of arthritis in SLE patients.

Results

Demographic and clinical features of SLE patients are given in Table I.

The mean ages of the SLE subjects were 42 ± 16 years, while the mean ages of controls was 41 ± 17 years. Thirty-three SLE patients (78.6%) and 35 subjects (79.5%) in control group were female. There were no significant differences between patient group with SLE and healthy controls in terms of age and gender distribution (p=0.628, p=0.912, respectively).

Table I. Main clinical characteristics of the patients with systemic lupus erythematosus and of the controls*

	SLE patients n=44	Controls n=44
Sex, no. female/male	33/11	35/9
Median age, years (range)	42±16	41±17
Age at SLE onset, years(range)	32±8.9	-
Remission duration, days (range)	12±4.9	-
Butterfly rash	28/44	-
Discoid lesions	11/44	-
Photosensitivity	23/44	-
Mouth ulcers	14/44	-
Arthralgias/arthritis	44/44	-
Serositis	4/44	-
Pleurisy	4/44	-
Pericarditis	1/44	-
Renal disease	12/44	-
Neuropsychiatric manifestations	4/44	-
Antinuclear antibodies	41/44	-
Anti–double-stranded DNA	24/44	-

*Except where indicated otherwise, values are the number

MPV was significantly lower in Group 1 (7.66±0.89fL) than in Grouand Group 3(8.62±1.11fL) (p<0.0001); however, there was no difference between group 2 and group 3 (p=0.772). MPV levels were not correlated with ESR and CRP.

The mean platelet volume and WBC count did not differ among the groups. CRP and ESR values were significantly higher in Group 1 than Group 2 (p<0.0001). All study parameters are presented in Table II and III.

Table II. Relationship between blood parameters in Group 1and Group 2

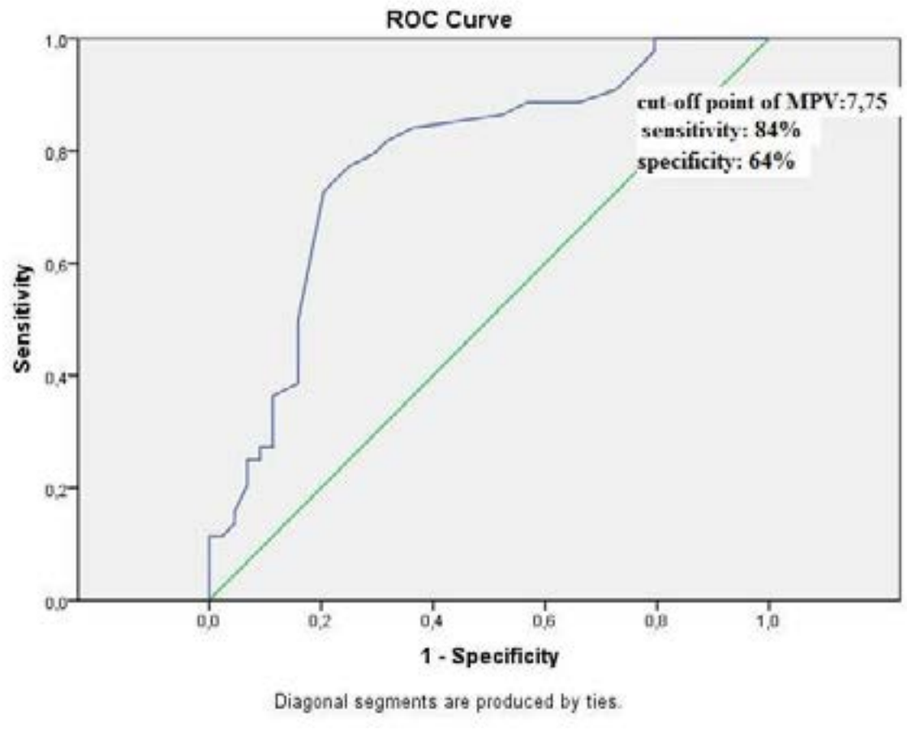
	Group 1 n=44	Group 2 n=44	P
Platelet (x10^9/L)	296.5±13.5	290.7±12.1	0.835
MPV (fL)	7.66±0.89	8.61±1.06	0.0001
Hb (g/dL)	11.9±1.4	12.3±1.6	0.356
Hct	36.35±3.70	36.96±4.69	0.503
WBC (x10^9/L)	7.72±4	8.29±3.26	0.493
CRP (mg/L)	71.4±22.3	5.1±6.1	0.0001
ESR (mm/h)	50.6±26.9	20.6±13.9	0.0001

Table III. Relationship between blood parameters in Group 1 and Group 3

	Group 1 n=44	Group 3 n=44	P
Platelet (x10^9/L)	296.5±13.5	275.5±45.8	0.333
MPV (fL)	7.66±0.89	8.62±1.11	0.0001
Hb (g/dL)	11.9±1.4	12.2±1.7	0.563
Hct	36.35±3.70	36.93±1.79	0.786
WBC (x10^9/L)	7.72±4	7.68±1.80	0.931

Correlation analysis showed that there was positive correlation between CRP (r= 0.534, p=0.001) and ESR (r= 0.556, p=0.001) and negative correlation between MPV (r=-0.445, p=0.001) in activation period SLE patients with arthritis (Figure I).

Figure I: Roc-curve analysis of MPV



ESR, CRP, MPV, platelet count, and WBC were entered in univariate analysis. CRP, ESR, and MPV were statistically important. These values were entered multivariate analyses to identify independent predictors of activation of arthritis in SLE patients.

Multivariate analysis showed that only MPV (odds ratio: 0,179, %CI: 0.048-0.671, p=0.011) and ESR (odds ratio: 1.134, %CI: 1.040-1.235, p=0.004) were independent predictors of arthritis activation in SLE patients (Table IV).

Table IV. Univariate and multivariate analyses

	Univariate analysis			Multivariate analysis		
	p	Odds ratio	CI(%)	p	Odds ratio	CI(%)
MPV	0.001	0.327	0.181-0.592	0.012	0.179	0.048-0.671
ESR	0.001	1.074	1.035-1.115	0.004	1.134	1.040-1.235
CRP	0.002	1.201	1.071-1.347	0.148	1.098	0.967-1.246
Platelet count	0.860	1.000	1.000-1.124			
WBC	0.489	1.000	1.000-1.214			

MPV: Mean platelet volume, WBC: White blood cell, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate

Discussion

In the present study, we demonstrated that MPV decreased in SLE patients during activation compared with remission and healthy controls. Low levels of MPV were associated with disease activity. We suggest its usefulness as a biomarker for global disease activity and clinical features. In patients with SLE, elevated ESR were found to be associated with disease activity [13], whereas serum CRP was only slightly elevated and was not correlated with disease activity[3, 14]. However, CRP and ESR may present some discordance in reflecting inflammation[4]. Recently, MPV has been considered a reliable marker for indicating platelet activation and inflammation. MPV is easily measured by automated cell counters under any storage conditions for blood samples. MPV is a marker of platelet function and activation, and it is also influenced by inflammation[15].

To our knowledge, there is only one study in the literature about MPV levels in adult SLE patients. In this study, low MPV (<7.2 fl) was recorded by 2 different hematology analyzers in 5 (14.3%) and 23 (65.7%) patients with SLE, mostly at active stage of the disease (n=28, 80%).[16] Results of this study, in which hematological parameters of SLE patients were studied, were in accordance with our results. A major difference of the present study from the ones in literature was that this is the first study evaluating MPV in SLE patients with arthritis in activation and remission periods.

Gasparyan et al.[15] stated that high-grade inflammation accompanies a decrease of MPV in RA and SLE, possibly due to the increased consumption of large platelets at the sites of rheumatoid inflammation.

Kisacik et al.[7] found that MPV was low in active ankylosing spondylitis and RA, and that MPV levels increased and then normalized with treatment. In another study lower MPV value of RA patients compared to controls were shown to increase after TNF-α treatment[17]. In the present study, lower MPV values of SLE patients with arthritis were normalized after treatment. There are two studies showing that MPV levels of FMF patients during the attack were significantly lower than those of healthy controls[18,19]. MPV has been reported to decrease in some inflammatory bowel diseases such as ulcerative colitis and it could be used for determination of disease activity[20]. This condition is thought to be related to the release of bioactive molecules of pro-inflammatory platelets in the presence of inflammation.

Two studies have suggested that SLE patients have increased platelet activation[21, 22]. Of these studies, Nagahama et al.[22] showed that plasma platelet-derived microparticle levels were significantly higher in SLE patients than in healthy subjects. Furthermore, Nagahama et al stated[22] that MPV levels were decreased in patients with arthritis of SLE activation as in our study. Several mechanisms for how complement components interact with platelets have been proposed, and most of these theories involve platelet activation.

Common trigger of platelets include immune complexes, which are frequently seen in SLE patients, shear stress due to atherosclerosis or inflammatory cytokines including interferon-alpha[21, 23, 24].

Limitations

The results of this study are subjected to some limitations. First, this study was not based on longitudinal observations but was conducted with a retrospective design. Second, since the study is retrospective, clinical activation indices of SLE patients with arthritis (SLEDAI, BILAG) were not calculated. Third, it is a single center study with a relatively small sample size, which might underestimate or overestimate the relationship between MPV and inflammation in SLE patients presented with arthritis. Fourth, the fact that MPV values may be affected by many factors.

Conclusion

we suggest that MPV levels decrease in patients with arthritis of SLE activation when compared to same patients with remission and healthy controls. Decreased MPV levels were observed in patients with SLE and these results may be related to active inflammatory states. Namely, MPV is associated with disease activity. The results of our study further expand perspectives of use of MPV in conditions associated with SLE with arthritis for monitoring treatment. So, more specifically designed prospective studies are needed to externally cross-validate our findings in a larger cohort of APS patients.

Authors' contributions:
Concept: SS; Data Collection and/or Processing: SS, AUU, SK; Interpretation: SS, TT, LA; Literature Review: SS, AUU, TT; Writer: SS, AUU, SK; Critical Review: SS. All authors read and approved the final manuscript.

Declaration of interest:
The authors report no conflict of interest.

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