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Impact of Mean Platelet Volume on Systemic Lupus Erythematosus Disease Activity

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ABSTRACT

Background: Previous research on mean platelet volume (MPV) in relation to disease activity in systemic lupus erythematosus (SLE) is sparse and conflicting. Although MPV is simple and inexpensive, few studies have investigated its role in patients with SLE and it remains unclear whether MPV is associated with SLE activity or not.

Objectives: This study aimed to ascertain MPV levels in SLE patients with and without activity. Additionally, to determine the association between MPV and lupus activity.

Patients and methods: 74 patients diagnosed with SLE and 74 healthy controls gender- and age-matched were registered in this research. Patients were split into two groups based on Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS). Data concerning sociodemographic information and MPV were recorded in both patients and controls.

Results: According to SLE-DAS, 41 patients with SLE were active, whereas 33 had inactive disease. Active SLE patients had diminished mean values of MPV compared to inactive disease group and control group (8.4 ± 0.7 fl versus 10.2 ±1.3 fl versus 10.9 ± 0.4 fl respectively, p=0.001). MPV correlated significantly to lupus activity determined by SLE-DAS (r=0.44, p=0.01).

Conclusions: MPV levels were significantly diminished in SLE patients than in healthy controls, and they were much diminished in active disease than in inactive group. MPV was correlated significantly with lupus activity. MPV can be used as a simple, available and low-cost laboratory assessment for evaluation of disease activity in SLE patients.

Keywords: Systemic Lupus Erythematosus Disease Activity Score, Mean platelet volume, Disease activity.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a multifaceted autoimmune illness marked by its inclusion of numerous organ systems, unpredictable disease history, and complex clinical presentation [1, 2].

Thus, the discovery of trustworthy and easily obtainable biomarkers is crucial for precise SLE diagnosis, prognosis, and disease activity monitoring [3, 4].

SLE disease activity assessment is indispensable in clinical trials, observational studies, and daily clinical practice [5, 6]. At present, the SLE disease activity index-2K is the most often employed indicator in clinical practice and trials (SLEDAI-2K). The primary benefit of SLEDAI-2K is its user-friendliness. Nevertheless, it is also notable for its failure to account for numerous severe manifestations, its inability to measure changes within an organ system, and its fixed severity weightings, which are frequently deemed incorrect [7].

As a result, the Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) was created to address the constraints that are widely acknowledged in conventional instruments. Featuring 17 weighted clinical and laboratory markers, comprising continuous assessments for leukopenia, thrombocytopenia, proteinuria, and arthritis, a proven tool for determining global disease activity is SLE-DAS [8-11].

Also of significance is the activation of the platelet system, which is critical in development of SLE. In SLE, platelets are primarily activated by anti-phospholipid antibodies, infectious organisms including viruses, and circulating immune complexes [12].

Mean platelet volume (MPV), for example, is becoming recognized as a trustworthy gauge of platelet function and activity [13] and in many chronic illnesses, including RA, it is frequently regarded as a sign of inflammation [14], acute rheumatic fever [15], familial Mediterranean fever [16] and systemic sclerosis [17].

Although MPV is simple and inexpensive, few studies have investigated MPV role in patients with SLE and it is yet unclear whether MPV is linked to SLE activity. The objective of this current work was to ascertain levels of MPV in SLE patients with and without activity. Additionally, to ascertain the relationship between MPV and disease activity as defined by SLE-DAS.

PATIENTS AND METHODS

Patients: This is a prospective cross-sectional research, which included 74 established SLE patients as per SLE International Collaborating Clinics disease classification criteria for SLE [18]. From November 2023 to June 2024, patients were gathered from Minia University Hospital's Rheumatology Department. As a comparative group, 74 healthy participants of age- and sex-matched from secretary and relatives of patients were included in this research. A comprehensive clinical and rheumatological examination was conducted on all patients, in addition to a

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comprehensive history-taking process. MPV was measured in both patients and controls.

Exclusion criteria: Those who were less than 18 years, smoking, other chronic autoimmune disease, hematological disorder, or malignancy.

SLE activity: SLE-DAS, which was graded by a rheumatologist, was employed to evaluate the illness's existing state [8]. SLE-DAS comprises 17 items, greater values on SLE-DAS indicate more disease activity [8]. The weighting scheme is well-balanced, assigning lower marks to localized skin rashes compared to those with systemic vasculitis and mucocutaneous skin rashes. Additionally, the SLE-DAS incorporates less common manifestations of SLE that have a significant impact on affected patients, comprising, hemolytic anemia, GIT, ophthalmological, and cardiopulmonary inclusion. This renders the assessment a comprehensive instrument for assessing the activity of SLE illness and depending on positive findings, it can be completed in 1-2 minutes per patient. Patients were classified according their activity score into two groups: Patients in activity and patients without activity. Derived cut-offs of SLE-DAS were: Remission; SLE-DAS $\leq$ 2.08, mild activity; SLE-DAS > 2.08 to $\leq$ 7.64 and moderate/severe activity; SLE-DAS >7.6 [19].

Investigations: A complete laboratory assessment was performed on each patient, which included measurements of platelets (PLT), erythrocyte sedimentation rate (ESR), white blood cells (WBC), lymphocytes (LYM), complement levels C3 and C4, anti-dsDNA, and 24-hour protein in urine. Abdominal ultrasonography, slit lamp and fundus examination, chest X-ray and CT, serum creatine phosphokinase, and EEG were done when indicated.

MPV measurement: 5 ml of venous blood were taken from each participant and placed into an EDTA tube for the purpose of measuring MPV and other blood counts. MPV was analyzed an hour after samples were collected and assessed by fully automated counter (Celltac G, Nihon Kohden Corporation Automated Hematology Analyser, Japan) and recorded by the same reader. Since all analyses were completed in Minia University Hospital laboratory within an hour of sample collection, all patients received the same lab equipment. MPV typically ranges from 7 to 11.5 fl [20].

Ethical approval: The research protocol was communicated to each participant who offered an informed consent and was authorized by Medical Ethical Committee of Minia Faculty of Medicine. The study adhered to Helsinki Declaration.

Statistical analysis:

SPSS windows version 25 software (SPSS Inc., Chicago, IL, USA) was employed to examine the data. Number and percent were utilized to convey categorical data. Normally dispersed ongoing variables were examined utilizing the mean and standard deviation. The Chi square test was employed to analyze categorical data across two groups and Student t test was utilized to contrast normally dispersed ongoing variables across two groups. Three groups were compared using quantitative variables that followed a normal distribution using the one-way ANOVA test. To assess parametric correlation between continuous variables, Pearson correlation was done. P-value of < 0.05 has been deemed significant.

RESULTS

The studied SLE patients group included 69 females (93.2%) and 5 males (6.8%) versus 91.9% females and 8.1% males of control group. Age of SLE patients varied from 21 to 49 years with a mean of 32.56 ± 4.9 years versus 33.98 ± 2.7 years of the control group. Duration of illness in SLE group varied from 1 to 13 years with a mean of 5.81 ± 4.7 years (Table 1).

Table (1): Demographic characteristics of study groups

	SLE group (n= 74)	Control group (n=74)	t/ (χ^2)	p
Sex, n (%)				
Female	69 (93.2%)	68 (91.9%)	0.36	0.55
Male	5 (6.8%)	6(8.1%)		
Age (years)				
Range	21-49	22-48	1.08	0.29
Mean ± SD	32.56 ± 4.9	33.98 ± 2.7		
Disease duration (years)				
Range	1-13	-	-	-
Mean ± SD	5.81 ± 4.7			

Among the 74 SLE patients and based on SLE-DAS, lupus disease was active in 41 patients (55.4%) and non-active in 33 (44.6%). The majority of the active group reported moderate/severe activity, which represent 36 patients (87.8%) and the remaining five patients (12.2%) represent mild activity. By comparing both groups of SLE; active and non-active, no significant variations were existed in sex, age, or disease duration in both groups. Lower hemoglobin levels (p=0.01), lymphopenia (p=0.003), and hypocomplementemia (p=0.001) were significantly more common in active SLE group. While 1st hour of ESR was significantly greater in active group than in inactive one (p=0.001). The average platelet or WBC count did not vary statistically between the two SLE subgroups (Table 2).

Table (2): Comparison between demographic and laboratory data in SLE patients' group with and without activity

	Active SLE (n=41) Mean ± SD/n (%)	**Non-active SLE (n=33) Mean ± SD/n (%)**	***t/ χ²***	***P***
Sex, n (%)				
Male	3 (8.1%)	2 (5.4%)	0.75	0.46
Female	34 (91.9%)	35 (94.6%)		
Age (years)	30.82 ± 6.9	33.56 ± 4.8	0.43	0.66
Disease duration (years)	5.81 ± 4.7	5.16 ± 3.2	-0.29	0.82
Hb (g/dl)	10.1 ± 1.2	12.4 ± 0.9	2.74	0.01
WBCs (10^3/mm^3)	6.02 ± 1.7	7.18 ± 1.5	0.49	0.61
Lymphocytes (10^3/mm^3)	1.4 ± 0.3	1.8 ± 0.1	4.01	0.003
PLTs (10^3/mm^3)	234±50	263±50	0.36	0.89
ESR (mm/h)	70 ± 18	39 ± 6	-6.19	0.001
Consumed C3	35 (85.3%)	16 (48.5%)	7.2	0.001
Consumed C4	28 (68.3%)	15 (45.4%)	7.9	0.001

Hb, hemoglobin; WBC, white blood cells; PLTs, platelets; ESR, erythrocyte sedimentation rate; C, complement. Significant p value <0.05; Highly significant p value <0.001.

For testing the differences in the means of MPV, we used One-way Analysis of Variance (ANOVA). Mean level of MPV was significantly lowered in SLE patients, in particular those who possess active disease (8.4 ± 0.7 fl) compared to both SLE patients with no activity (10.2 ±1.3 fl) and healthy individuals (10.9 ± 0.4 fl) and a significant statistical significance was seen in difference (p=0.001) (Table 3).

Table (3): Mean values of MPV in the study groups

	MPV (fL) Mean ± SD	**One-way ANOVA F**	**p-value**
SLE with activity (n=41)	8.4 ± 0.7		
SLE without activity (n=33)	10.2 ±1.3	7.31	0.001
Healthy controls (n=74)	10.9 ± 0.4		

Additionally, MPV was correlated significantly with lupus activity as determined by SLE-DAS (r=0.44, p=0.01) (Table 4).

Table (4): Correlation between MPV levels with demographic and different SLE disease parameters

	MPV	
	r	**p**
Age (years)	*0.18*	*0.33*
Disease duration (years)	*0.32*	*0.07*
SLE-DAS	0.44	0.01
Arthritis	0.07	0.43
CNS affection	0.1	0.40
Renal affection	0.07	0.49
Cutaneous affection	0.09	0.54
ANA	0.23	0.42
Anti-ds-DNA	0.08	0.44

MPV, mean platelet volume; SLE-DAS, systemic lupus erythematosus disease activity index; ANA, antinuclear antibody; Anti ds-DNA, anti-double stranded deoxyribonucleic acid.

DISCUSSION

SLE is an autoimmune condition that may cause damage to multiple organs simultaneously or asynchronously [21, 22]. It is linked to a high rate of morbidity and death caused by accumulation of irreparable end-organ damage [23]. Numerous investigations have established a connection between SLE and markers of activity such as serum complement and anti-dsDNA autoantibodies [24]. Alterations in peripheral blood cell components are utilized by authors to identify disease activity in some collagen tissue illnesses, including RA [14, 25] and systemic sclerosis [17].

The MPV, a platelet size measurement, has been utilized as an inflammatory biomarker in numerous rheumatic disorders and to evaluate platelet function and activation. Nevertheless, there have been few and inconsistently conducted prior research on MPV in SLE [26-28]. Whether MPV and SLE disease activity are connected remains unknown. The connection between MPV levels and disease activity was examined in our study.

In the current research and as opposed to earlier ones, we assessed disease activity by SLE-DAS, which is considered the initial research to quantify MPV pertaining to SLE activity using a different tool. Our results demonstrated a substantial decrease in MPV in SLE patients, particularly those with active disease in contrast to both SLE patients with no activity and healthy individuals. Additionally, this was verified by the existence of statistically significant connection between SLE-DAS score and MPV in our patients. This is in agreement of a study by **Delgado-García *et al.*** [26] who contrasted two groups of SLE adults organized by disease activity (36 per group), MPV was dramatically reduced in patients with active SLE. Likewise, **Khan *et al.*** [27] and **Hartmann *et al*.** [28] who discovered that adult patients with active disease exhibited a reduced MPV in contrast to those with inactive disease. In contrast to our results, **El-Garf** [29] studied MPV in patients with juvenile SLE and found no significant variation between MPV in 18 active patients in contrast to 11 patients with inactive disease. Additionally, he did not identify any statistically significant connections between MPV and disease activity as assessed by SLEDAI score (r =0.19, p= 0.33). Conversely, **Uzkeser *et al.*** [30] reported in his research that MPV was significantly higher in SLE patients in contrast to controls, and reported a significant positive connection between MPV and lupus activity measured by SLEDAI.

In our study, we were unable to provide a precise explanation for biological basis of a decreased MPV in individuals with SLE and its correlation with increasing disease activity. MPV has been proposed as a potential indicator of the inflammatory process and platelet activation. Perhaps the presence of inflammation as a result of disease activity, the existence of inflammatory cytokines, and the dysregulation of complement system results in a rise in the need for platelets. Platelets that are younger and larger may be released by the bone marrow, which ultimately leads to a decrease in MPV values. In addition, several illnesses that are linked with disease activity might impact platelet' synthesis, activation, and destruction, which can in turn affect MPV readings. Consumption of big platelets at areas of inflammation is another potential mechanism that could elucidate the connection between lower MPV and disease activity [26, 31, 32].

In reality, the findings on the values of MPV in SLE are incongruous. This may be due to the notion that cell counters measure MPV by utilizing optical effects and impedance. The interchangeable use of MPV is restricted by the discrepancy between the results of several cell counters [14, 27]. However, in our study, we tried to overcome this obstacle by measuring MPV using the same lab machine and the same reader, and justifying the time of storage until the analysis to be within one hour to overcome this variation.

Limitations: This study has some constraints. First and foremost, the MPV levels were only assessed once during the investigation, which may not correctly represent the chronic inflammation that persisted for an extended period. The second limitation of this investigation was that the cross-sectional methodology employed in this investigation hinders the development of a causal connection between disease activity and MPV. Thirdly, solitary center study of this research. It is necessary to conduct a future prospective multicenter investigation to verify any potential links.

CONCLUSIONS

MPV levels were significantly diminished in SLE patients than in healthy controls, and they were much

reduced in active disease than in inactive one. MPV is considered a simple, available, inexpensive laboratory and an easily measurable parameter. We suggest that MPV to be considered as one of the disease activity markers in SLE patients. Further prospective longitudinal research may provide more evidence to more precisely establish the role of MPV in SLE by analyzing the changes of MPV during various stages of disease activity.

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