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Association of Mean Platelet Volume (MPV) in Relation to Disease Activity in Lupus

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Introduction: Among the various clinical and biochemical parameters which are employed to monitor the disease activity in Systemic Lupus Erythematosus (SLE), Mean Platelet Volume, which is a platelet activation biomarker has been recently studied. We intended at evaluating the MPV in patients with active SLE and comparing it with the same patients who were in clinical remission, and to study the correlation between MPV and SLEDAI. We also studied the correlation between MPV and ESR, complements C3 and C4.

Methods: This is a prospective study conducted for a period of 12 months, in which 50 consecutive patients who were recently diagnosed with SLE according to the SLICC classification criteria were included. Complete blood count with MPV levels along with ESR, were measured at the first visit to the hospital and were repeated at every visit till they attained clinical remission. Analysis of MPV was done at first visit and at remission. Complements C3 and C4 was done at the first visit and at remission. The results were then tabulated and statistically analysed using SPSS 25. A Pearson's correlation test was done to assess the relation between MPV, ESR and SLEDAI.

Results: Patients with active disease had a decreased MPV as compared to those in clinical remission (10.91fl, 13.11fl, p=0.011). We observed a weak positive correlation between MPV and SLEDAI (r=0.034, p=0.011). We observed no correlation between MPV and ESR, C3 and C4. Meanwhile, SLEDAI showed a positive correlation with C3 and C4; there was no correlation with ESR though.

Conclusion: MPV is reduced in patients with active SLE and displayed an inverse correlation with SLEDAI.

Keywords: Mean platelet volume (MPV); systemic lupus erythematosus (SLE); SLEDAI; ESR; C3; C4.

1. INTRODUCTION

Systemic lupus erythematous (SLE) is a chronic autoimmune disorder of unknown aetiology that can affect any organ of the body [1]. The development of autoimmunity in SLE is attributed to the loss of immunological tolerance and immunoregulatory control [2,3].

SLE predominately affects women of child bearing age group, with a female to male ratio of 8-15:1 and an annual incidence of 5 per 100,000 of the general population [1,4]. The usual onset of lupus is between the ages of 16 and 40, although a particularly severe form of lupus can occur before the age of 16, known as juvenile SLE [1,5]. The clinical presentation of SLE is variable, ranging from constitutional symptoms such as fever, sweating, weight loss, joint pain and skin rashes, to life threatening features including the involvement of central nervous system and kidneys [1]. Although the manifestations are variable, the clinical symptoms do not occur concurrently and can occur at any stage of the disease [6]. Lupus with its multifaceted manifestations is characterised by periods of remissions and relapses, and has a propensity to vary from acute progressive to chronic indolent forms [1,7,8]. According to the American College of Rheumatology (ACR), presence of 4 out of a total 11 criteria, must be present to make a clinical diagnosis of SLE [1,9,10]. The recent SLICC criteria 2012, needs 4 manifestations, out of which one has to be clinical and one immunological.

The SLE disease activity can be measured by SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), which is a complex tool composed of 24 clinical and laboratory variables [2,11]. The other validated tools to measure disease activity include Lupus Activity Index, European Consensus Lupus Activity Measurement, and British Isles Lupus Activity Group (BILAG) [1,12]. Taking into account the remitting and relapsing nature of most cases of SLE, it is of utmost importance to have a biomarker to monitor it's disease activity [1]. The routinely employed method to diagnose and assess the disease activity in SLE is to measure to the serum levels of individual complement components [2]. Significantly decreased levels of serum C1q, C3 and C4 are associated with an active disease and a consistently decreased level of C3 post treatment is a sign of worst prognosis [2,12,13]. One of the parameters of a complete blood cell count (CBC) is mean platelet volume (MPV). It indicates the function and activation of platelets, and it is variable in many inflammatory, cardiovascular and cerebrovascular disease [7,14-18].

In the recent past, MPV has proven to be an effective and a practicable marker of disease activity in SLE [1]. On the other hand, a similar study not only validate an inverse relationship between MPV and disease activity; higher the disease activity, lower is the MPV but also proposed serum albumin as an effective indicator for prognosis in patients with SLE [1,19].

2. MATERIALS AND METHODS

This is a prospective study conducted in the Department of General Medicine and Rheumatology, Saveetha Medical College & Hospital, Chennai between June 2020 and June 2021. Sample size was calculated to be 50 and patients who satisfied the inclusion and exclusion criteria were included in the study. The diagnosis of lupus was based on the presence of at least 4 criteria (1 immunological and 1 clinical) of the SLICC 2012 classification criteria. 50 consecutive SLE patients in the age group of 18-70 years who satisfied the SLICC 2012 criteria with active SLE were included. Active SLE was defined as SLEDAI score of >3 points.

Patients who had an active infectious disease, haemoglobin >16.5g/dl, thrombocytopenia, anti-phospholipid syndrome, recurrent miscarriage, thrombosis and acute/chronic renal failure were excluded from the study. Patients who had history of an associated autoimmune disorder other than SLE, such as rheumatoid arthritis or scleroderma, (overlap syndrome) were also excluded from the study. As these factors are possible confounders, including them would have resulted in a selection bias in our study. Blood samples of patients who were newly diagnosed with SLE were collected at their first visit. A total of 5ml of venous blood was withdrawn from every patient. These samples were then sent for measurement of complete blood count, which includes haemoglobin, white blood cell count, platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), mean platelet volume (MPV), and compliments C3 and C4 levels. SLEDAI values at the time of diagnosis of SLE was calculated. Based on the clinical and

laboratory evidence, they were treated and were followed up monthly with needed investigations. At the time of clinical remission with drugs,(SLEDAI of 0, while on drugs) bloods samples were collected and analysed again for C3, C4 and MPV. All the haematological parameters were analysed using the haematology analyser, Sysmex XN-1000 (6 part, fully automated). The C3 and C4 levels are measured by immunoturbidimetry in the Cobas Integra 400 automation equipment. The results were then tabulated and statistically analysed using SPSS 25 software. A Pearson's correlation test was done to assess the relation between MPV, ESR and SLEDAI. A probability (p) value of less than 0.05 was considered statistically significant.

3. RESULTS

A total of 50 patients were included in the study, of which 88% were female and 12% were male. The mean age of all the patients was 34.28 years and the age ranged from 18-58 years. The time taken to achieve a clinical remission was 8±2.8 months.

The mean MPV of patients with active SLE was 10.91±1.0fl, while that of patients in clinical remission was 13.11±3.4fl. The mean ESR was higher in patients with active disease (83.72±29.8) than those of patients in clinical remission (30.86±11.7).

3.1 Active SLE

The MPV, in patients with active SLE, showed an inverse correlation with the SLEDAI, which, although weak, was statistically significant (r=0.034, p=0.011). MPV results in active SLE did not show statistically significant correlation with ESR, C3 and C4 (p=0.120, p=0.07 and p=0.166, respectively). SLEDAI showed an inverse correlation with C3 and C4 complements, which was statistically significant (p<0.00001 and p=0.00007, respectively). However, SLEDAI did not demonstrate a statistically significant correlation with ESR (r=0.0013, p=0.075).

3.2 Clinical Remission

The MPV, of patients in clinical remission, showed an inverse correlation with SLEDAI, which, although weak, was statistically significant (r=0.1109, p=0.011). MPV showed a statistically significant correlation with ESR (p=0.004). However, MPV did not demonstrate a statistically significant correlation with C3 and C4 (p=0.3 and p=0.5, respectively).

4. DISCUSSION

SLE, which predominantly affects women, has a female to male ratio of 9:1 [1,20]. In our study, 44 (88%) patients were females and 6 (12%) were males. Most of the patients in our study were in their third decade of life.

Besides MPV, ESR has routinely been used as a marker of disease activity in patients with inflammatory conditions, and SLE, especially [1,21]. In the year 1985, SLEDAI was reported as a marker to assess disease activity in SLE, and in the year 2002, it was modified and reinstated as SLEDAI-2000 [1,22]. SLEDAI is an important predictor of prognosis and mortality [1,23]. An increase in ESR and SLEDAI value is often associated with a high disease activity [1,22,24].

In our study, it was found that MPV was significantly lower in patients with active SLE when compared to those in remission. In SLE, platelet activation has been associated with a lower platelet size. The key event in the pathogenesis of SLE is platelet system activation [2]. Likewise, it was observed that, lower levels of MPV was associated with a higher level of ESR in patients with active disease and vice versa. In addition, MPV had a convincing inverse relationship with both SLEDAI and ESR. From the above observation, we can say that, MPV was as effective as both ESR and SLEDAI-2000, as an indicator of disease activity in patients with SLE.

MPV has been contemplated as a possible marker of platelet activation and inflammatory process [2,7]. The presence of inflammatory cytokines and degranulation of the complement system, which interferes with the activation of platelets, is the pathophysiology behind SLE [2,19]. A potential mechanism that could explain the decrease in MPV levels and the disease activity is the utilisation of platelets at the sites of inflammation [2,19,24].

Despite the fact that our MPV results did not show statistically significant correlation with ESR, C3 and C4 compliments, we established a positive inverse correlation between MPV and SLEDAI.(higher the SLEDAI lower the MPV, in active disease) In a similar study conducted by

Table 1. Shows demographic details of patients with active SLE and patients in clinical remission

Demographic details			
	Patients with active disease	**Patients in clinical remission**	**P value**
Age	34.2	N/A	N/A
Gender	Female 88%; Male 12%	N/A	N/A
Duration of illness	1 year	N/A	N/A
SLEDAI	15.42±8.2	1.32±0.8	<0.01
MPV	10.91±29.8	13.11±11.7	0.05
ESR	83.72±1.0	30.86±3.4	<0.01
C3	59.26±24.9	112.64±22.4	<0.01
C4	8.74±12.4	31.73±5.7	<0.01

Khan A., et al. [1] a negative correlation between MPV and SLEDAI were established. Similarly, MPV results did not show statistically significant correlation with ESR, C3 and C4 compliments. Similar results were observed in a study conducted by Hartmann et al. [2].

In the case of rheumatoid arthritis, a study observed reduced levels of MPV in active disease. In the same study, the values of MPV were on the higher side after treatment [2,25]. In another study conducted in patients with active ankylosing spondylitis, where MPV levels were evaluated before and after treatment, the results demonstrated a considerable increase in the MPV levels after treatment [2,24].

Although, most of the studies found an inverse association between active SLE and MPV in adults, a few studies on juvenile SLE observed a positive correlation between MPV and active disease [1,26]. The results of our and a few similar studies are in contrast to the findings observed between MPV and disease activity in juvenile SLE [1,7,27].

5. CONCLUSION

We conclude by saying that MPV is reduced in patients with active SLE and displays a significant inverse correlation with SLEDAI and ESR.

CONSENT AND ETHICAL APPROVAL

Permission was obtained from the Institutional Ethics Committee (IEC) to conduct the study. A written informed consent was obtained from all the patients at the beginning of the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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