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Original Research Article

Profile of mean platelet volume, neutrophil - lymphocyte ratio and platelet - lymphocyte ratio in patient with psoriasis

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ABSTRACT

Background: Psoriasis is a chronic, inflammatory, systemic disease. In response to therapy in psoriasis patients, the psoriasis area severity index (PASI) is used to evaluate the disease activity. However more objective laboratory tools should be developed besides PASI. In various inflammatory diseases, mean platelet volume (MPV), neutrophil-lymphocyte ratio (NLR), and platelet lymphocyte ratio (PLR) are inflammatory biomarkers that are known to be evaluated. The aim of the study was to assess the frequency of platelet activation and leukocyte infiltration by measuring MPV, NLR, and PLR.
Methods: This was a case-control observational study conducted at department of dermatology and venereology at Bangabandhu Sheikh Mujib Medical University from July 2016 to December 2017. A total of 55 psoriasis cases and 55 healthy controls were included according to inclusion and exclusion criteria.
Results: We have investigated a total of 55 psoriasis patients and another 55 age-sex matched control. There were 31 males (56.36%) and 24 females (43.44%) psoriasis patients in the study. The mean age of the patient was 34.27±13.44 years. Mean±standard deviation (SD) value of MPV, NLR, and PLR in our study cases were 9.92±1.21, 4.32±8.53, and 292.96±88.80 whereas in the case of control values were 9.46±0.636, 4.54±8.51, and 162.26±103.38 respectively.
Conclusions: In conclusion, we suggest MPV is a strong indicator of psoriasis severity. MPV and PLR should be followed up routinely to take preventive measures against psoriasis-related micro and macro vascular thrombotic complications.

Keywords: Psoriasis, MVP, PLR, Severity, NLR, PASI

INTRODUCTION

Psoriasis is a common inflammatory condition of the skin where concomitant proliferation also happens. Both genetic and environmental factors are responsible for psoriasis. Platelets, leukocyte, and endothelial cells interaction have been evaluated in the inflammatory process.[1] Increased keratinocyte proliferation and infiltration of T cells, macrophages, and neutrophils seem to be the main pathophysiology of psoriasis.[2] It is also evidenced by histopathology of psoriatic lesions that a leukocyte infiltration is seen especially rich in T-lymphocytes and neutrophils. Coimbra et al have studied peripheral blood of both psoriatic individual and control groups and found significantly increased levels of leukocyte, monocytes, and neutrophils and decreased levels of lymphocytes.[3] In psoriasis, reactive oxygen species causes the release of cytokines, proteases, and cationic proteins such as elastase and lactoferrin which ultimately activate neutrophils. However, thrombocytes

also suggested to play an important role in the pathogenesis of psoriasis and the activation of thrombocytes ultimately increase leukocyte migration in the skin and release inflammatory cytokines. Evidence for an in vivo platelet activation, followed by thrombotic complication development has been established in a psoriasis patient. Activation of platelets can be done by various stimuli which are known to mediate the immune-inflammatory process.[4] In inactive condition platelets remain in a quiescent disc-shaped state. After activation they become spherical and a pseudopod is formed, followed by an increment in their size. These activated platelets show hyper-responsiveness to adenosine diphosphate (ADP) or collagen-induced aggregation as they contain denser granules and produce large amounts of thromboxane A2. Karabudak et al has been demonstrated that platelet activation, e.g. platelet hyper aggregability and increased levels of platelet-derived microparticles and soluble P-selectin is increased with the severity of psoriasis.[5] Measurement of platelet activation can be done in various ways like measurement of secretory molecules, such as adhesion proteins, cytokines, chemokines.[6] Mean platelet volume (MPV), a measure of platelet size, is a valuable indicator for platelet activation along with function, MPV is one of the most extensively studied and reported markers of platelet activation.[7] Furthermore, MPV is of low cost, reliable, easy, and available parameter, estimated with automated hematology analyzer and also included in routine complete blood cell count (CBC). Cardiovascular disease, peripheral artery disease, systemic lupus erythematosus, systemic sclerosis, rheumatoid arthritis (RA), osteoarthritis, vascular dementia, and Alzheimer's disease, and many other inflammatory diseases cause significantly increased MPV levels.[8] Platelet activation and aggregation are the basic processes in the pathophysiology of micro-and macrovascular (e.g. cerebrovascular, coronary, and peripheral arterial) disease.[9] Altered platelet morphology and function have been reported in psoriatic patients. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are the two new systemic inflammatory biomarkers.[10] To evaluate inflammation in different chronic inflammatory diseases such as coronary arterial disease, psoriasis, chronic kidney disease, ulcerative colitis, gastric cancer, chronic obstructive pulmonary disease, familial Mediterranean fever, and ankylosing spondylitis, NLR have been studied exclusively.[11] The NLR is a simple, relatively inexpensive, more available than any other derived marker. It has established itself as a good predictor for other multiple cardiovascular outcomes that reflect an imbalance in the inflammatory cells and the role of activated neutrophils in atherogenesis. Moreover, NLR is shown to be an independent risk factor in cardiovascular diseases. Central pathology to increase NLR level in psoriasis patients have increased levels of tumor necrosis factor (TNF)-α and many other cytokines (IL-6, IL-7, IL-8, IL-12, IL-17).[10] Again, lymphopenia has been observed as an independent mortality risk in cardiovascular diseases. NLR is potentially an unrecognized predictor of subclinical atherosclerosis in patients with psoriasis. Subclinical atherosclerosis may be predicted by NLR in patients with psoriasis.[12] In many diseases for predicting inflammation and mortality, the PLR is a novel inflammatory marker, which is established to be used. Increased proliferation of megakaryocytic series and decreased lymphocyte count due to apoptosis causes altered PLR in the chronic inflammatory process.[13] Recent studies show that a high PLR reflects inflammation, atherosclerosis, and platelet activation.[14] Increased PLR has been shown to be associated with adverse outcomes in cardiovascular diseases and decreased survival in malignancies such as pancreatic, colorectal, and endometrial cancers.[15] This study would be done to compare MPV, NLR, and PLR in patients with psoriasis and healthy individuals and to find out any relationship of this parameter with disease severity.

Objectives

General objectives

General objective was to assess MPV, NLR and PLR in patient with psoriasis.

Specific objectives

Specific objectives were to measure MPV, NLR and PLR in psoriasis patient; to compare mean MPV, NLR and PLR in psoriasis and healthy control; to categorize disease severity according to psoriasis area severity index (PASI) score; and to correlate disease severity with MPV, NLR and PLR.

METHODS

This was a case-control observational study conducted at department of dermatology and venereology at Bangabandhu Sheikh Mujib Medical University (BSMMU) from July 2016 to December 2017. Study populations are individuals diagnosed with psoriasis. The sample populations were extracted via purposive sampling. Individuals were screened on the basis of the inclusion and exclusion criteria of the study. Patients with psoriasis were diagnosed clinically and/or histopathologically by dermatologists attending the outpatient department of dermatology and venereology, BSMMU were recruited as the study population. Individuals who had apparently no physical complaints during history taking or presented the clinical finding of disease during my examination were selected as the control. The objective and procedure of the study were explained in both cases and controls in an easily understandable local language and then the respondents were signed in written consent form who felt interested to participate in my study. A detailed history and complete physical examination and necessary laboratory tests were

carried out. Than 55% with psoriasis and 55 age, sex-matched healthy control who were free from known comorbid diseases was enrolled finally for this study according to the inclusion and exclusion criteria. Duration of disease was measured in years. The disease severity of each and every patient was measured by PASI. The score of PASI usually varies between 0 and 72. PASI score of less than or equal to 10 is classified as a mild disease, whilst a score of greater than 10 was considered to be moderate to severe. 2 cc of venous blood was drawn from each participant and sent to the main hematology department or clinical pathology, department of BSMMU for blood complete analysis by an auto-analyzer. Mean platelet volume was measured as a part of blood complete analysis and NLR, PLR also was calculated from the report. Statistical analysis was carried out by using the statistical package for the social sciences (SPSS) software version 23.0 for windows. Continuous data were expressed as the mean±standard deviation (SD) and categorical variables were expressed as percentages. All data were processed with student's independent tests to compare between psoriatic and healthy individuals. Spearman correlation coefficient test was used to correlate MPV, NLR, and PLR with PASI. For all statistical tests, the p value is less than 0.05 was considered statistically significant. Prior to the commencement of this study, the research protocol was approved by the ethical review committee of BSMMU, Dhaka.

RESULTS

Table 1 showed the age distribution of the study patients. Age range of the cases and control was 17 to 67 years and 18 to 64 years respectively. The mean age of cases was 34.27±13.44 years and control was 33±13.26 years.

Table 1: Distribution of the study patients by age (n=110).

Age in years	Case (n=55)		Control (n=55)	
	N	%	N	%
15-24	16	29.09	12	21.81
25-34	16	29.09	16	29.09
35-44	9	16.36	11	20.0
45-54	6	10.91	8	14.55
>55	8	14.55	8	14.55
Mean age±SD	34.27±13.44		33±13.26	
Range (years)	17-67	18-64		

Table 2 showed mean±SD value of MPV, NLR and PLR in study cases were 9.92±1.21, 4.32±8.53 and 292.96±88.80 where as in case of control values were 9.46±0.636, 4.54±8.51, 162.26±103.38 respectively. Both the MPV and PLR means are high in case of psoriasis patient.

Table 2: Mean value of MPV, NLR, PLR in cases and control (n=110).

Parameter	Case (mean±SD)	Control (mean±SD)
MPV	9.92±1.21	9.46±0.636
NLR	4.32±8.53	4.54±8.51
PLR	292.96±88.80	162.26±103.38

The calculated OR is 1.95 and 95% CI 0.9102-4.186. So patient with psoriasis have higher risk of increased MPV in comparison to healthy control.

Table 3: Odds ratio for MPV.

Parameter	Cases	Control	Total
MPV increased	35	26	61
MPV not increased	20	29	49
Total	55	55	110
	Odds	**Odds ratio**	**95% CI**
Case	1.75	1.95	0.9102-4.186
Control	0.8966		

The calculated OR is 0.89 and 95% CI 0.34-2.30.

Table 4: Odds ratio for NLR.

Parameter	Cases	Control	Total
NLR increased	10	11	21
NLR not increased	45	44	89
Total	55	55	110
	Odds	**Odds ratio**	**95% CI**
Case	0.222	0.8889	0.3431-2.3027
Control	0.25		

The calculated OR is 1.49 and 95% CI 0.6789-3.271. So patient with psoriasis have higher risk of increased PLR in comparison to healthy control.

Table 5: Odds ratio for PLR.

Parameter	Cases	Control	Total
PLR increased	22	17	39
PLR not increased	33	38	71
Total	55	55	110
	Odds	**Odds ratio**	**95% CI**
Case	0.667	1.4902	0.6789-3.271
Control	0.4474		

Table 6 showed there was significant increase in MPV and PLR in psoriasis patient then healthy control group (p value was <0.05). NLR has not shown any significant difference in psoriasis and control group (p=0.895).

Table 6: Comparison of MPV, NLR and PLR in psoriasis and healthy control (n=110).

Parameters	t value	P value	Significance status
MPV	2.424	0.019	Significant
NLR	1.33	0.895	Not significant
PLR	6.861	0.000	Significant

Table 7 showed the severity of psoriasis patient on the basis of PASI score: 65.45% patient had moderate to severe psoriasis and 34.55% had mild psoriasis.

Table 7: Distribution of psoriasis patient group on basis of PASI score into mild and moderate to severe group (n=55).

Severity of psoriasis	N	%
MILD	19	34.55
Moderate to severe	36	65.45
Total	55	100.0

Table 8: Psoriasis severity between male and female according to PASI score.

Severity of psoriasis	Male		Female	
	N	%	N	%
Mild	11	35.48	8	33.33
Moderate to severe	20	64.52	16	66.67
Total	31	100.0	24	100.0

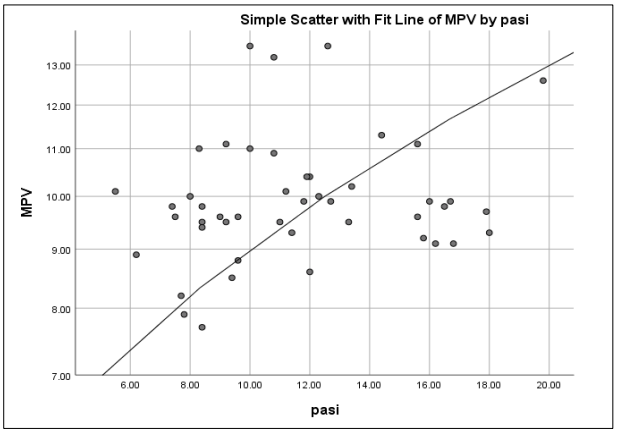

Figure 1: Scatter diagram showing correlation with MPV and PASI score.

Table 9 revealed gender distribution of severity of psoriasis patient, around two third percent of male and female suffering from moderate to severe disease (64.52% and 66.67%), rest one third suffers from mild disease (35.48% and 33.33% respectively in male and female).

Table 9 showed only MPV is positively correlated with severity of psoriasis. MPV increases when disease severity increased. NLR and PLR had no significant correlation with disease severity.

Table 9: Severity correlation between MPV, NLR, and PLR with PASI by Spearman's correlation test.

Parameter	Rho	P value	Significance level
MPV	0.283	0.036	Significant
NLR	0.060	0.662	Not significant
PLR	0.068	0.624	Not significant

DISCUSSION

Chronic inflammatory condition of the skin is known as psoriasis. Inflammation results from interactions among platelets, leukocytes, and endothelial cells.[1] Thrombocyte also aid in the pathogenesis of psoriasis and the activation of thrombocytes increase leukocyte migration in the skin and release inflammatory cytokines like tumor necrosis factor-alpha (TNFα), interleukin-1, interleukin-6, interleukin-17, interleukin-22, and interleukin-36. None of these mediators have proved to be reliable biological markers for psoriasis or its severity. As platelet plays an important role, platelet and their products have investigated whether it fits as a biological marker of an inflammatory condition like psoriasis, systemic lupus erythematosus, cardiovascular disease, systemic sclerosis, rheumatoid arthritis, and osteoarthritis. The platelet-related parameters that have been evaluated so far thus, include a PLR, CD-62, p-selectin, PDW, and MPV. MPV has attracted the most attention among these. NLR and PLR are the two novel inflammatory biomarkers used in the assessment of systemic inflammation.[10] For predicting inflammation and mortality, these markers are established to be used in many diseases. Recent studies show that a high PLR reflects inflammation, atherosclerosis, and platelet activation.[14] NLR may predict subclinical atherosclerosis in patients with psoriasis.[12] This case-control study was carried out with the aim to see the level of these inflammatory markers (MPV, NLR, and PLR) and to see the correlation of these markers with disease severity. In our study, we have investigated a total of 55 psoriasis patients and another 55 age-sex matched control. There were 31 males (56.36%) and 24 females (43.44%) psoriasis patients in the study. The age range of the psoriasis patient was 17 to 67 years. The mean age of the patient was 34.27 (SD-13.44) years. Maximum patients (32) belong to two age groups 16 patients of 25-34 years and 16 of 35- 44 years. We have found MPV is significantly higher in comparison to the healthy individuals ($p<0.05$) with OR of 1.95(CI=0.9102-4.186) which is in the agreement with Canpolat et al, Kilic et al, Karabudak et al, Chandrasekar et al, Kim et al, Asahina et al, and Ahmed et al showed that MPV was higher in psoriasis patients in relation to healthy individuals in a case-control study of a total of 60 subjects.[5,16-21] MPV shows significantly higher by using independent sample t-test. P value was significant ($p=0.001$). MPV values were 8.248±1.150 and 7.442±1.626 in psoriasis and control group and found significant $p<0.001$. In a study

done by Kim et al it was found that MPV is not only increased in psoriasis but also has a positive correlation with disease severity of psoriasis calculated by PASI score.[22] A total of one hundred and seventy-six (167) psoriasis patients and 101 healthy controls were observed in this study. In psoriasis patients, they observed that PASI, significantly correlated with MPV (r=0.189, p=0.006). Chandrasekar et al in their case-control study on 62 psoriasis patients along with age and sex-matched controls; found that MPV values were higher in patients as part of overall activation of platelets.[18] Karabudak et al in a study carried out on 20 patients with mild to moderate psoriasis, found significantly higher values for MPV in patients compared to controls.[23] In another study, done on 106 patients with psoriasis and psoriatic arthritis Canpolat et al was able to demonstrate a significantly higher MPV in psoriasis as well as psoriatic arthritis.[16] In another study, Kilic et al found significantly elevated MPV in both psoriatic patients and psoriatic arthritis patients.[17] A case-control study was carried out on 50 psoriatic patients and 50 healthy control subjects. Mean values for MPV were significantly different between the two groups (control and patients). The MPV values in male patients showed a strong positive correlation with the PASI score. They came to the conclusion that rising MPV may be good indicators of disease severity and progression. Again psoriasis patients were grouped by PASI score to see the difference between disease severity but there was no significant correlation between the disease activity and mean platelet volume values (p>0.05). It may be due to the small sample size of 49 only. The study has not found any significance. The mean MPV values were 8.96±1.03 fL for psoriasis and 8.75±1.07 fL for control groups. No significant difference was also found between the patients and controls regarding mean MPV values (p=0.231 and p=0.295, t-test and Mann Whitney-U test, respectively). They also measured no correlation between PASI scores and MPV levels. As they did not found any significance, so suggested for large population study for further clarification. In marked contrast to our study, Saleh et al also failed to see any significant association between psoriasis and MPV in their study.[24] They also failed to find a link between psoriasis and MPV where the p value was 0.435. In our study, we have found NLR is not significantly raised in psoriasis patients in comparison to the control group. PLR to be increased significantly in psoriasis patients in relation to control group which shows the similar result by Asahina et al, and Cereman et al conducted study over forty-nine patients with psoriasis and forty-seven controls which reveals NLR levels were significantly higher in patients with psoriasis than in healthy controls (p<0.001).[11,20] Again psoriasis patients were grouped by PASI score to see a difference between disease severity but there was no significant correlation between the disease activity and neutrophil-lymphocyte ratio (p>0.05). Asahina et al investigated to evaluate the clinical significance of novel inflammatory biomarkers, NLR, PLR and MPV in Japanese patients a significant correlation was found between NLR and PLR.[20] The NLR-high and PLR-high subgroups exhibited significantly higher PASI scores compared with the NLR-low and PLR-low subgroups, respectively. Polat et al evaluate the relationship between disease activity and NLR and PLR in patient's psoriasis through a retrospective case-control study over 46 patients and a control group of 46 healthy volunteers.[25] NLR and PLR were significantly elevated in patients with psoriasis (p=0.0001 and p=0.003, respectively). After PASI calculation and categorization of psoriasis patient into mild and moderate to severe psoriasis result shows positive correlation with NLR, PLR, (r=0.313, p=0.034; r=0.394, p=0.017; respectively). The investigator suggested that NLR and PLR are low-cost tests that can be used to determine the severity of current systemic inflammation in patients with chronic plaque psoriasis. PASI score is a worldwide accepted scoring system to categorize psoriatic patients in mild and moderate to severe groups. When psoriasis patient is divided under mild and moderate to the severe group, it found that MPV correlates with severity of psoriasis. MPV showed a significant positive correlation in the moderate to severe group with a p value <0.05 in relation to the mild group. NLR and PLR were not found to correlate with disease severity which differs from a study done by Asahina et al and Polat et al.[20,25] MPV positively correlated with disease severity has been reported by Canpolat et al.[16] Same result was also obtained by Kilic et al but weekly positive.[17] Ahmed et al also reported that MPV correlates significantly with the severity of the disease.[26] When the gender-based analysis was done no significant change in the overall study result found. Both male and female group shows significant MPV rises and it also correlated with disease severity. There are no significant NLR values in psoriasis but PLR shows significant elevation. Again PLR is not significantly increasing with disease severity.

Limitations

The present study had few limitations such as this study was conducted in a single hospital and had a small sample size that may not reflect the whole scenerio.

CONCLUSION

In our present study, we have found MPV and PLR significantly high in psoriatic individuals in comparison to the control group. PASI score-based disease severity positively correlates with MPV values. The gender-based analysis does not alter any result. In conclusion, we suggest MPV is a strong indicator of psoriasis severity. MPV and PLR should be followed up routinely to take preventive measures against psoriasis-related micro and macrovascular thrombotic complications.

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