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Platelet Parameters, Neutrophil–Lymphocyte Ratio, Platelet Lymphocyte Ratio, Red Cell Distribution Width: Can they Serve as Biomarkers in Evaluation of Severity of Psoriasis?

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Abstract:

BACKGROUND: Psoriasis has a multifactorial pathogenesis encompassing genetic, environmental, and immunological factors. There is a dire need for specific, cost effective, reliable, and universally accepted laboratory marker as indicator of severity of psoriasis.

MATERIALS AND METHODS: A cross-sectional study was conducted on 50 psoriasis patients and 50 healthy controls. Hematological parameters including platelet indices (platelet count [PC], plateletcrit, mean platelet volume [MPV], platelet large cell ratio, platelet distribution width [PDW]), neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR), and red blood cell distribution width (RDW) were evaluated and correlation of these indices among themselves and with Psoriasis Area and Severity Index (PASI) analyzed. Statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

RESULTS: A statistically significant difference in RDW, PC, MPV, PDW, NLR, and PLR was observed between psoriasis versus controls and mild versus moderate to severe psoriasis. There was a significant positive correlation between PASI and RDW, MPV, platelets, PLR while erythrocyte sedimentation rate showed a significant correlation with MPV. MPV and RDW, RDW and NLR, and RDW and PLR were also found to be correlated. MPV showed highest sensitivity and specificity both. MPV (area under the curve: 0.970, $P < 0.001$) demonstrated better predictive power as per area under curve of receiver-operator curve as compared to other parameters for psoriasis.

CONCLUSION: The present study assessed the role of simple and low-cost parameters easily computed from routine tests like complete blood count as biomarkers for severity of psoriasis. Mean values of MPV, RDW, NLR, and PLR were found to be higher in psoriasis patients compared to controls. Moreover, a significant correlation was observed between PASI and these novel markers. However, additional large-scale, multicenter studies need to be conducted before application of these parameters in clinical practice.

Keywords:

Mean platelet volume, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, psoriasis, psoriasis severity index, red cell distribution width

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Introduction

Psoriasis is a chronic inflammatory disease with a prevalence ranging from 0.91 to 8.5% in the adult population. It is an ongoing, progressive, immunologically mediated disease accompanied by periods of attacks and remissions.[1] Several comorbidities such

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as diabetes, hypertension, and lipid abnormalities have been observed in psoriatic patients. Moreover, there is an increased risk of metabolic syndrome and cardiovascular disorders in patients with psoriasis.[2]

A gamut of potential markers for psoriasis has emerged including inflammatory cytokines, C-reactive protein (CRP), hyperhomocystinemia, and platelet hyperactivity.[3] The different parameters which represent the condition of platelets are platelet count (PC), plateletcrit (PCT) (total mass of platelets), and mean platelet indices that are mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (PLCR). Among these, MPV is a reflection of the average size of platelets and is most extensively researched and has been found to increase in myocardial infarction (MI),[4] coronary artery disease[5] as well as psoriasis.[2,6-8] Platelet indices which reflect platelet morphology, namely PDW, PLCR, and PCT also play a significant role in atherosclerosis and thrombosis, however, there is a dearth of literature on these parameters in psoriasis.

The neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) have both emerged as good indicators of subclinical systemic inflammation in a variety of diseases such as cancer, cardiovascular diseases, and autoimmune inflammatory diseases. NLR and PLR have an advantage of being relatively stable compared to individual blood cell parameters. There are only a few studies in the literature regarding these novel biomarkers in psoriasis.[8,9]

Red blood cell distribution width (RDW) is an indicator of variation in size of the red blood cells (RBCs) and has been used traditionally to differentiate types of anemia. Recently, RDW has gained importance as an inflammatory marker in many diseases.[10]

The objectives of present study were to evaluate the various hematological parameters including platelet indices (PC, PCT, MPV, PLCR, PDW), NLR, PLR, and RDW in psoriasis patients and controls and to study whether any correlation exists between these indices and Psoriasis Area and Severity Index (PASI).

Materials and Methods

This is a cross-sectional study comprising of 50 psoriasis patients attending dermatology clinics (OPD) and 50 age-matched controls over a period of 6 months (November 2018 to April 2019). The study was approved by institutional ethics committee.

Inclusion criteria

All patients with established diagnosis of psoriasis on the basis of clinical and histopathological criteria were included in the study.

Exclusion criteria

The patients with a history of cardiovascular disease, metabolic syndromes, inflammatory bowel disease, hematological disorders, kidney or liver disease, and any other disease that might alter the hematological parameters and patients on antiplatelet medication were excluded from the study.

All the patients meeting the inclusion criteria and those who gave consent were included in the study. The demographic information and clinical details of the patient were recorded including duration of disease, family history, drug history, PASI, special reference to any complications, or comorbidities.

PASI[11] was calculated by using the formula:

PASI = 0.1 (EH + IH + DH) AH + 0.2 (EU + IU + DU) AU + 0.3 (ET + IT + DT) AT + 0.4 (EL + IL + AL) AL

Where E – Erythema, I – Indurations, D – Desquamation, A – Area of skin affected, H – Head, U – Upper limb, T – Trunk, L – Lower limb.

The severity of erythema, induration, and desquamation of the psoriasis was assessed as none (0), mild (1), moderate (2), severe (3), or very severe (4). The area of affected skin was expressed as nil (0), 1%–9% (1), 10%–29% (2), 30%–49% (3), 50%–69% (4), 70%–89% (5), or 90%–100% (6). Once the score is derived, the psoriasis was classified as mild when PASI score of ≤ 10, moderate to severe when PASI score is >10.

Venous blood samples were collected in the potassium ethylenediaminetetraacetic acid for estimation of hematological indices and tested within 1 h of collection to minimize variations due to sample. Complete blood count (CBC) was performed on 5 part hematology analyzer (Sysmex XN 1000).

Statistical analysis

Continuous parameters were expressed as mean ± standard deviation while qualitative parameters as numbers and percentages. To determine differences between groups (psoriasis vs. controls and mild psoriasis versus moderate to severe psoriasis), student's *t*-test, Mann–Whitney test, and Chi-square test were used. The correlation between various parameters was evaluated with Pearson's test. The parameters indicating psoriasis were analyzed by receiver-operator curve (ROC) analysis. Area under the curve (AUC) was calculated and if a significant cutoff was observed, the sensitivity and specificity were presented. Statistically significant differences were considered if $P < 0.05$. Statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

Results

The present study was conducted on 50 psoriasis patients and 50 age-matched healthy controls. The psoriasis patients were further categorized into mild (PASI <10, n = 27) and moderate to severe psoriasis (PASI >10, n = 23) based on the PASI score for the assessment of severity of the disease.

The mean age of the psoriasis group was 39.8 ± 11.59 years while the average age at onset of disease was 34.5 ± 12.54 years. The PASI score, erythrocyte sedimentation rate (ESR), and CRP positivity were significantly higher in moderate to severe psoriasis compared to mild psoriasis. A positive family history was observed in 11/50 (22%) of the patients. The clinicopathological parameters in the various groups are depicted in Table 1.

On comparing psoriasis patients (n = 50) versus healthy controls (n = 50), there was a statistically significant difference in RDW, PC, MPV, PDW, NLR as well as PLR between the two groups. All these parameters were found to be elevated in psoriasis patients. Comparison of hematological parameters between psoriasis and controls is shown in Table 2.

Moreover, when psoriasis was further classified into mild and moderate to severe psoriasis according to the PASI score, RDW, MPV, NLR, and PLR were observed to show statistically significant difference between these two categories [Table 2]. Bar diagrams depicting differences in novel hematological parameters (RDW, MPV, PDW, NLR) between psoriasis versus controls and mild versus moderate to severe psoriasis are shown in Figure 1.

There was a significant moderately positive correlation between various parameters with PASI, namely RDW (r: 0.479, P < 0.001), MPV (r: 0.466, P < 0.001), platelets (r: 0.395, P < 0.001), PLR (r: 0.474, P < 0.001), and ESR (r: 0.340, P: 0.001) [Figure 2]. A significant moderate positive correlation was observed between ESR and MPV (r: 0.387, P < 0.001), MPV and RDW (r: 0.302, P = 0.002), RDW and NLR (r: 0.406, P < 0.001), and RDW and PLR (r: 0.430, P < 0.001). The correlation of various parameters with each other and with severity indices is depicted in Table 3. Figure 2 shows scatter plot graphics showing correlation between PASI and MPV, RDW, NLR and PLR.

Table 1: Clinicopathological parameters in the various study populations

Parameter	Mean±SD		
	Mild psoriasis PASI<10 (n=27)	Mod to severe psoriasis PASI ≥ 10 (n=23)	Psoriasis (n=50)
Age (years)	41.5±12.34	37.8±10.58	39.8±11.59
Age at onset of psoriasis	37±10.75	31.35±13.94	34.5±12.54
Male:female	17:10	19:4	36:14
Duration of disease	4.35±4.68	6.68±7.57	5.34±6.19
Positive family history	3/27	8/23	11/50
PASI score	4.73±2.26	22.26±6.23	12.79±9.9
CRP positivity	7/27	16/23	23/50
ESR (mm/1st h)	15.15±8.66	20.52±9.19	18.00±9.12

CRP=C-reactive protein; ESR=Erythrocyte sedimentation rate; SD=Standard deviation; PASI=Psoriasis area and severity index

Table 2: Comparative analysis of hematological parameters in psoriasis patients versus controls and mild versus moderate to severe psoriasis patients

Parameter	Mean±SD		P	Mean±SD		P
	Psoriasis patients (n=50)	Controls (n=50)		Mild psoriasis PASI <10 (n=27)	Mod to severe psoriasis PASI ≥ 10 (n=23)	
Hemoglobin (g/dl)	14.05±1.78	14.52±2.12	0.23	14.35±1.38	13.69±2.13	0.19
TLC (10^3/µl)	8.06±1.49	7.18±1.84	0.01	8.39±1.72	7.68±1.09	0.09
RDW (%)	14.44±1.33	13.67±1.26	0.0037	13.97±1.18	14.99±1.30	0.0055
ESR (mm/h)	18.00±9.12	11.29±8.45	0.0002	15.15±8.66	20.52±9.19	0.05
Platelet count (10^3/µl)	238.7±76.53	207.9±65.8	0.033	227.85±68.92	251.43±84.36	0.28
MPV (fL)	12.40±1.43	9.40±1.35	<0.0001	11.48±1.43	12.93±1.44	0.008
PDW (fL)	17.63±3.73	15.60±3.12	0.004	17.94±3.67	17.25±3.84	0.5
PCT (%)	0.29±0.07	0.31±0.06	0.12	0.28±0.06	0.31±0.08	0.13
PLCR (%)	43.93±10.99	41.04±9.84	0.16	44.51±10.89	43.24±11.32	0.68
NLR	2.31±0.96	1.81±0.67	0.003	2.08±0.75	2.56±1.16	0.016
PLR	107.96±42.3	88.42±38.92	0.02	94.7±29.4	123.5±49.96	0.014

MPV=Mean platelet volume; PDW=Platelet distribution width; RDW=Red blood cell distribution width; NLR=Neutrophil-lymphocyte ratio; PLR=Platelet-lymphocyte ratio; ESR=Erythrocyte sedimentation rate; PASI=Psoriasis area and severity index; PLCR=Platelet large cell ratio; PCT=Plateletcrit; TLC=Thin-layer chromatography; SD=Standard deviation

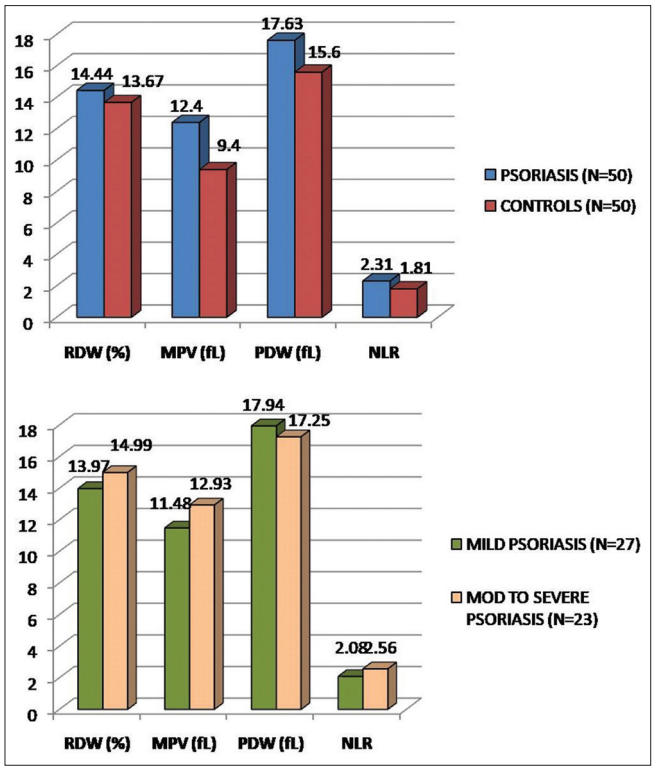


Figure 1: Bar diagrams depicting differences in novel hematological parameters (red blood cell distribution width, mean platelet volume, platelet distribution width, neutrophil–lymphocyte ratio) between psoriasis versus controls and mild versus moderate to severe psoriasis

Using ROC curve, the cutoff values for MPV, platelet, PDW, RDW, NLR, and PLR for diagnosing psoriasis were determined. MPV showed highest sensitivity and specificity both. Platelets count had a high specificity but low sensitivity [Table 4]. MPV (AUC: 0.970, $P < 0.001$) demonstrated better predictive power as per area under curve of ROC as compared to other parameters for psoriasis identification [Figure 3].

Discussion

Psoriasis has a multifactorial pathogenesis encompassing genetic, environmental, and immunological factors. Although no specific, universally accepted laboratory marker for the determination of psoriasis activity exists, elevated levels of cytokines, certain adhesion molecules etc., in circulation reflects their role in systemic inflammation which underlies psoriasis. Therefore, the need for more practical, cost-effective, and reliable indicators of severity of psoriasis is strongly felt.[1,3]

The role of platelets in the inflammatory process which underlies many diseases has been extensively studied. Mean platelet volume is an indicator of average platelet size, platelet function, and activation which in turn is a factor in the causation of atherosclerosis. Elevated MPV has emerged as an independent risk factor in acute MI as well as other vascular diseases such as diabetes mellitus and hyperlipidemia.[6,12,13] The literature on MPV in psoriasis is relatively limited compared to other diseases. In the current study, MPV emerged as a marker with the strongest predictive power for psoriasis with highest sensitivity and specificity. The comparative analysis of various studies on MPV in psoriasis is depicted in Table 5.

NLR and PLR are being appreciated as novel markers of subclinical systemic inflammation as well as poor prognosis in cancers, cardiovascular disease, metabolic syndrome, and autoimmune diseases.[8] The advantage of NLR and PLR compared to individual blood cell parameters is that they are relatively stable and are not affected by dehydration/overhydration, diluted blood samples, and blood specimen handling.[21] Moreover, these can be easily computed from routine CBC parameters without the need for any additional costly, time-consuming tests. NLR is a simple, economical index reflecting overall inflammatory burden. Bhat *et al*.[22] considered NLR to have a superior predictive ability as it is a ratio encompassing the detrimental effects of neutrophils which are the hallmark of active nonspecific inflammation as well as lymphopenia which in turn implies poor general health.

The role of NLR and PLR in psoriasis has been studied by several authors.[17,19,23-25] Qin *et al*.[21] studied NLR and PLR in psoriasis patients and found that both were significantly associated with PASI scores in multivariate analysis and both were statistically significant predictors for the presence of psoriatic arthritis in these patients. Among these parameters, NLR emerged as the strongest predictor similar to results obtained by Asahina *et al*.[8] In addition, another important finding was a time course decrease of NLR and PLR after treatment with biologics. However, Ataseven *et al*. did not find any association between NLR and PASI scores.[25]

An *et al*.[19] observed that NLR, MPV, and CRP values were significantly higher in psoriatic arthritis patients compared to controls and a significant relationship was observed between CRP and NLR and MPV values. Contrary to most studies in the literature, Yavuz and Yavuz[18] did not find any significant differences in these markers (NLR, PLR, and MPV) in 60 psoriasis patients versus 30 controls.

RDW is an index which indicates the variation in red cell size and has conventionally been used to aid in differentiating various types of anemia. Nowadays, RDW has emerged as an inflammatory marker in many diseases.[10,26] The exact cause of elevated RDW in these studies is unclear. However, it is proposed that increased

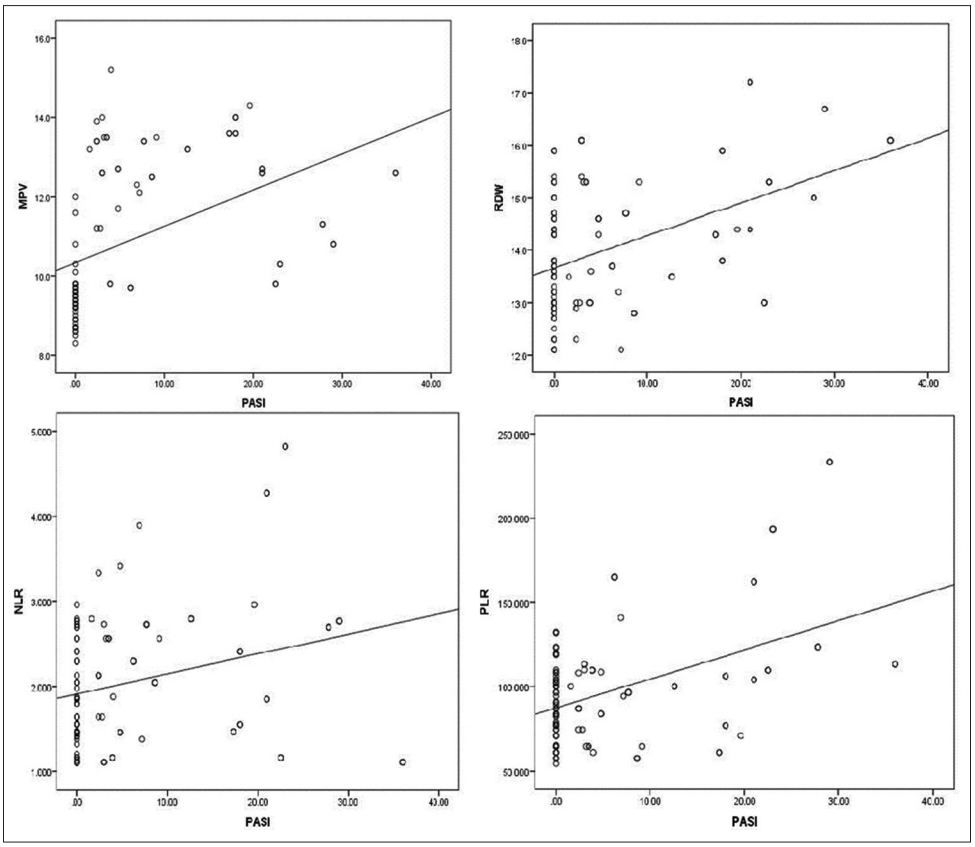
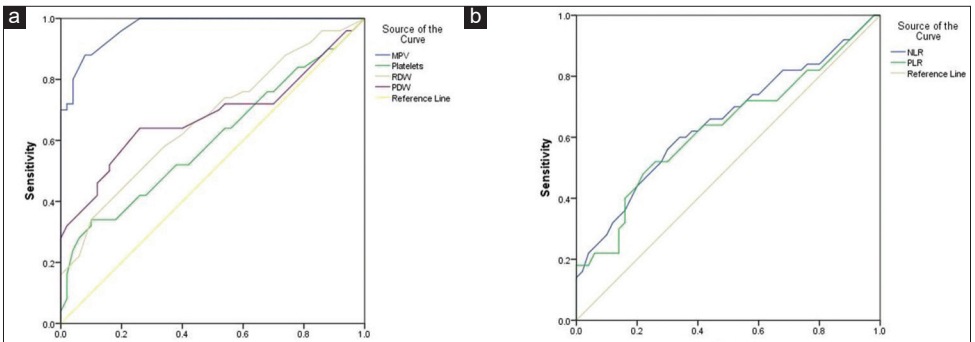


Figure 2: Scatter plot graphics showing correlation between psoriasis area and severity index and mean platelet volume, red blood cell distribution width, neutrophil–lymphocyte ratio, and platelet–lymphocyte ratio



Test Result Variable(s)	Area	Asymptotic Sig.[b]
MPV	.970	.000
Platelets	.601	.082
RDW	.668	.004
PDW	.680	.002

Test Result Variable(s)	Area	Asymptotic Sig.[b]
NLR	.651	.009
PLR	.630	.025

Figure 3: Receiver-operator curves to determine cutoff values for the presence of psoriasis with (a) mean platelet volume, platelets, red blood cell distribution width, platelet distribution width and (b) neutrophil–lymphocyte ratio and platelet–lymphocyte ratio

inflammatory cytokines in such diseases might lead to RDW elevation. Cytokines such as interferon-gamma, tumor necrosis factor-alpha, interleukin (IL)-1, IL-6, and IL-10-induced alterations are RBC precursors, erythropoietin, and RBC lifespan which can lead to RDW elevation.[26,27]

Kim *et al*.[10] observed that RDW is increased in patients with psoriasis vulgaris in a retrospective study on 261 patients. They also found that RDW was significantly higher in moderate to severe psoriasis compared to mild psoriasis. Raghavan *et al*.[7] also found a statistically significant difference in RDW between psoriasis patients

Table 3: Correlations between the novel laboratory markers for psoriasis and the indices for severity of psoriasis

	MPV	PDW	Platelets	NLR	PLR	ESR	PASI
RDW							
Pearson correlation	0.302**	0.195	0.196	0.406**	0.430**	0.218*	0.479**
Significance (two-tailed)	0.002	0.051	0.050	0.000	0.000	0.029	0.000
n	100	100	100	100	100	100	100
MPV							
Pearson correlation		0.638**	−0.155	0.244*	−0.043	0.387**	0.466**
Significance (two-tailed)		0.000	0.123	0.014	0.667	0.000	0.000
n		100	100	100	100	100	100
PDW							
Pearson correlation			−0.580**	0.065	−0.387**	0.197*	0.066
Significance (two-tailed)			0.000	0.522	0.000	0.050	0.512
n			100	100	100	100	100
Platelets							
Pearson correlation				−0.036	0.651**	0.014	0.395**
Significance (two-tailed)				0.721	0.000	0.888	0.000
n				100	100	100	100
NLR							
Pearson correlation					0.479**	0.166	0.268**
Significance (two-tailed)					0.000	0.100	0.007
n					100	100	100
PLR							
Pearson correlation						0.238*	0.474**
Significance (two-tailed)						0.017	0.000
n						100	100
ESR							
Pearson correlation							0.340**
Significance (two-tailed)							0.001
n							100

MPV=Mean platelet volume; PDW=Platelet distribution width; RDW=Red blood cell distribution width; NLR=Neutrophil-lymphocyte ratio; PLR=Platelet-lymphocyte ratio; ESR=Erythrocyte sedimentation rate; PASI=Psoriasis area and severity index; * weak correlation; ** moderate correlation

Table 4: Receiver-operator curve to determine cutoff value for predicting the presence of psoriasis

Variables	Cut off	Sensitivity/specificity
MPV	10.55	84/94
Platelet	225	38/78
PDW	16.25	68/52
RDW	14.05	58/66
NLR	1.82	66/56
PLR	101	52/70

MPV=Mean platelet volume; PDW=Platelet distribution width; RDW=Red blood cell distribution width; NLR=Neutrophil-lymphocyte ratio; PLR=Platelet-lymphocyte ratio

and controls. In the present study as well, similar results were obtained.

Balevi *et al*.[17] investigated RDW, MPV, NLR, PLR at monthly intervals during treatment for psoriasis among 45 patients with moderate to severe psoriasis. They observed that MPV increased at month 3 while lymphocytic counts increased significantly at all months. However, PCs decreased significantly only at months 6, 9, and 12, while RDW decreased significantly only at month 3.

Sharma *et al*.[20] studied the lifestyle factors, platelets, and platelet indices in 42 psoriasis patients and compared with twenty healthy controls and observed that PASI correlated with smoking ($P = 0.042$) as well as psychological stress level ($P = 0.002$). PLT ($P = 0.043$) and PCT ($P = 0.043$) were significantly higher whereas PDW ($P = 0.05$) was lower in psoriasis patients. A significant correlation of PASI with PDW ($P = 0.031$), mean platelet volume ($P = 0.050$), and PLCR (0.028) was found similar to our results.

Aman *et al*.[28] conducted a cross-sectional study of hematological parameters in 100 psoriasis patients. MPV was significantly higher in patients with psoriasis vulgaris ($P < 0.05$) with a positive correlation between PASI and MPV. Mean MPV was 8.63 ± 0.67 fL. However, in the current study, the mean MPV was 12.40 ± 1.43 fL.

Limitations of the present study were the small sample size and in statistical analysis, not all variable confounding factors could be included. Moreover, ours was a single institutional study. Even though exhaustive list of exclusion criteria was followed, some

Table 5: Comparative analysis of the literature on mean platelet volume in psoriasis

Authors	Year	Study population	Findings
Canpolat *et al*.[6] (Turkey)	2010	PsA *n*=48 PV=58 Control=95	MPV findings were higher in PsV as control. Statistically significant difference between MPV levels in patients with and without arthritis. MPV showed positive correlation with PASI and disease duration
Saleh *et al*.[14] (Egypt)	2013	PV - 25 Control - 25	MPV was not increased in PV compared to controls
Kim *et al*.[15] (Korea)	2015	PV - 176 Control - 101	PDW and MPV were significantly higher in patients with Psoriasis than controls. Positive correlation between PASI and MPV was observed
Işik *et al*.[2] (Turkey)	2016	PV - 45 Control - 44	No statistically significant difference between MPV values in two groups
Kılıç *et al*.[16] (Turkey)	2017	PsA - 116 PV - 41 Control - 90	MPV of PsA and PV group were significantly higher than controls. Weak statistically positive correlation between PASI and MPV
Raghavan *et al*.[7]	2017	PV - 50 Control - 50	Mean MPV was higher in PV than controls. MPV in male patient has a strong positive correlation with PASI score
Asahina *et al*.[8] (Japan)	2017	PV - 186 PsA - 50	MPV was significantly higher in PV than in PsA. MPV was negatively associated with the presence of arthritis
Balevi *et al*.[17] (Turkey)	2018	PV - 45 (moderate to severe PASI ≥ 7)	Studied levels of RDW, MPV, NLR, PLR at monthly intervals during treatment. MPV increased at month 3 while lymphocytic counts increased significantly at all months
Yavuz and Yavuz,[18] (Turkey)	2019	PV - 60 Control - 30	No significant difference was found in MPV, NLR, PLR between PV and control
An *et al*.[19]	2019	PsA - 74 Control - 77	MPV and NLR were significantly higher in patients. Statistically significant relation between CRP and NLR, MPV in PSA patients.
Sharma *et al*.[20]	2020	PV - 42 Control - 20	A significant correlation of PASI with PDW (*P*=0.031), mean platelet volume (*P*=0.050), and PLCR (0.028) was noted
Present study		PV - 50 Control - 50	MPV was significantly higher in psoriasis versus controls as well as in moderate to severe psoriasis versus mild psoriasis. There was a significant correlation of MPV with PASI and ESR

PsA=Psoriatic arthritis; PV=Psoriasis vulgaris; PASI=Psoriasis area and severity index, MPV=Mean platelet volume; PDW=Platelet distribution width; PLCR=Platelet large cell ratio; RDW=Red blood cell distribution width; NLR=Neutrophil-lymphocyte ratio; PLR=Platelet-lymphocyte ratio; CRP=C-reactive protein; ESR=Erythrocyte sedimentation rate

of the inflammatory markers could be altered by many other conditions which are difficult to control such as dehydration, dilution of blood samples, and specimen handling.

Conclusion

The present study assessed the role of simple and low-cost parameters easily computed from routine tests like CBC as biomarkers for severity of psoriasis. A significant positive correlation was observed between PASI and RDW, MPV, platelets, PLR while ESR showed a significant correlation with MPV. MPV and RDW, RDW and NLR, and RDW and PLR were also found to exhibit correlation. MPV (AUC: 0.970, $P < 0.001$) demonstrated better predictive power as per area under curve of ROC as compared to other parameters for psoriasis identification. However, additional large scale, multicenter research is required before these parameters can be used in clinical practice.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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