Platelet mass index as early indicator of subclinical atherosclerosis in psoriasis: a case–control study

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Background
Psoriasis is a chronic systemic disease. Inflammatory pathways activation in psoriasis may play a role in atherosclerosis development, independent of conventional risk factors. Platelets may have roles in psoriasis and atherosclerosis. Cardiovascular diseases prevention is based on early diagnosis of atherosclerosis. Platelet mass index means platelet count×mean platelet volume. Platelet mass index is a good indicator of inflammation, platelets activation, and atherosclerosis.

Objective
To evaluate platelet mass index as a marker of early diagnosis of subclinical atherosclerosis in psoriasis and its relation to different disease characteristics.

Patients and methods
In this case–control study, 100 psoriasis patients and 100 well-matched healthy controls were included. In all participants, common carotid intima-media thickness, platelet count, mean platelet volume, platelet mass index, and Psoriasis Area Severity Index (PASI) score were estimated.

Results
There were significant increases in platelet mass index and common carotid intima-media thickness in patients compared with controls and in atherosclerotic patients compared with nonatherosclerotics. There was significant increase in psoriasis duration in atherosclerotic patients compared with nonatherosclerotics, whereas PASI score showed nonsignificant difference between them. There were significant positive correlations between platelet mass index and patient age, psoriasis duration, common carotid intima-media thickness, whereas there was significant inverse correlation between platelet mass index and age of psoriasis onset and no correlation with PASI score. Platelet mass index was more predictor of atherosclerosis than platelet count and mean platelet volume. Platelet mass index was valid as predictor for atherosclerosis with cutoff value 3322.

Conclusion
Platelet mass index may be a good marker of platelet activity and subclinical atherosclerosis in psoriasis. Disease duration is more important than severity in atherosclerosis development. Dermatologists should advice patients to avoid traditional cardiovascular risk factors and to do routine cardiovascular checkup.

Keywords:
atherosclerosis, MPV, platelet, PMI, psoriasis

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Introduction

Psoriasis is a chronic immune-mediated relapsing inflammatory disease involving skin and joints of genetically predisposed individuals affecting 2%–3% of the world wide population [1]. Psoriasis is considered as systemic condition associated with various comorbidities [2]. Atherosclerosis is caused by chronic low-grade inflammation that results from an interaction between immune mechanisms and metabolic abnormalities within the vessel wall. Psoriasis increases the inflammatory load of the patient through activation of inflammatory pathways and increase levels of inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6, and tumor necrosis factor α. Also, it causes a state of insulin resistance and abnormal lipid profile that results in endothelial cell dysfunction. Thus, psoriasis itself may be a risk factor for atherosclerosis development, independent of conventional risk factors. In addition, psoriasis treatment, for example, acitretin, may induce hyperlipidemia [3].

Platelets have roles in inflammatory reactions, immune responses, and endothelial damage leading to atherosclerosis. Platelets also participate in psoriasis pathogenesis as activated platelets increase migration of white blood cells to skin and release many cytokines [4,5]. In addition, mean platelet volume (MPV), which reflects platelet activation and microvascular dysfunction; is significantly high in psoriasis especially in patients at high risk for atherothrombotic diseases [6,7].

Platelet mass index (PMI) is a new approach and is used in the neonatal intensive care unit to reduce unnecessary transfusions [8,9]. PMI is related to platelet functionality and is a useful parameter for platelets atherosclerotic plaque formation capacity. Also, PMI may be a better parameter of inflammation and platelet activation than MPV. Furthermore, high PMI in psoriasis may be an indicator of atherosclerosis vulnerability [10]. Despite the reported values of PMI, few studies assessed the PMI in psoriasis. The aim of our study was evaluation of PMI as a marker can be used in early diagnosis of subclinical atherosclerosis in psoriasis patients and its relation to different disease characteristics.

Patients and methods

This hospital-based case–control study was carried out on 100 adult psoriasis vulgaris patients (patients group) and 100 well-matched healthy adult volunteers from those attended the outpatient clinic of Dermatology at Mansoura University Hospital for esthetic procedures without known dermatological or systemic diseases and no history of use of any systemic medication in the last one month (control group). An informed written consent was obtained from any participant before enrollment in the study. Institutional Research Board, Faculty of medicine, Mansoura University approved this study (No: MS.18.05.147).

Participants with a history or clinical evidence of any dermatological disease other than psoriasis, systemic disease (e.g., hypertension, obesity, hyperlipidemia, diabetes mellitus, renal or hepatic disease, and ischemic heart diseases), history of using any systemic drugs in the last 1 month, for example, acitretin, smoking, and drinking alcohol, or showing active infection were excluded.

All participants were subjected to detailed history taking, complete general examination (including body mass index [BMI] calculation, joints examination, measurement of blood pressure), and full dermatological examination including skin, hair, nail, and oral mucosa. Psoriasis Area Severity Index (PASI) score was used to assess severity of psoriasis in each patient [11].

From each participant in the study, 3 ml of venous blood was withdrawn under complete aseptic condition from the cubital vein. Two milliliters were put in a test tube containing 20 µl of ethylenediaminetetraacetic acid (EDTA) for complete blood count and 1 ml was put in dry test tube for random blood sugar (RBS) estimation. The complete blood count was done as soon as possible using Sysmex XN 1000 cell counter (Sysmex Corporation, Kobe, Japan). Platelet count and MPV were estimated. Normal range of platelet count is $150–400\times10^3$/µl in both sexes and typical range of MPV is 9.4–12.3 femtoliter (fl) in both sexes. PMI was determined by the formula: platelet count×MPV [12].

Common carotid artery (CCA) ultrasound for common carotid intima-media thickness (CCIMT) estimation in millimeters was done using high-resolution B-mode ultrasonography (Philips Xario 200, Sysmex Corporation, Kobe, Japan). CCIMT is defined as a double-line pattern visualized by echo 2D on both walls of CCA in a longitudinal view [13]. The result of estimated CCIMT was interpreted as follows [14]:

(1) The thickness of CCIMT ≤0.9 mm was considered normal.
(2) The thickness of CCIMT >0.9 mm was considered atherosclerotic.

Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 software (SPSS Inc., Chicago, IL). Categorical data were presented as number and percentages. The χ^2 or Fisher's exact test was used to analyze categorical variables. Quantitative data were tested for normality using the Kolmogorov–Smirnov test assuming normality at $P>0.05$. Quantitative data were expressed as mean±SD, median, and range. Student's t test was used to analyze normally distributed variables among two independent groups, or Mann–Whitney U test for nonparametric ones. Spearman's correlation coefficient (rho) was used to assess correlation between nonparametric variables. Receiver operating characteristic (ROC) curve was used to detect cutoff values with optimum sensitivity and specificity in early diagnosis and prediction of

diagnosis of atherosclerosis. $P<0.05$ is considered statistically significant.

Results

Ages of the patients ranged from 18 to 76 years (mean ±SD: 45.37±13.11), whereas the range of ages of controls was from 18 to 60 years (mean±SD; 42.06 ±12.44). Patients were 56 females and 44 male, whereas controls were 67 females and 33 males. There were no significant differences between patients and controls regarding age, sex, occupation, and marital status.

No special habit was reported in patients and controls. No family history of psoriasis was reported in the control group, whereas it was detected in 7 patients (7%). The age of psoriasis onset ranged from 10 to 72 years (mean±SD: 36.41±13.59), early onset psoriasis (<40 years age) in 56 patients and late onset psoriasis (>40 years age) in 44 patients, whereas the duration of psoriasis ranged from 0.25 to 37 years (mean±SD: 9.03 ±7.748). Regarding psoriasis severity, PASI score for patients ranged between 2 and 43 (mean±SD: 13.50 ±7.44) with scalp affection in 51 patients (51%), nails affection in 10 patients (10%), and no joints affection was reported.

There were no statistically significant differences between patients and controls regarding body weight, height, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), and RBS. On the other hand, there were significant increases in platelet count, MPV, PMI, and CCIMT in patient group compared with control group (Table 1).

According to CCIMT, at cutoff value 0.9 mm, the controls were classified into atherosclerotic (n=18) and nonatherosclerotic (n=82) and patients were classified into atherosclerotic (n=39) and nonatherosclerotic (n=61), respectively. Percentage of atherosclerosis was significantly higher in patients than controls (P=0.001). The mean age of the atherosclerotic patients was 48.21±11.58 years (mean±SD), whereas the mean age of the nonatherosclerotic patients was 43.56±13.79 years (mean±SD) without significant difference (P=0.084). Atherosclerotic patients were 22 females and 17 males, whereas nonatherosclerotic patients were 34 females and 27 males without significant difference (P=0.947). Atherosclerotic controls were 15 females and 3 males with mean age 42.22±12.56 years (mean±SD). There were nonsignificant differences between age and sex of atherosclerotic patients vs. atherosclerotic controls ($P>0.05$).

Table 1 Comparison between patient group and control group regarding anthropometric measurements, blood pressure, random blood sugar, platelet count, MPV, PMI, and CCIMT

	Patient group (mean±SD)	Control group (mean±SD)	*t* test	*P* value
Weight (kg)	90.02±22.87	85.40±19.05	2.896	0.07
Height (cm)	165.19±10.34	167.54±6.59	1.346	0.180
BMI (kg/m^2)	29.92±9.64	28.38±7.99	2.025	0.06
SBP (mmHg)	121.92±13.07	121.62±9.97	0.183	0.855
DBP (mmHg)	75.70±8.35	76.95±6.431	–1.186	0.237
RBS (mg/dl)	123.05±48.05	114.90±25.08	1.504	0.134
Platelet count (10^3/μl)	416.20±207.39	312.27±142.58	4.13	0.000*
MPV (fl)	9.8±1.001	8.2±0.9	–21	0.028*
PMI	3877.95 ±2137.34	2863.26 ±1221.36	4.12	0.000*
CCIMT (mm)	0.77±0.29	0.53±0.38	5.082	0.000*

t: Student's *t* test. BMI, body mass index; CCIMT, common carotid intima-media thickness; DBP, diastolic blood pressure; fl, femtoliter; MPV, mean platelet volume; PMI, platelet mass index; RBS, random blood sugar; SBP, systolic blood pressure. *$P<0.05$ is considered statistically significant.

In addition, there were nonsignificant differences between atherosclerotic and nonatherosclerotic psoriatic patients regarding body weight, height, BMI, SBP, DBP, RBS, PASI score, and psoriatic nail affection. However, there was significant increase in psoriasis duration, scaly scalp affection, platelet count, MPV, and PMI in atherosclerotic psoriatic patients compared with nonatherosclerotic patients (Table 2).

There were significant positive correlations between PMI and each of age of the patient, psoriasis duration, platelet count, MPV, and CCIMT, whereas there was significant negative correlation between PMI and age of psoriasis onset. In addition, there were significant positive correlations between platelet count and each of age of the patient, psoriasis duration, body weight, BMI, MPV, and CCIMT, whereas there was a significant negative correlation between platelet count and age of psoriasis onset. Both PMI and platelet count showed nonsignificant negative correlations with PASI score (Table 3).

There were significant positive correlations between MPV and each of psoriasis duration, BMI, CCIMT, and PASI score, whereas there was significant negative correlation between MPV and age of psoriasis onset. In addition, there were significant positive correlations between CCIMT and each of psoriasis duration, body

Table 2 Comparison between atherosclerotic and nonatherosclerotic psoriatic patients regarding anthropometric measurements, blood pressure, random blood sugar, platelet count, MPV, PMI, CCIMT, scalp, and nail affection

	Atherosclerotic psoriatic patients (No.=39) (mean±SD)	Nonatherosclerotic psoriatic patients (No.=61) (mean±SD)	*t* test	*P*
Weight (kg)	97.21±22.57	91.98±23.00	1.115	0.268
Height (cm)	166.87±11.71	167.39±9.46	–0.245	0.807
BMI (kg/m^2)	29.46±10.32	26.92±9.12	1.285	0.202
SBP (mmHg)	121.03±9.95	122.50±14.80	–0.547	0.586
DBP (mmHg)	75.13±6.44	76.07±9.40	–0.546	0.587
RBS (mg/dl)	124.33±62.86	122.23±36.12	0.213	0.832
Psoriasis duration (year)	13.690±8.75	6.04±5.23	5.477	0.000*
PASI	13.63±8.64	13.42±6.63	0.137	0.892
Platelet count (10^3/μl)	535.31±229.27	340.05±150.19	5.150	0.000*
MPV (fl)	9.56±0.79	9.00±1.06	2.839	0.005*
PMI	5131.93±2277.74	3076.22±1605.04	5.293	0.000*
CCIMT	1.03±0.13	0.61±0.25	9.941	0.000*
Scalp	Absent (*n*, %)		8.503	0.004*
psoriasis	12 (30.8%)	37 (60.7%)		
	Present (*n*, %)			
	27 (69.2%)	24 (39.3%)		
Nail psoriasis	Absent (*n*, %)		7.115	0.310
	33 (84.6%)	56 (91.8%)		
	Present (*n*, %)			
	6 (15.4%)	4 (8.2%)		

t: Student's *t* test. BMI, body mass index; CCIMT, common carotid intima-media thickness; DBP, diastolic blood pressure; fl, femtoliter; MPV, mean platelet volume; PASI, Psoriasis Area Severity Index; PMI, platelet mass index; RBS, random blood sugar; SBP, systolic blood pressure. *$P<0.05$ is considered statistically significant.

Table 3 Correlation between PMI, platelet count, MPV, CCIMT, and other variables

Variables	PMI		Platelet count		MPV		CCIMT	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Age of the patient	0.223	0.026*	0.203	0.004*	0.107	0.289	0.110	0.122
Age of psoriasis onset	–0.213	0.034*	–0.226	0.024*	–0.219	0.029*	–0.106	0.293
Psoriasis duration	0.737	0.000*	0.745	0.000*	0.284	0.004*	0.584	0.000*
Weight	0.075	0.457	0.184	0.009*	0.127	0.207	0.222	0.002*
Height	0.066	0.516	0.027	0.701	–0.009	0.932	–0.005	0.941
BMI	0.028	0.787	0.146	0.040*	0.139	0.016*	0.205	0.004*
PASI	–0.143	0.157	–0.146	0.147	0.021	0.037*	–0.113	0.263
SBP	–0.048	0.635	–0.093	0.194	0.076	0.456	–0.072	0.318
DBP	–0.032	0.753	–0.127	0.073	–0.024	0.812	–0.145	0.042*
RBS	0.148	0.383	0.051	0.474	0.108	0.283	0.090	0.207
Platelet count	0.975	0.000*	–	–	–	–	–	–
MPV	0.465	0.000*	0.323	0.001*	–	–	–	–
CCIMT	0.622	0.000*	0.592	0.000*	0.202	0.044*	–	–

BMI, body mass index; CCIMT, common carotid intima-media thickness; DBP, diastolic blood pressure; MPV, mean platelet volume; PASI, Psoriasis Area Severity Index; PMI, platelet mass index; *r*, Pearson's correlation; RBS, random blood sugar; SBP, systolic blood pressure. *$P<0.05$ is considered statistically significant.

weight, and BMI, whereas there was significant negative correlation between CCIMT and DBP; and nonsignificant negative correlation between CCIMT and PASI score (Table 3).

Regression analysis was conducted for prediction of atherosclerosis in psoriasis patients using platelet count, MPV, and PMI as covariates. PMI was more predictor than platelet count and MPV (Table 4). Validity of PMI in diagnosis of atherosclerosis in psoriasis patients (as shown by ROC curve) presented that PMI was a significant good predictive factor at cutoff value 3322, area under the curve 0.74, sensitivity 55.1%, specificity 76.5%, positive predictive

value 69.2%, negative predictive value 63.9%, accuracy 56%, and significant *P* value 0.00 (Fig. 1).

Discussion

In the present study, sociodemographic data are like Mahrous [15] who found nonsignificant differences between atherosclerotic and nonatherosclerotic patients regarding their ages. However, Farag *et al.* [16] reported that atherosclerotic patients were significantly elder than nonatherosclerotics. In the current study, it was found that psoriasis duration was significantly higher in atherosclerotic patients, whereas PASI score showed nonsignificant differences. Mahrous [15] and Farag *et al.* [16] reported significant increases in psoriasis duration and PASI score in atherosclerotic patients compared with nonatherosclerotics. Duration of the disease and age of onset seem to be more important than disease severity in development of atherosclerosis in psoriasis patients.

Regarding BMI, SBP, DBP, and RBS, the present results are like several studies [17–19]. However, this may contradict with other studies [20–22]. In addition, estimated CCIMT in this study is confirming what was reported by several studies that psoriasis may be associated with subclinical atherosclerosis [15–17,22–28]. Despite the nonexistence of atherosclerotic risk factors, psoriasis patients were more vulnerable for development of atherosclerosis than healthy individuals denoting that psoriasis with its induced state of generalized inflammation encourages atherosclerosis [29].

Moreover, regarding platelet count, MPV, and PMI, the results of the present study indicate significantly increased platelet activity in psoriasis that was more obvious in patients with atherosclerosis. Platelet activation may share in psoriasis pathogenesis and may facilitate atherosclerosis plaque formation in the absence of other risk factors such as aging, high BMI, hypertension, and diabetes. The current results agree with many studies [4,6,10,15,16,30–33]. However, others found no significant differences between patients and controls [19,34–38]. These conflicting results may be due to small samples sizes in the lastly mentioned studies.

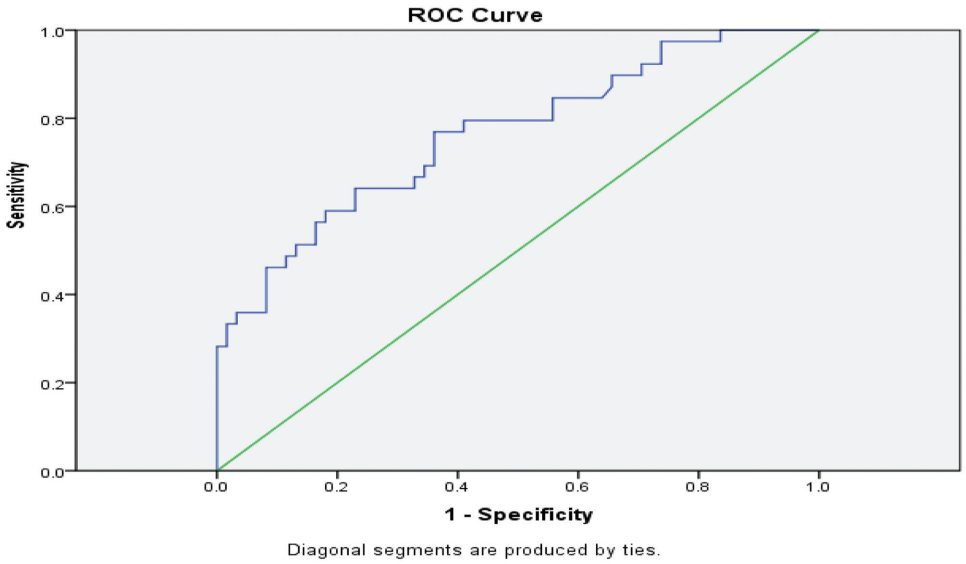
Comparing correlations between platelet count and other parameters (age of the patient, psoriasis duration, MPV, PMI, CCIMT, age of psoriasis onset, and PASI score) in this study with other studies revealed some controversies. Unal [10] and Pektas *et al.* [30] found no correlation between platelet count and PASI score. However, Raghavan *et al.* [36] reported significant inverse correlation

Table 4 Regression analysis for prediction of atherosclerosis in psoriasis patients

	Exp (B)	95% CI for Exp (B)	
		Lower	Upper
Platelet count	0.77	0.61	1.001
MPV	0.63	0.47	1.002
PMI	1.2	1.00	1.024

CI, confidence interval; MPV, mean platelet volume; PMI, platelet mass index.

Figure 1



ROC curve for the validity of platelet mass index in diagnosis of atherosclerosis psoriasis cases.

between platelet count and PASI score. Unal [10] found inverse correlation between platelet count and MPV and no correlations between platelet count and both disease duration and age of onset. On the other hand, correlations between MPV and other parameters (age of the patient, psoriasis duration, PMI, CCIMT, age of psoriasis onset, and PASI score) in the present study agrees with many studies [4,6,15,16,30,32], whereas they show controversies with other studies [10,34,37–39].

Also, the current work shows positive correlations between PMI and each of age of the patient, psoriasis duration, and CCIMT, whereas it showed inverse correlation with age of psoriasis onset and no correlation with PASI score. Unal [10] reported that PMI had inverse correlation with age of psoriasis onset and no correlation with PASI score and disease duration. Patients who had psoriasis at younger ages showed high PMI, increased cytokines released from platelets, pronounced inflammatory environment, more psoriasis activity, and more atherothrombotic complications due to longer exposure [10].

According to the results of the present study, it was noticed that the duration of disease is the pivotal factor in the development of complications in psoriasis. All markers of platelet activity, inflammation, and atherosclerosis showed significant positive correlations with duration of disease rather than with severity of the disease.

The diversity in all the previously mentioned results may be due to differences in the numbers, races, ages, health status, physical activity, psoriasis duration, disease severity, methods of case ascertainment, weight, or BMI of the studied population. Also, the time at which each study was performed as psoriasis is more active in winter. Moreover, the course of the disease as psoriasis has periods of exacerbation and remission, with a variable PASI score along the time/overtime. Hence, a considerable variation in disease activity (PASI) along the time/over time makes it difficult to demonstrate the relationship with the presence of subclinical markers of atherosclerosis such as CCIMT [40–43]. Population-based studies in general do not allow a comprehensive assessment of the association between disease-related variables such as disease activity, markers of inflammation, and medication use and cardiovascular risk [3]. In addition, in the current study, obese, diabetic, and hypertensive patients were excluded from the start as established cardiovascular risk factors can influence MPV and CCIMT [38,44–46].

PMI can be considered superior predictor of atherosclerosis, platelet activity, and inflammatory status in psoriasis than platelet count and MPV as it showed more regular correlations with different variables that well co apt with others results. Unal [10] reported the same outcome as PMI correlated with inflammatory markers, for example, hs-CRP and ESR, and has no contradictory studies.

Conclusion

Platelet activity, evaluated by high PMI, may have an active role in psoriasis development and its outcome. A simple inexpensive complete blood count including PMI can be a good test for early detection of atherosclerosis in psoriasis patients who should receive close clinical attention. Dermatologists should advice their patients with high PMI to avoid traditional cardiovascular risk factors and to routinely checkup. Also, it is recommended to study the prophylactic antiplatelet therapy in psoriasis to reduce the cardiovascular disease risk.

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Conflicts of interest

There are no conflicts of interest.

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