PLATELETCRIT IS POTENTIAL BIOMARKER FOR PRESENCE AND SEVERITY OF PSORIASIS VULGARIS

Suzan Demir Pektas[*], Emine Tugba Alatas[*], Nigar Yilmaz[**]
[*]Mugla Sitki Kocman University, Faculty of Medicine, Department of Dermatology, Mugla - [**]Mugla Sitki Kocman University, Faculty of Medicine, Department of Biochemistry, Mugla

ABSTRACT

Introduction: Psoriasis vulgaris (PV) is characterized by erythrosquamous plaques in skin and associated with systemic inflammation. Platelets modulate immune and inflammatory processes in the skin. Platelets are indicated with PCT which is produced of PLT and the MPV and reflects total platelet mass. PCT is found as a marker that shows platelet activity. PCT is associated with severity of inflammation in some diseases. NLR and PLR in venous blood are increased in systemic inflammatory responses. We aimed to investigate the association between Psoriasis Area and Severity Index (PASI) and platelet indices including plateletcrit (PCT), the value of platelet to lymphocyte ratio (PLR), platelet count (PLT), mean platelet volume (MPV) and the value of neutrophil to lymphocyte ratio (NLR).

Materials methods: A total of 172 patients with psoriasis and 128 healthy controls were included in the study. Age, sex, PCT, PLR, NLR, PASI, PLT, neutrophil count (NC) and lymphocyte count (LC), MPV, lipid profile of the patients were recorded. We measured the severity of skin disease using PASI.

Results: When compared with controls, patients with psoriasis had higher PCT, platelet count, MPV, PLR and NLR. We observed significant association between the presence of psoriasis and PCT, NLR, MPV. There were significant differences between platelet indices including PLT, PCT, MPV, PLR in the severe and moderate groups. PASI was positively correlated with PCT, MPV and PLR. In ROC analysis, PCT value greater than 0.321 predicted psoriasis with 55% sensitivity and 90% specificity. Using binary logistic regression analysis, we found that PCT, especially those values >0.321, were independent predictors of psoriasis (OR=2.810, 95% Cl=1.28-3.33, p=0.000).

Conclusion: PCT value should be used as a predictor for precense of psoriasis. It could also be highlighted that PCT is a noninvasive, easily available marker and so it can be used in predicting patients with psoriasis.

Keywords: Psoriasis vulgaris, plateletcrit, platelet, platelet to lymphocyte ratio, neutrophil to lymphocyte ratio, MPV.

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Introduction

Psoriasis vulgaris is a chronic inflammatory immune-mediated skin disease affecting 2 to 4% of the world population which decrease quality of life[1]. Platelets modulate immune and inflammatory processes in the skin[2]. Platelet activation in pathogenesis of the some inflammatory diseases was described in previous studies[3]. The elevated platelet levels have been implicated in increasing inflammation and trombosis.

Also, the activated platelet may increase the effect of leukocytes in the skin, and result worsenning of the disease or presenting of disease. Platelets are indicated with PCT which is produced of PLT and the MPV and reflects total platelet mass. PCT is newly found as a marker that shows platelet activity[4]. It was indicated that PCT is associated with severity of inflammation in some diseases including Behcet's disease, Crohn's disease, inflammatory bowel diseases and malignancies[5-7].

It was reported that increased NLR and PLR indicate elevated inflammation. PLR is an another new biomarker used for determining the inflammation. PLR is related to atherosclerosis in patients with coronary artery disease and also assumed to be a prognostic factor in some inflammatory disease[8-10]. NLR and PLR in venous blood are increased in systemic inflammatory responses. The level of MPV was recently described as an indicator of larger, more reactive platelets resulting from an elevation in platelet turnover. MPV is an easy and accurate biomarker of the functional status of platelets. The larger platelets the more reactive they are well established in previous studies[11].

No research was found about investigating the association with PCT and psoriasis. Firstly, this study was designed to determine the platelet activation which is showed by the level of PCT in patients with psoriasis and the correlation with PASI which shows the severity of psoriasis. Also, we aimed to compare the levels of PCT, NLR, PLR, MPV, PLT in patients with psoriasis and healthy controls. Also, we evaluated the association between PASI and PCT, NLR, PLR, MPV, PLT as well as other laboratory findings including lipid levels.

Material and methods

The study included 172 patients with psoriasis and 128 healthy individuals. We included the patients with psoriasis as following: age over 18 years who applied to the Mugla Sitki Kocman University, Faculty of Medicine and Aydin State Hospital, Outpatient Department of Dermatology from October 2013 to December 2015. The exclusion criteria for patients with psoriasis and healthy individuals were the following: age under 18 years, the presence of pregnancy, malignancies, hepatic and renal disease, infectious diseases and diabetes mellitus. Age, sex, PCT, PLR, NLR, PASI, NC, PLT, LC, MPV, lipid profile of the patients were recorded. We measured the severity of skin disease using PASI score. A PASI score below 10 was defined as "moderate" and above 10 was defined as "severe" disease (according to British Association of Dermatologists Guidelines)[12].

Statistical Analysis

Statistical analyses were performed using IBM SPSS version 20.0 software program (IBM Corp, Armonk, USA). Qualitative variables were calculated as frequency and percentage. Continuous variables were described as mean ± standard deviation. The Kolmogorov-Smirnov test was used to determine the normality of the distribution of variables. The Mann-Whitney U-test, Student's t-test were used for determining the differences in continuous variables. The correlation between PASI and platelet indices and NLR were determined with pearson correlation analysis. Binary logistic regression analysis was performed to identify the independent predictors of psoriasis. In addition, patients with psoriasis were grouped according to PASI score and the two groups were compared. In all our analyses, a p value of under 0.05 was accepted as significant. A cut off point for PCT, PLT, MPV, NLR and PLR were calculated for predicting the presence of psoriasis with a receiver operating characteristics (ROC) curve analysis. The results were conducted as odds ratio (OR), area under the curve (AUC) and sensitive-specific values with 95% confidence intervals (CIs).

Results

The demographic and laboratory characteristics of the study and control groups were shown in Table 1.

Variables	Patients with psoriasis n= 172	Control n= 128	Value of p
Age (year)	42.17±11.98	40.6±12.69	>0.05
Male gender, n (%)	84(48.8)	65(50.7)	>0.05
BMI	26.73±3.90	23.08±2.03	<0.01
PASI	7.75±6.89	156.92±23.65	<0.01
TC (mg/dl)	197.59±38.64	47.67±17.10	>0.05
HDL (mg/dl)	50.82±14.78	94.11±24.81	<0.01
LDL (mg/dl)	12.23±33.10	117.24±33.45	<0.01
TG (mg/dl)	145.45±69.33	1.33±0.66	<0.01
NC (10³/ul)	2.19±0.83	250.31±71.43	>0.05
LC (10³/ul)	236.15±61.65	9.72±1.28	<0.01
MPV (fl)	1.42±1.73	239.43±59.27	<0.01
PLT (10³/ul)	295.12±81.32	0.201±0.064	<0.01
PCT (%)	0.273±0.108	0.201±0.064	<0.01
PLR	137.53±61.3	105.01±45.68	<0.01
NLR	2.19±0.83	1.33±0.66	<0.01

Table 1: Baseline characteristics of patients with psoriasis and control.

BMI= body mass index, PASI=psoriasis area and severity index, TC=total cholesterol HDL=high-density lipoprotein, LDL=low-density lipoprotein, TG= triglyceride, MPV=mean platelet volume, PLT=platelet count, PCT=plateletcrit, PLR=platelet-to-lymphocyte ratio, NLR=neutrophil-to-lymphocyte ratio.

Variables	OR	95% Cl	Value of p
MPV	2.209	1.99-2.42	0,000
PLT	1.012	1.009-1.015	0,000
PCT	2.810	1.283-3.337	0,000
PLR	1.013	1.000-1.018	0,000
NLR	5.181	4.740-5.610	0,000

Table 2: Binary logistic regression model for the presence of patients with psoriasis.

MPV=mean platelet volume, PLT=platelet count, PCT=plateletcrit, PLR=platelet-to-lymphocyte ratio, NLR=neutrophil-to-lymphocyte ratio, Cl= confidence interval, OR= odds ratio

Charecteristics	PASI<10 (n=124)	PASI>10 (n=48)	p value
Age(year)	42.2±12.04	41.94±11.91	>0.05
Gender (M/F)	70/54	23/25	>0.05
BMI	26.81±3.85	26.44±4.15	>0.05
TC (mg/dl)	198.48±37.69	194±44.74	>0.05
HDL (mg/dl)	52.43±14.76	44.32±13.22	0,002
LDL (mg/dl)	122.46±33.22	121.21±33.52	>0.05
TG (mg/dl)	145.88±68.9	143.71±72.11	>0.05
NC (10³/ul)	2.04±0.77	2.83±0.79	0,000
LC (103/ul)	237.53±62	230.58±60.82	>0.05
MPV (fl)	10.02±1.46	12.05±1.83	0,000
PLT (10³/ul)	287.61±78.86	325.62±85.21	0,016
PCT (%)	0.26±0.01	0.35±0.12	0,000
PLR	131.23±57.17	163.13±71.19	0,007
NLR	2.03±0.77	2.83±0.79	0,000

Table 3: The comparison of clinical characteristics of psoriasis patients with PASI<10 and PASI≥10.

BMI= body mass index, TC=total cholesterol HDL=high-density lipoprotein, LDL=low-density lipoprotein, TG= triglyceride, NC= neutrophil count, LC=lymphocyte count, MPV=mean platelet volume, PLT=platelet count, PCT=plateletcrit, PLR=platelet-to-lymphocyte ratio, NLR=neutrophil-to-lymphocyte ratio, PASI=psoriasis area and severity index

	Correlation coefficient (r)	p value
NC	0.316	0.001
LC	-0.033	0.669
MPV	0.410	0.001
PLT	0.114	0.137
PCT	0.114	0.001
PLR	0.325	0.001
NLR	0.111	0.148

Table 4: Pearson correlation between PASI and different variables.

NC=neutrophil count, LC=lymphocyte count, MPV-mean platelet volume, PLT=Platelet count, PCT- plateletcrit; PLR-platelet to lymphocyte ratio; NLR-neutrophil to lymphocyte ratio

	AUROC	cut-off value	Sensitivity %	Specifity %	p value
MPV	0.787(0.736-0.838)	10.49	46	94	0.000
PLT	0.711(0.653-0.768)	308	38	90	0.000
PCT	0.745(0.689-0.800)	0.321	55	90	0.000
PLR	0.673(0.612-0.735)	138.8	38	85	0.000
NLR	0.812(0.763-0.861)	2.31	68	80	0.000

Table 5: Correlation between hematological parameters and psoriasis vulgaris.

MPV-mean platelet volume; PLT=platelet count, PCT- plateletcrit; PLR-platelet to lymphocyte ratio; NLR-neutrophil to lymphocyte ratio
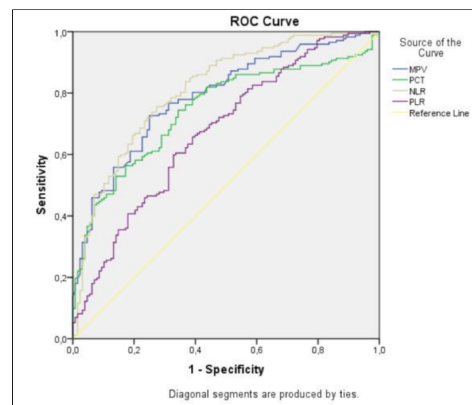

Fig. 1: Receiver-operator curve to determine cut off value for predicting the presence of patients with psoriasis with MPV-mean platelet volume, PCT- plateletcrit, PLR-platelet to lymphocyte ratio, NLR-neutrophil to lymphocyte ratio.

MPV=mean platelet volume; PCT=plateletcrit; PLR=platelet to lymphocyte ratio; NLR=neutrophil to lymphocyte ratio

There was no significant differences in age and gender between patients with psoriasis and controls. The mean of PASI score was 7,75±6,89. We determined significant differences in total cholesterol (TC), LDL cholesterol (LDL), trigliceride (TG) levels in patients with psoriasis when compared with controls. TC, HDL, LDL and TG levels were not correlated with PASI. We observed significant platelet activation in patients with psoriasis, as shown by the significant increase in platelet indices (PLT, PCT, MPV). When compared with controls, patients with psoriasis had higher PLT, PCT and MPV. NLR and PLR levels were significantly higher in patients with psoriasis when compared with healthy individuals.

We observed significant association between the presence of psoriasis and NLR, PCT, MPV levels in binary regression analysis. NLR was found as the strongest predictor of the presence of psoriasis

vulgaris. PCT and MPV were less strong predictor when compared to NLR.

Next, we grouped patients with psoriasis into two according to their PASI score. PASI≥10 is reported as severe. There were 48 patients with psoriasis enrolled as severe. One hundred twenty four patients had PASI<10. Age, sex, BMI, TC, LDL, TG levels, LC were similar between the moderate and severe patients with psoriasis. There were statistically significant differences between platelet indices including PLT, MPV, PCT, PLR of the severe and moderate groups. NC, HDL, NLR were significantly higher in the severe disease when compared with moderate patients.

We also found significantly positive correlations between PASI score and NC, MPV, PCT and PLR. However, among the platelet indices, platelet only did not show correlation with PASI.

The ROC analysis yielded a cutoff value of 0.321 for PCT to predict the presence of patients with psoriasis with 55% sensitivity and 90% specificity. The AUC of MPV value was 0.787 with 46% sensitivity and 94% specificity. The AUC of NLR value was 0.812 with 68% sensitivity and 80% specificity. The AUC of PLR value was 0,673 with 38% sensitivity and 85% specificity. The AUC of platelet count value was 0.711 with 38% sensitivity and 90% specificity.

Discussion

In the current study, mainly we investigated the relation between the PCT level and PASI. This is the first study that show the relation between PCT and psoriasis in the literature. Also, we suggest that PCT is a novel biomarker of the presence and severity of psoriasis. PCT, PLT, MPV, NLR and PLR were significantly increased in patients with psoriasis than healthy individuals in our study. In addition, the level of PCT is related to elevated disease severity. PCT is a parameter of the routine complete blood count which is cheap and for diagnosis of patients with high PCT level. In previous studies, it was described that PCT correlates with inflammation. PCT was explained as a specific and sensitive biomarker for some inflammatory disease[7]. PCT is a new marker that shows PLT and activity. The measurement of platelet volume has been of interest for investigators concerned with platelet production[13]. Platelets are deeply involved initiating and modulation of inflammation and immune response as immune cells in the skin[14].

According to some studies, the platelets may be related to the regulatory processes of skin inflammatory diseases[15,16]. PCT is calculated by the produce of the platelet count and the mean platelet volume. PCT is an inexpensive and easily measurable parameter. We focused on the risk factors including elevated platelet and platelet hyperactivity which may be a direct consequence of psoriasis inflammation. Bain et al. demonstrated that PCT indicates the number of circulating platelets in blood[17]. The activated platelets may participate the development of inflammation in the skin and result in increasing the severity of the disease. In contrast, it was mentioned that the systemic inflammation in psoriasis may led to the activation of platelets[18]. There was a positive correlation between PASI and PCT in current study. In previous study, it was mentioned that PCT was shown to correlate with inflammation marker including CRP. In an another study, it was mentioned that hs CRP and IL-6 were correlated positively with platelet activity and disease severity[19]. It shows that psoriasis is a disease which has relationship with cytokins and other inflammatory markers. We suggest that PCT may reflect the inflammation in patients with psoriasis. We showed that high PCT may predict the presence of psoriasis in patients. The value of PCT appears effective in predicting the severity of inflammation in patients with psoriasis.

Psoriasis is closely related to cardiovascular events such as atherosclerosis and thromboembolism. The combination of platelet and leukocytes, particularly neutrophils, has a synergistic effect on increased risk of atherogenesis[20].

In our study, we found increased NC and PLT in patients with psoriasis. It may show the potential cardiovascular risk in psoriasis. In previous studies, it was described that platelets interact with leukocytes and effect the count of leukocytes. NLR was found as a diagnostic marker diseases characterized by systemic or local inflammatory response including coronary artery disease, crohn's disease, inflammatory arthritis and ulcerative colitis[21,22]. NLR is an useful biomarker in showing the presence of inflamatory conditions. Similar to the literature, we found that the levels of NLR in patients with psoriasis significantly higher than the healthy individuals, and also it was correlated to PASI[23]. In addition, using binary logistic regression analysis, we found that NLR was the strongest predictor of the presence of psoriasis vulgaris.

The relationship between NLR and psoriasis has been evaluated in only one study which was similar to our study. PLR is explained as a sensitive biomarker in some diseases[24,25]. In our study, PLR was found positively correlated with PASI more than NLR.

The level of MPV was significantly higher in patients with psoriasis vulgaris than in the control group. Increased MPV shows the average size of platelets that is biologically more active. In previous studies, MPV in psoriasis was regarded, however with different results. Saleh et al. reported that there was no difference between psoriasis patient and MPV level according to control group[26]. Canpolat et al. found that significantly increased MPV level in psoriasis patients compared to healthy individuals and also found positive correlation with PASI[27]. For this reason, they mentioned that the activity of platelet is strongly related to the pathogenesis of psoriasis. Platelet activation is thought to be an important pathogenic factor in psoriasis. In an another way, some proinflammatory mediators stored in platelets are closely associated with pathogenesis of psoriasis[28]. The increased platelet activation and aggregation is regarded with MPV and PCT, which is related to reactive thrombocytosis and inflammation. In contrast, the decreased MPV and platelet count ratio, was mentioned that related to higher PLT along with relatively small platelets.

Psoriasis is associated with endothelial dysfunction, atherothrombotic diseases and dislipidemia. Dyslipidemia is well-described that confers adverse cardiovascular risk in patients with psoriasis. In our study, the mean value of TC, HDL, LDL, TG were not increased in patients with psoriasis, but TC, LDL, TG were higher than control groups. And TC, HDL, LDL, TG were not correlated with PASI. In contrast, some dyslipidemia studies in psoriasis patients have shown an association with PASI scores[29,30]. The differences may depend on the age of patient with psoriasis. The mean of age was lower in previous studies. And also, we excluded the comorbidities in psoriasis such as hepatic and renal disease, diabetes mellitus. It should effect the level of lipids in sera.

To the best of our knowledge, our study is the first that determines the predictive value of PCT in patients with psoriasis. The PCT cut off value for psoriasis in our study was 0.321. PCT value > 0.321 were seen as independent predictor of psoriasis. The diagnostic value of PCT should indice in the severity of the disease activity in psoriasis. It could also be highlighted that PCT is a noninvasive, easily available marker and so it can be used in predicting patients with psoriasis.

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Corresponding author
SUZAN DEMIR PEKTAS, Assistant Professor Dr.
Mugla Sitki Kocman University,
Faculty of Medicine, Department of Dermatology
Mugla 48000
(Turkey)