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Original Article

Evaluation of mean platelet volume, neutrophil/ lymphocyte ratio and platelet / lymphocyte ratio relationship with disease severity and metabolic syndrome in patients with psoriasis vulgaris

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Abstract

Aim: Psoriasis is one of the diseases caused by chronic inflammation. It is associated with a number of comorbidities (metabolic syndrome, cardiovascular disease, obesity, non-alcholic fatty liver...). Recently, mean platelet volume (MPV), neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) were found to be related to systemic inflammation. At the end of this study, the risk of metabolic syndrome in psoriasis will be evaluated and the effect of MPV, NLR, PLR levels will be determined on predicting metabolic comorbidities in psoriasis patients.

Material and Methods: This research was planned prospectively. The study consisted of 40 patients with psoriasis vulgaris and 40 healty control group which was similar in age and gender . Patients' informations were recorded and blood pressure, height, weight values were measured. Hemogram parameters, biochemistry values were determined.

Results: The count of neutrophiles was higher in the psoriasis; but disease severity and neutrophil count were not related each other. According to our study, MPV values, high density lipoprotein (HDL), fasting blood glucose and body mass index (BMI) were meaningful findings in estimating the development of metabolic syndrome.

Conclusion: The use of neutrophil activation markers in addition to neutrophil count in patients with psoriasis may be useful in determining disease severity and activation. In the follow-up of patients with psoriasis, fasting glucose, HDL, BMI value and MPV can help predicting possibility of metabolic syndrome and cardiovascular diseases that may develop in these patients.

Keywords: Metabolic syndrome; neutrophil; platelet; psoriasis

INTRODUCTION

Psoriasis occurs as a result of immune-mediated genetic factors (1). In addition to genetic factors; external and internal triggers such as trauma, infections, drugs, endocrine and metabolic changes are responsible for its etiology and pathogenesis (2). According to our current knowledge, it is not only a cutaneous disease but also a systemic condition.

Psoriasis can affect many systems depending on the severity of inflammation. The best-known comorbidity of psoriasis is psoriatic arthritis. Other comorbidities include obesity, metabolic syndrome, cardiovascular-cerebrovascular diseases, non-alcoholic liver fatty, obstructive sleep apnea, migraine, malignancies, chronic kidney diseases, autoimmune diseases, chronic obstructive pulmonary disease, psychiatric problems (3). In particular, its relationship with cardiovascular disease and metabolic syndrome ,which consists of obesity, hyperlipidemia, diabetes mellitus, hypertension, is significant. Because it both shortens the expected life time and reduces the quality of life, patients should be informed and screened for these comorbidities from time to time.

Today, there are many markers that show systemic inflammatory response; however, there is a need for cost-effective biomarkers that are simple to access. MPV, NLR and PLR have recently become prominent as markers of systemic inflammation. In many studies, these

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parameters correlated with the prognosis of inflammatory diseases, cardiovascular diseases, malignancies (2-4) and inflammation severity in acne, psoriasis (5-7). For example, in the study conducted by Saraç et al. on urticaria, NLR was found to be significantly higher (8). The number and ratio of circulated leukocytes in blood, alter during the inflammatory response. In response to stress, the number of neutrophils increases, while the lymphocytes decrease (4). High MPV value is related to activate platelets. Increased MPV is an independent risk factor in diseases such as diabetes mellitus, hyperlipidemia, hypertension and acute myocardial infarction (9). But these hematological parameters were compared between patients with rosacea and the control group, but no significant difference was found (10).

We planned this article to assess the usability of hemogram parameters for screening metabolic syndrome in psoriasis. We also investigated comorbidities such as hyperlipidemia, hypertension, obesity, metabolic syndrome accompanying psoriasis. Furthermore, we analyzed that frequency of metabolic syndrome in psoriasis and control groups.

MATERIAL and METHODS

The participants in our study were selected from patients who applied to Mugla Sitki Kocman University Training and Research Hospital Dermatology outpatient clinic between 01.10.2017 and 01.02.2018. Fourty patients with psoriasis and fourty control groups which were similar to age and gender, were accepted to the study. Patients, who were defined as chronic plaque type psoriasis clinically or histopathologically, were included to the study. All patients were over 18 years old. These conditions were determined as exclusion criterias: a history of chronic disease (chronic liver disease, coronary artery disease, lung diseases, chronic kidney failure, connective tissue diseases), a history of malignancy, thyroid disease, active infection, pregnant women, smoking, alcohol users and patients who used systemic drugs in last 1 month before the study.

Patients who included in the control group were individuals over the age of 18. The selected person did not have an inflammatory disease or chronic disease, did not use cigarettes / alcohol, were not pregnant, and did not use medication in the last month.

Mugla Sitki Kocman University Clinical Research Ethics Committee approved this study. (date: 14.09. 2017, number: 2017/3). All contributors were told in detail about the study and their written consent was obtained.

The patients' age, gender, the age at which the disease first appeared, duration of the psoriasis, family history, nail and joint involvement, and the treatments they received before were recorded. Disease severity was determined using Psoriasis Area Severity Index (PASI) value. Platelet, lymphocyte and neutrophil counts, MPV, PDW, RDW values and fasting glucose, HDL and triglyceride levels were saved. NLR and PLR were obtained by the ratio of white blood cells to each other (NLR=neutrophil/lymphocyte, PLR=platelet/lymphocyte). Patients with metabolic syndrome were determined according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) -2001.

Metabolic Syndrome Diagnostic Criteria: abdominal obesity (waist circumference: > 102 cm for men, > 88 cm for women), hypertriglyceridemia (≥150 mg / dl), low HDL (< 40 mg / dl in men, < 50 mg / dl in women), hypertension (≥ 130 / 85 mmHg), hyperglycemia (fasting blood glucose ≥ 110 mg / dl).

Metabolic syndrome severity was divided into 3 groups depending on how many of the diagnostic criterias were carried: 3 criteria, 4 criteria and 5 criteria.

Statistical analysis

The dispersion of the data was analyzed with the Shapiro-Wilk test graphically. In comparison of continuous data, Student's t test (normally distributed data), Mann Whitney U test (non-normally distributed data) and chi-square test (categorical data) were utilized. The correlation between parameters was measured by Pearson and Spearman correlation tests. To predict the development of metabolic syndrome, it was made use of logistic regression analysis. When p value was less than 0.05, it was considered significant.

RESULTS

There were 80 participants in the study, 40 of them were psoriasis group and 40 of them were control group patients. The average age of the patients was 47.06 ± 13.74, the mean height was 168.70 ± 7.27 and the mean weight 74.76 ± 14.31.

It was found that the weight and BMI values were meaningfully higher in the psoriasis group than control group (p = 0.005 and p = 0.002). Accordingly, the number of obese patients was evidently higher in the psoriasis group (p = 0.032). Waist circumference, glucose levels, systolic and diastolic blood pressure were significantly higher in the psoriasis group (p <0.05), while HDL values were significantly lower than the control group (p <0.05) (Table 1).

Neutrophil values were found to be higher in the psoriasis group than the control group (p = 0.018). There was no significant difference between the groups in terms of other hemogram parameters (p>0.05) (Table 2).

In the psoriasis group, 19 patients (47.5%) had joint involvement and 29 patients (72.5%) had nail involvement. The average age at which the disease first appeared was 36.25 ± 12.48 years, disease duration was 10 (1-40) years, and PASI values were 5.75 (2-29.7) (Table 3).

When psoriasis patients were seperated into 3 groups according to disease severity (PASI <7, PASI 7-12, PASI > 12), there was no significant difference between the groups (p > 0.05). In the correlation analysis, no respectable correlation was found between PASI values and hematological parameters (p>0.05) (Table 4).

Table 1. Distribution of demographic and biochemical findings of the groups

	Psoriasis			Control			
		95% CI			95% CI		p
	Mean	SD	Min – Max	Mean	SD	Min - Max	
Age	48.98	13.90	44,53-53.42	45.15	13.48	40.84-49.46	0.215
Height	169.10	7.33	166.76-171.44	168.30	7.28	165.97-170.63	0.626
Weight	79.18	15.34	74.27-84.08	70.35	11.82	66.57-74.13	**0.005**
BMI	27.64	4.84	26.09-29.19	24.75	3.22	23.71-25.77	**0.002**
	n	%			n	%	p
Sex							
Woman	14	35.0			20	50.0	0.258
Man	26	65.0			20	50.0	
Obesity							
Normal	12	30.0			18	45.0	**0.032**
Overweight	16	40.0			19	47.5	
Obese	12	30.0			3	7.5	
Metabolic syndrom							
Yes	10	25.0			5	12.5	0.252
No	30	75.0			35	87.5	
	Median	Minimum	Maksimum	Median	Minimum	Maksimum	p
Waist circumference	90.50	61.00	126.00	78.00	63.00	118.00	**0.025**
Systolic	125.00	90.00	160.00	120.00	90.00	150.00	**0.018**
Diastolic	85.00	60.00	100.00	80.00	60.00	100.00	**0.010**
Glucose	100.00	77.00	142.00	91.50	69.00	150.00	**0.006**
HDL	45.00	28.00	105.00	53.00	34.00	100.00	**0.044**
Triglyceride	131.00	49.00	342.00	107.50	49.00	309.00	0.082

Table 2. Distribution of laboratory values

	Psoriasis				Control				
			95% CI				95% CI		p
	Mean	SD	Min	Max	Mean	SD	Min	Max	
Lymphocyte	2.51	0,91	2.22	2.80	2.25	0.61	2.05	2.44	0.130
Neutrophil	5.02	1.47	4.55	5.49	4.33	1.09	3.97	4.67	**0.018**
Platelet	267.95	60.06	248.74	287.16	267.38	63.09	247.20	287.55	0.967
N/L	2.27	1.17	1.90	2.65	2.07	0.84	1.80	2.33	0.364
P/L	122.24	62.12	102.37	142.11	128.16	46.38	113.32	142.99	0.631
MPV	10.85	0.97	10.54	11.16	10.93	1.09	10.57	11.27	0.763
PDW	13.46	2.20	12.75	14.16	13.47	2.37	12.70	14.22	0.996
RDW	41.72	3.42	40.62	42.81	40.89	3.05	39.911	41.86	0.255

N/L: Neutrophil/Lymphocyte, P/L: Platelet/ Lymphocyte, MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

When psoriasis patients were compared in terms of PASI values, no significant difference was found in demographic data at different PASI values (p > 0.05) . In the correlation analysis between clinical data and hematological data in psoriasis patients, a mild positive correlation was found between lymphocyte values and triglyceride values (Rho=0.359; p=0.023) .

Table 3. Distribution of clinical findings in psoriasis patients

	Psoriasis (n= 40)
Disease duration (years) Median (min-max)	10 (1 - 40)
PASI Median (min-max)	5.75 (2 – 29.7)
Nail Involvement (n)	29
Joint Involvement (n)	19
Age of onset (mean ± standard deviation)	36.25±12.48

Table 4. Correlation between PASI values and hematological parameters in psoriasis patients

		Lymphoyte	Neutrophil	Platelet	NL	PL	MCV	PDW	RDW
PASI	r	0.034	-0.046	-0.134	0.121	0.107	0.193	0.222	-0.161
	p	0.837	0.779	0.410	0.458	0.510	0.233	0.168	0.321

Patients with psoriasis were compared in terms of severity of the metabolic syndrome and there was no difference between hematological parameters and the degree of metabolic syndrome (p>0.05) . Metabolic syndrome was detected in 25% of patients with psoriasis (Table 5) .

Table 5. Distribution of psoriasis patients according to BMI and metabolic syndrome severity

		n	%
BMI	Normal	12	30.0
	Overweight	16	40.0
	Obese	12	30.0
Metabolic Syndrome Severity	3 criteria	3	30.0
	4 criteria	4	40.0
	5 criteria	3	30.0

The logistic regression analysis revealed that the most important factors in predicting the development of metabolic syndrome were BMI and HDL values. While a decrease of 1 unit in BMI values decreases the risk of developing metabolic syndrome by 48.5% (p=0.006), 1 unit decrease in HDL values increases the risk 1.2 times (p=0.045) (Table 6).

By removing the constant value from the regression equation, the effect on other factors was increased; logistic regression analysis was performed again. In this case, the most effective factors in predicting the development of metabolic syndrome were BMI , HDL , glucose and MPV values (p<0.05). A decrease of 1 unit in BMI values will decrease the risk of developing metabolic syndrome by 42.5% (p=0.005) and a decrease of 1 unit in glucose will decrease the risk of metabolic syndrome by 6.1% (p = 0.025). Increasing the risk by 3 times (p = 0.010), 1 unit increase in MPV values increases the risk by 3.6 times (p = 0.010) (Table 7).

Table 6. Logistic regression analysis results for factors that may be effective in predicting metabolic syndrome development

	B	S.E.	p	Exp (B)
PLR	-0.026	0.042	0.535	0.975
Age	0.158	0.158	0.317	1.171
NLR	-0.794	1.083	0.463	0.452
Sex	1.912	1.606	0.234	6.766
MPV	0.856	0.600	0.154	2.353
BMI	-0.664	0.241	**0.006**	0.515
HDL	-0.177	0.088	**0.045**	1.193
Triglycerid	-0.019	0.010	0.068	0.981
Glucose	-0.067	0.035	0.058	0.935
Psoriasis	165.162	5201.325	.975	5.356E+071
Fixed Value	23.590	9.272	0.011	17577701451.593

p<0.05 statistically significant, SE: Standard Error, Exp(B): Risk rate, PLR: Platelet to lymphocyte ratio, NLR: Neutrophil to lymphocyte ratio, MPV: Mean platelet volume, BMI: Body mass index, HDL: High density lipoprotein

Table 7. Logistic regression analysis results of factors that may be effective in predicting the development of metabolic syndrome (fixed value is not included in the equation)

	B	S.E.	p	Exp (B)
Age	0.047	0.102	0.645	1.048
NLR	-0.213	0.907	0.814	0.808
PLR	0.012	0.019	0.547	1.012
Sex	1.874	1.578	0.235	6.516
Triglycerid	-0.011	0.008	0.167	0.989
BMI	-0.553	0.197	**0.005**	0.575
HDL	-0.239	0.092	**0.010**	1.270
Glucose	-0.063	0.028	**0.025**	0.939
MPV	1.288	0.503	**0.010**	3.627
Psoriasis	200.683	5532.105	0.971	1.431E+087

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, BMI: Body mass index, HDL: High density lipoprotein, MPV: Mean platelet volume

DISCUSSION

Psoriasis, a chronic disease, is now known as a cytokine-mediated inflammatory disease (1). With the prominence of inflammation in psoriasis, their association with conditions with chronic inflammation has gained importance. There is a need for biomarkers that can easily be applied under polyclinic conditions to identify these conditions that will cause various morbidity.

NLR is an easily accessible inflammatory marker. In recent studies, it has been investigated in many diseases with inflammation (2-4). Besides it was found higher in the patient group than in control, it was also associated with prognosis in colorecral cancer (4). Also, in the study of Coimbra et al, neutrophil count was higher and lymphocyte count was lower in psoriasis (1). In our study, NLR was higher in the psoriasis group, but it was not statistically significant.

Increased platelet volume indicates the presence of reactive platelets in the circulation. MPV value may be helpful to assess platelet activation (9). There is an independent relationship between thrombosis susceptibility and platelet activation and inflammation, and there is a study in which it is evaluated as a cardiovascular risk marker (11). In our study, we found MPV as an effective factor in predicting metabolic syndrome development.

Metabolic syndrome and psoriasis share similar inflammatory and cytokine-mediated mechanisms. Changes in transcription in renin, CTLA4 and TLR3 gene in psoriasis and metabolic disorders have been described (12). In recent studies, it has shown that proinflammatory mediators locally produced in psoriasis, join the systemic circulation. And these cytokins lead to insulin resistance, endothelial dysfunction, hypercoagulability, oxidative stress and angiogenesis, so metabolic changes occur (13).

Sen et al. detected that patients with psoriasis had higher neutrophils (5.48 x 10^9 / L) and lower lymphocyte counts (2.3 x 10^9 / L) and higher NLR (2.71). When NLR ratio was checked against disease severity, it was seen that NLR value increased as PASI score increased (14). In patients treated with biological agents, there was a decrease in NLR and PLR values in parallel with the decrease in PASI (15; 16). We did not determine a relationship between disease severity and NLR in our study. In the retrospective study of Kim et al. in psoriasis, PDW and MPV values were higher in the group with psoriasis. While MPV value was found to be correlated with disease severity positively, it had no correlation between PDW and disease severity (15). In another study performed, both NLR and MPV were found to be higher in the psoriatic arthritis group compared to healthy controls (16). In the study of Chandrashekar et al., MPV and PDW were found relatively high in psoriasis group. While no relationship was observed between PDW and disease severity, it had a positive correlation with disease severity and MPV (17). In the light of these studies, platelet activation may be thought to increase in psoriasis pathogenesis. We did not observe any distinction between the groups in terms of MPV and PDW values.

Unlike most studies on this subject, we planned our study prospectively. As a result of the power analysis, we determined the number of samples required to obtain meaningful results as 32 people per group. We included 40 patients with psoriasis and the same number of healty control groups according to the criteria we have specified. We saw that the mean age of groups was similar in our study. We found that the average disease duration of patients with psoriasis was 10 years, and the average onset age was 36.2. We determined that the average PASI value of the patients was 5.75 (<7, mild severity).

When we compared the groups, we found that the neutrophil count was higher in psoriasis (psoriasis neutrophils: 5.02 x 10^9 / L, control neutrophils: 4.33 x 10^9 / L, p = 0.018). NLR and RDW values were higher in psoriasis; but we couldn't discover a remarkable difference between the groups.

In recent studies, RDW has been referred to be associated with cardiovascular risk and the prognosis of inflammatory illnessess like ankylosing spondylitis (18). In one of the studies performed to evaluate systemic inflammation in patients with vitiligo, RDW was determined to be significantly higher in vitiligo compared to controls (19). Kim et al. found that RDW was elevated in psoriasis compared to control group. And they were concluded that RDW increased as an indicator of chronic inflammation in psoriasis patients, but it was not a parameter indicating the severity of the disease (20). Based on these studies, we compared RDW values in our study, but we could not achieve a meaningful result. Perhaps in this result, it may be effective that our study consists of less sample groups.

When the neutrophil count was evaluated separately, it was was generally found to be higher in patients with psoriasis (14-21). Similarly, in our study, the count of neutrophils was meaningfully higher in psoriasis (psoriasis group's neutrophil: 5,02 x 10^3 /µl; control group's neutrophil: 4,33 x 10^3 /µl).

In a study made by Sommer et al., it was reported that metabolic syndrome was observed two times more in psoriasis patients (22). In our study, 25% of psoriasis group had metabolic syndrome, while 12.5% of the control group had metabolic syndrome.

In our study, 30% (n =12) of patients with psorasis were obese, while 7.5% (n =3) of the patients in the control group were obese. Also, patients with psoriasis had higher BMI and waist circumference than the control group. In our study, systolic and diastolic blood pressure was significantly higher in psoriasis than in the control.

Milčić et al. found that there was a positive correlation between psoriasis and type II DM prevalence, similar to many studies. They also stated that individuals with severe psoriasis had a bigger risk of developing DM (23). In our study, fasting blood glucose was higher in patients with psoriasis than in the control group and the mean triglyceride value of patients with psoriasis was 131, while the control group's triglyceride level was 107.5. HDL level was 45 in the psoriasis and 53 in the control . In many studies, it has been revealed that there is a relationship between psoriasis and atherogenic dyslipidemia (high total cholesterol, triglyceride, LDL, VLDL level; low HDL, apolipoprotein B level) (23). Some authors have determined that abnormalities in lipid metabolism of patients with psoriasis are genetically encoded (24).

When patients were compared according to the severity of metabolic syndrome, it was seen that as the severity of metabolic syndrome increased, NLR, PLR, MCV and PDW values increased; however, this increase was not statistically significant. Büyükkaya et al. compared 70 metabolic syndrome patients and 71 control groups and they showed that as the severity of metabolic syndrome increases, NLR increases (25). In other studies, the individuals carrying metabolic syndrome criterias and patients without metabolic syndrome were compared and it was observed that the number of leukocytes increased in patients with metabolic syndrome compared to control. In these studies, NLR was not related with metabolic syndrome (26). However, these studies are only studies on those with and without metabolic syndrome. In the literature, we could not find any studies on the evaluation of hemogram parameters with the severity of metabolic syndrome in patients with psoriasis.

In our article, the most effective factors in predicting the occur metabolic syndrome in psoriasis were BMI, HDL, glucose and MPV. According to our study, a 1-unit decrease in BMI reduces the risk of metabolic syndrome by 42.5% while a 1-unit decrease in glucose value decreases the risk of metabolic syndrome by 6.1%. 1 unit increase in HDL value decreases the risk by 1.3 times, while 1 unit increase in MPV increases the risk of metabolic syndrome by 3.6 times. More comprehensive studies are needed regarding the clinical importance of MPV in the prediction of the risk of developing metabolic syndrome in psoriasis and the role of activated platelets in psoriasis.

CONCLUSION

Metabolic syndrome is one of the well-known comorbidities of psoriasis. Therefore, psoriasis should be closely observed for the occurance of comorbidities. There is a need for objective, reliable, inexpensive, easily applicable laboratory parameters that can be useful in predicting disease severity and course in psoriasis. Parameters such as NLR, PLR, MPV, PDW, RDW obtained from hemogram are frequently used in the routine as a marker of chronic inflammation and cardiovascular risk. We researched the relationship between these parameters and metabolic syndrome in psoriasis. Especially, we found that MPV and HDL levels associated with metabolic syndrom in patients with psoriasis. This article is the first study on predicting metabolic syndrome which can develop in patients with psoriasis.

Competing interests: The authors declare that they have no competing interest.

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