RESEARCH ARTICLE / *Araştırma Makalesi*

Is There Any Association Between the Monocyte / Lymphocyte Ratio and the Presence and Severity of the Disease in Patients with Psoriasis?

Psöriyazis Hastalarında Monosit / Lenfosit Oranı ile Hastalığın Varlığı ve Şiddeti Arasında Bir İlişki Var Mıdır?

Nur Cihan Cosansu, Bahar Sevimli Dikicier, Mahizar Yaldız, Berna Solak

Sakarya University, Education and Research Hospital, Department of Dermatology

Yazışma Adresi / *Correspondence:*
Nur Cihan Cosansu

Department of Dermatology, Sakarya University, Education and Research Hospital Sakarya/Turkey, 54100
T: **+90 507 287 47 50** E-mail **: mimaroglu5@hotmail.com**

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Orcid :
Nur Cihan Cosansu https://orcid.org/0000-0001-6156-6380
Berna Solak https://orcid.org/0000-0002-1683-2421
Bahar Sevimli Dikicier https://orcid.org/0000-0002-1912-3946
Mahizar Yaldiz https://orcid.org/0000-0001-6981-457X

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Abstract

Objective	Patients with psoriasis have increased systemic inflammation and monocytes levels compared with the general population. However, the role of monocytes in modulating inflammation in these patients is not clearly known. Psoriasis patients, where inflammation plays a role, are also at risk for cardiovascular diseases. The monocyte-to-lymphocyte ratio (MLR) may reflect a systemic inflammatory status. The aim of this study was to investigate the usefulness of MLR in patients with psoriasis.
Materials and Methods	A total of 180 consecutive patients who had been routinely referred to psoriasis outpatient clinic,and 40 healthy individuals were included in our case-control study between January 2015, and January 2017. Demographic features, Psoriasis Area and Severity Index (PASI) scores,and laboratory data were collected from electronic database system.
Results	Patients with psoriasis had higher leukocyte, neutrophil, monocyte counts and MLR compared with control group (p=0.003, p<0.001, p=0.032, p<0.001, respectively). The PASI scores positively correlated with MLR (r=.244, p=0.001). The monocyte counts(p=0.004) and MLR (p<0.001) were significantly higher in the moderate-severe psoriasis group than in the mild psoriasis group. After adjusted for confounding factors,only MLR and body weight were found independently associated with moderate-severe psoriasis in multivariate regression analysis (p=0.005; p=0.037,respectively). The ROC analysis showed that MLR predicted moderate-severe psoriasis with a sensitivity of 84% and with a specificity of 56%, using a cut-off value of 0,192. The AUC (area under curve) was found 0.71(p<0.001).
Conclusion	The MLR, an inexpensive and easily measurable variable,is significantly associated with the presence and severity of psorisis. More comprehensive studies are needed to validate and elaborate this relationship.
Key Words	Inflammation ; monocyte ; lymphocyte ; psoriasis.

Abstract

Amaç	*Psöriyazis'li hastalar, genel popülasyona kıyasla artmış sistemik inflamasyon ve monosit seviyelerine sahiptir. Bununla birlikte, bu hastalarda monositlerin enflamasyonu modüle etmedeki rolü açıkça bilinmemektedir. Enflamasyonun rol oynadığı psöriyazis hastaları kardiyovasküler hastalıklar içinde risk altındadır. Monosit-lenfosit oranı (MLO) sistemik bir enflamatuar durumu yansıtabilir. Bu çalışmanın amacı psöriyazis hastalarında MLO'nın yararlılığını araştırmaktır.*
Gereç ve Yöntemler	*Vaka-kontrol çalışmamıza Ocak 2015 ile Ocak 2017 arasında psöriyazis polikliniğine rutin olarak yönlendirilen toplam 180 ardışık hasta ve 40 sağlıklı birey dahil edildi. Demografik özellikler, Psöriyazis Alan ve Şiddet İndeksi (PASI) skorları ve laboratuvar verileri elektronik veri tabanı sisteminden toplandı.*
Bulgular	*Psöriyazis hastalarında kontrol grubuna kıyasla daha yüksek lökosit, nötrofil, monosit sayısı ve MLO vardı (sırasıyla p = 0.003, p <0.001, p = 0.032, p<0.001). PASI skorları MLO ile pozitif korelasyon gösterdi (r = .244, p = 0.001). Monosit sayıları (p = 0.004) ve MLO (p <0.001) orta-şiddetli psöriyazis grubunda hafif psöriyazis grubuna göre anlamlı derecede yüksekti. Karıştırıcı faktörler ayarlandıktan sonra, çok değişkenli regresyon analizinde sadece MLO ve vücut ağırlığının orta-şiddetli psöriyazis hastalığı ile bağımsız ilişkili olduğu bulunmuştur (sırasıyla p = 0.005; p = 0.037). ROC analizi, MLO'nın 0,192'lik bir cut-off değeri kullanılarak %84 sensitivite ve %56 spesifite ile orta-şiddetli psöriyazisi öngördüğünü gösterdi. EAA (eğrinin altındaki alan) 0.71 (p<0.001) bulundu.*
Sonuç	*Ucuz ve kolayca ölçülebilen bir değişken olan MLO, psöriyazis varlığı ve ciddiyeti ile önemli ölçüde ilişkilidir. Bu ilişkiyi doğrulamak ve detaylandırmak için daha kapsamlı çalışmalara ihtiyaç vardır.*
Anahtar Kelimeler	*inflamasyon; monosit ; lenfosit ; psöriyazis*

INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory skin disease which affects 1–2% of the global population.[1] It is important to determine the severity of the disease for appropriate, safe and effective treatment in psoriasis patients. However, evaluation of the severity of psoriasis is complex and, unfortunately there is no single tool that can evaluate every aspect.[2] One of the most commonly used scales in identifying psoriasis severity is the Psoriasis Area Severity Index (PASI).[3] PASI score is based on the intensity of redness, thickness, and scaling of the representative lesions, and it ranges from 0 to 72. According to the European S3 guidelines on the systemic treatment of psoriasis vulgaris, moderate-to-severe disease is defined as a PASI score >10.[4] However, PASI is limited due to the high degree of variation between clinicians, a lack of objective evaluation criteria, and insufficient evaluation of chronic microvascular inflammatory conditions underlying the disease. Disease activity has been evaluated in patients with psoriasis by measuring cytokines, adhesion molecules, and parameters used in routine blood tests such as C-reactive protein (CRP).[5-7] In patients with systemic and chronic psoriasis, new parameters are necessary for evaluating systemic inflammation.

The role of monocytes in psoriasis is not completely clear. Recent studies suggested the role of CD14+ and CD16+ monocytes in the pathogenesis of psoriasis. Monocytes is increased in patients with psoriasis, suggesting their important role in the disease.[8] Monocyte-to lymphocyte ratio (MLR) can be derived from white blood cell count, and is a low-cost, effective, and readily available new marker. MLR has recently been used as new indicator of systemic inflammation, morbidity, and mortality.[9-11] Inflammation influences the development and progression of coronary atherosclerosis.[12] Psoriasis patients, where inflammation plays a role, are at risk for cardiovascular diseases.[13]

To the best of our knowledge, the relation among psoriasis and the MLR has not been studied. The aim of this study was to compare MLR between patients with psoriasis and healthy volunteers, and examines the relationship between PASI and MLR for the assessment of disease severity.

MATERIALS and METHODS

Study design, settings and ethics

This was a case-control, single-center study. The current study included 180 consecutive patients (103 females, 77 males) who were diagnosed with plaque-type psoriasis and followed by dermatology outpatient clinic in Sakarya University Education and Research Hospital, Sakarya, Turkey between January 1, 2015, and January 1, 2017. Fourty healty individuals (23 females, 17 males) without any systemic and/or any dermatological disease was also included consecutively in the study as control group. Patients, who did not receive systemic treatment for psoriasis during the previous 3 months were included in the study. The patients who had an another inflammatory, autoimmune or active infectious diseases, malignancy or pregnancy were excluded from the study. Clinical features, demographic features, and comorbidities were also recorded from patient charts. Complete blood count parameters (CBC) and CRP levels were recorded retrospectively. MLR (was calculated as the monocyte count divided by the lymhocyte count) was obtained from the CBC results. According to observations from clinical practice, physicians on the expert panel strongly agreed that psoriasis should be classified into two categories: mild and moderate-to-severe.[14] In the current study, patients with PASI> 10 were taken as moderate to severe, and ≤ 10 were taken as mild psoriasis. The study was approved by Sakarya University Education and Research Hospital Ethics Committee (02/10/2019, E.12307).

Statistical analysis

For the statistical analysis, the Statistical Package for the Social Sciences (SPSS), version 16.0 for Windows (SPSS Inc., Chicago, IL) was used. Continuous data were expressed as mean ± standard deviation, and the categorical data were expressed as percentages. The normal distribution of the data was assessed by the Kolmogorov–Smirnov

test. Comparisons between groups were performed using a chi-square or Fisher's exact tests for qualitative variables, as appropriate. An independent t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was conducted for non-normally distributed continuous variables, as appropriate. A receiver operating characteristic curve (ROC) was plotted in the psoriasis group to analyse the predictive capacity of MLR to determine optimal cut-off points for moderate-severe disease activity. The variables with a p<.10 in the univariate analysis were included in the multivariate logistic regression analysis to evaluate MLR's relation with moderate-severe disease activity measured by PACI. Statistical significance was described as p< 0.05.

RESULTS

A total of 180 patients diagnosed with chronic plaque-type psoriasis (77 males, 103 females; mean age: 41.7 ± 14.0 years old) and 40 healthy control subjects (17 males, 23 females; mean age: 43.8 ± 12.7 years old) were included in this study. Demographic features and comorbid conditions of patients with psoriasis and healthy controls are shown in Table 1.

Table 1. Baseline demographics and clinical characteristics of patients with psoriasis and healthy controls.

Variables	Psoriasis (n=180)	Healthy Controls (n=40)	p-value
Age, years	41.7 ± 14.0	43.8 ± 12.7	0.379
Gender (Male), n (%)	77 (42.8)	17 (42.5)	0.975
PASI	7.7 ± 6.8	-	-
Diabetes mellitus, n (%)	10 (5.7)	-	-
Hypertension, n (%)	28 (15.9)	-	-
Body Height	166.5 ± 8.6	166.7 ± 9.9	0.875
Body Weight	76.3 ± 15.1	71.2 ± 13.8	0.059
Glucose, mg/dL	103.6 ± 35.2	92.4 ± 16.4	0.055
Triglycerides, mg/dL	143.9 ± 76.9	142.0 ± 119.8	0.924
LDL, mg/dL	128.1 ± 36.2	121.7 ± 42.7	0.341
HDL, mg/dL	45.4 ± 12.1	48.7 ± 10.4	0.122
CRP, mg/L	7.8 ± 2.9	4.2 ± 1.6	0.451
eGFR, mL/min/1.73 m2	106.5 ± 25.4	101.5 ± 14.0	0.093

Data presented as mean ± standard deviation or number (%). PASI, Psoriasis Area Severity Index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate.

There was no difference between the patient and the control group in terms of age and gender. Moreover, there was no statistically significant difference in terms of other demographic features and blood parameters between the patient and control group. The mean disease duration was 154.5 ± 114.9 months among the psoriasis patients.

Comparation of complete blood count data, leukocyte subgroup values, and MLR results are presented in Table 2. There was a statistically significant difference in terms of leukocyte, neutrophil, and monocyte between the psoriasis and control group (p = 0.003, p <0.001, p = 0.032, respectively). The MLR was significantly higher in patients with psoriasis than in controls (p <0.001). The difference between the MLR values of the groups originated from the difference between the monocyte counts of the groups. There was no significant difference in lymphocyte counts between groups.

Table 2. Complete blood count parameters of patients with psoriasis and healthy controls.

Variables	Psoriasis (n=180)	Healthy Controls (n=40)	p-value
WBC, (10^9/l)	7.92 ± 2.23	7.05 ± 1.48	**0.003**
Neutrophils, (10^9/l)	4.80 ± 1.76	3.83 ± 0.98	**<0.001**
Lymphocytes, (10^9/l)	2.36 ± 0.76	2.49 ± 0.65	0.314
Hemoglobin, (g/dl)	13.75 ± 1.69	13.97 ± 1.69	0.442
Platelet, (10^9/l)	272.32 ± 66.66	275.38 ± 68.15	0.795
Eosinophil, (10^9/l)	0.18 ± 0.16	0.19 ± 0.15	0.732
Monocyte, (10^9/l)	0.53 ± 0.18	0.47 ± 0.14	**0.032**
MLR	0.25± 0.14	0.19 ± 0.05	**<0.001**

Data presented as mean ± standard deviation. WBC, white blood cell count; MLR, monocyte-to lymphocyte ratio.

The severity of disease was determined using the PASI values in patients with psoriasis. The mean PASI was 7.7 ± 6.8. When the association between PACI score and CBC parameters was investigated in Pearson correlation analysis, a significant correlation was found only between PACI scores and monocyte and lymphocyte counts (r = .245, p = 0.001; r = -.152, p = 0.042, respectively). Moreover, the PASI score showed a significant correlation with MLR (r = .244, p = 0.001) (Table 3). When the patient group

with psoriasis was divided into two subgroups according to PACI scores as mild disease or moderate-severe disease and compared in terms of CBC parameters, and MLR; there was no significant difference between groups according to these parameters (p> 0.05), except monocyte counts (0.50 ± 0.18 vs 0.60 ± 0.17; p= 0.004) and MLR (0.23 ± 0.13 vs 0.31 ± 0.15; p <0.001) (Table 4).

Table 3. Correlation analysis of PASI score and blood count parameters and MLR

		PASI
WBC	**r**	.048
	p	0.528
Neutrophils	**r**	.107
	p	0.155
Lymphocytes	**r**	**-.152***
	p	**0.042**
Hemoglobin	**r**	.042
	p	0.577
Platelet	**r**	-.066
	p	0.377
Eosinophil	**r**	-.078
	p	0.297
Monocyte	**r**	**.245****
	p	**0.001**
MLR	**r**	**.244****
	p	**0 .001**

PASI, Psoriasis Area Severity Index; MLR, monocyte-to lymphocyte ratio; WBC, white blood cell count.

Table 4. Comparison of blood count parameters in patients with mild and moderate-severe psoriasis

Variables	Mild Psoriasis (n=135)	Moderate-severe Psoriasis (n=45)	p-value
WBC, (10^9/l)	7.88 ± 2.32	8.03 ± 1.96	0.488
Neutrophils, (10^9/l)	4.71 ± 1.81	5.07 ± 1.59	0.101
Lymphocytes, (10^9/l)	2.43 ± 0.78	2.15 ± 0.69	0.053
Hemoglobin, (g/dl)	13.65 ± 1.68	14.02 ± 1.70	0.215
Platelet, (10^9/l)	275.30 ± 68.03	263.47 ± 62.30	0.199
Eosinophil, (10^9/l)	0.19 ± 0.18	0.16 ± 0.11	0.577
Monocyte, (10^9/l)	0.50 ± 0.18	0.60 ± 0.17	**0.004**
MLR	0.23± 0.13	0.31 ± 0.15	**<0.001**

Data presented as mean ± standard deviation. WBC, white blood cell count; MLR, monocyte-to lymphocyte ratio.

MLR, body weight, CRP and neutrophil count were found to be in relation with moderate-severe psoriasis in univariate logistic regression analysis (p: 0.047, p: 0.043, p: 0.019, p: 0.021, respectively). However, when adjusted for confounding factors, only MLR and body weight were found independently associated with moderate-severe psoriasis in multivariate regression analysis (B: 141.53; 95% CI: 4.60 to 4346.98, p: 0.005; B: 1.03; 95% CI: 1.00 to 1.06, p: 0.037, respectively). The ROC analysis showed that MLR predicted moderate-severe psoriasis with a sensitivity of 84% and with a specificity of 56%, using a cut-off value of 0,192. The AUC (area under the curve) for the MLR was found 0.71 (95% CI, 0.62-0.79; p <0.001) (Figure 1).

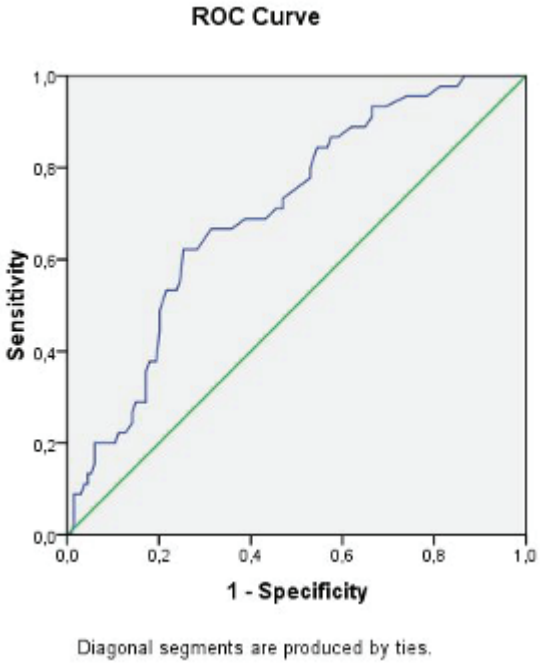

Figure 1. ROC curve of, monocyte-to lymphocyte ratio (MLR) for the prediction of moderate-severe psoriasis.

DISCUSSION

To the best of our knowledge, this was the first study to analyze the relationship between psoriasis and MLR. The present study demonstrate that leukocyte, neutrophil, monocyte counts and MLR increase in patients with psoriasis than the control group. In addition, PASI score showed

a significant correlation with MLR. Moreover, monocyte and MLR levels were significantly higher in patients with moderate-severe psoriasis compared with the mild psoriasis group. The results also revealed that MLR and body weight are a significant indicators for moderate-severe psoriasis.

Psoriasis is a common, inflammatory immune-mediated skin disease, and mainly presenting with plaques.[15] The underlying pathomechanisms involve complex interaction between the innate and adaptive immune system. Psoriasis leads to sustained inflammation and epidermal hyperplasia, ultimately resulting in the formation and persistence of lesions.[16] The macrophages were upregulated in dermal and epidermal layers of lesional skin in patients with psoriasis.[17]

Monocytes are the cornerstones of the immune system and critical drivers of inflammatory reactions.[18] A recent study revealed that a high percentage of circulating monocytes is present in patients with psoriasis, and the frequency of those cells correlated with disease severity.[19] Moreover, there is a relationship between psoriasis and cardiovascular diseases, in which monocytes play an important role in angiogenesis and atherosclerosis.[20,21] In the present study, monocyte counts was found to be higher in patients with psoriasis than the control group. In addition, monocyte counts was significantly higher in patients with moderate-severe psoriasis compared with the mild psoriasis group.

MLR or LMR (lymphocyte to monocyte ratio), which can be easily calculated from the peripheral blood, has been demonstrated as new expression of the systemic inflammatory indicator that can help in the diagnosis and evaluation of disease severity in many diseases, such as Behçet's disease and cancer.[22-24] Jiang et al found lower LMR levels in patients with Behçet's disease (BD) than in healthy controls, and found negatively correlation between the severity score and LMR levels. Moreover, LMR was found independent factor for BD by multivariate logistic analysis.[24] High monocytes and low lymphocytes were also confirmed to be independent risk indicators of cardiovascular diseases.[25] Therefore, the MLR could be used as a marker of coronary atherosclerosis. The main pathophysiological links between MLR and psoriasis can be endothelial dysfunction and inflammation. Inflammation in patients with psoriasis leads to monocyte secretion and aggregation.[19] Increased MLR is associated with systemic inflammation, and it is defined as a novel inflammation-based marker in cardiovascular diseases. Fan et al's study suggested that the MLR could be used to identify the vulnerable plaques in stable angina.[26] Moreover, Murat et al showed an inverse association between the LMR and bare-metal stent restenosis in patients with stable coronary artery disease.[11] In addition, the LMR has been found to be associated with in-hospital and long-term major adverse cardiac and cerebrovascular events in patients with ST-elevation myocardial infarction.[27] In our study, concordant with previous studies on cardiovascular disease, increased MLR was found to be related with the presence and severity of psoriasis, in whose pathophysiology inflammation plays a significant role.

Limitations

The present study had several potential limitations. Firstly, the data were obtained from only a single center; therefore, patient selection bias was not completely avoided. Secondly, this study was designed as a retrospective study. Thirdly, we did not explore the influence of treatment on these serum inflammatory parameters due to insufficient data.

CONCLUSIONS

To the best of our knowledge, this is the first report on the relationship between MLR and psoriasis. Based on the results of the present study, it can be suggested that assessment of MLR in psoriasis may provide additional information about inflammation. Also, the present study has demonstrated that there was association between MLR and disease activity in psoriasis. Moreover, MLR is an inexpensive and easily measurable laboratory variable that could

be used as a novel risk marker of cardiovascular disease in patients with psoriasis. Further controlled studies comprising a greater number of patients are needed to evaluate this relationship in more detail, and to validate the clinical value of MLR in psoriasis.

The study was approved by Sakarya University Education and Research Hospital Ethics Committee (02/10/2019, E.12307).

Kaynaklar

1. *Christophers E. Psoriasis–epidemiology and clinical spectrum. Clin Exp Dermatol 2001; 26: 314– 320.*
2. *Paul C, Gourraud PA, Bronsard V, Prey S, Puzenat E, Aractingi S, et al. Evidencebased recommendations to assess psoriasis severity: systematic literatüre review and expert opinion of a panel of dermatologists. J Eur Acad Dermatol Venereol 2010; 24:2–9.*
3. *Schmitt J, Wozel G. The Psoriasis Area and Severity Index is the adequate criterion to define severity in chronic plaque-type psoriasis. Dermatology 2005; 210:194–9.*
4. *Pathirana D, Ormerod AD, Saiag P, Smith C, Spuls PI, Nast A, et al. European S3-guidelines on the systemic treatment of psoriasis vulgaris. J Eur Acad Dermatol Venereol 2009;23 Suppl 2:1–70.*
5. *Uysal S, Yılmaz FM, Karatoprak K, Artüz F, Cumbul NU. The levels of serum pentraxin3, CRP, fetuin-A, and insulin in patients with psoriasis. Eur Rev for Med Pharmocol Sci 2014; 18:3453–8.*
6. *Dowlatsahi EA, van der Voort EA, Arends LR, Nijsten T. Markers of systemic inflammation in psoriasis: a systematic review and meta-analysis. Br J Dermatol 2013; 169:266–82.*
7. *Beygi S, Lajevardi V, Abedini R. C-reactive in psoriasis: a review of the literature. J Eur Acad Dermatol Venereol 2014; 28:700–11.*
8. *Fujisawa T, Murase K, Kanoh H, Takemura M, Ohnishi H, Seishima M, et al. Adsorptive depletion of CD14(+), CD16(+) proinflammatory monocyte phenotype in patients with generalized pustular psoriasis: clinical efficacy and effects on cytokines. Ther Apher Dial 2012; 16: 436– 444.*
9. *Han, LH, Jia, YB, Song, QX. Prognostic significance of preoperative lymphocyte-monocyte ratio in patients with resectable esophageal squamous cell carcinoma. Asian Pac J Cancer Prev 2015; 16: 2245–2250.*
10. *Ferro, M, Musi, G, Serino. A. Neutrophil, platelets, and eosinophil to lymphocyte ratios predict gleason score upgrading in low-risk prostate cancer patients. Urol Int 2019; 102: 43–50.*
11. *Murat, SN, Yarlioglues, M, Celik, IE. The relationship between lymphocyte-to-monocyte ratio and bare-metal stent in-stent restenosis in patients with stable coronary artery disease. Clin Appl Thromb Hemost 2017; 23: 235–240.*
12. *Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005; 352:1685-95.*
13. *Jindal S, Jindal N. Psoriasis and Cardiovascular Diseases: A Literature Review to Determine the Causal Relationship. Cureus 2018 Feb; 10(2): e2195.*
14. *Daudén E, Puig L, Ferrándiz C, Sánchez-Carazo JL, Hernanz-Hermosa JM. Consensus document on the evaluation andtreatment of moderate-to-severe psoriasis: Psoriasis Group ofthe Spanish Academy of Dermatology and Venereology. J EurAcad Dermatol Venereol 2016; 30 Suppl 2:1-18.*
15. *Boehncke, W.H.; Schon, M.P. Psoriasis. Lancet 2015, 386, 983–994.*
16. *K.E. Nograles, B. Davidovici, J.G. Krueger. New insights in the immunologic basis of psoriasis. Semin Cutan Med Surg 2010; 29(1): 3-9.*
17. *Wang Y, Edelmayer R, Wetter J, Salte K, Gauvin D, Leys L, et al. Monocytes/Macrophages play a pathogenic role in IL-23 mediated psoriasis-like skin inflammation. Sci Rep 2019 Mar 29;9(1):5310.*
18. *A.M. Zawada, K.S. Rogacev, B. Rotter, P. Winter, R.R. Marell, D. Fliser, et al., SuperSAGE evidence for CD14++CD16+ monocytes as a third monocyte subset, Blood 118 (2011) e50–e61.*
19. *J.B. Golden, S.G. Groft, M.V. Squeri, S.M. Debanne, N.L. Ward, T.S. McCormick, et al. Chronic psoriatic skin inflammation leads to increased monocyte adhesion and aggregation, J. Immunol 195 (2015) 2006–2018.*
20. *M. Augustin, J. Vietri, H. Tian, I. Gilloteau. Incremental burden of cardiovascular comorbidity and psoriatic arthritis among adults with moderate-to-severe psoriasis in five European countries, J. Eur. Acad. Dermatol. Venereol 2017; 31 (8): 1316–1323.*
21. *K.S. Rogacev, S. Seiler, A.M. Zawada, B. Reichart, E. Herath, D. Roth, et al. CD14++CD16+ monocytes and cardiovascular outcome in patients with chronic kidney disease, Eur. Heart J 2011; 32: 84–92.*
22. *J. Xiang, Zhou L, Li X, Bao W, Chen T, Xi X, et al. Preoperative monocyte-to-lymphocyte ratio in peripheral blood predicts stages, metastasis, and histological grades in patients with ovarian cancer, Transl Oncol 10 (1) (2017) 33–39.*
23. *S. Song, C. Li, S. Li, H. Gao, X. Lan, Y. Xue, et al. Derived neutrophils to lymphocyte ratio and monocyte to lymphocyte ratio may be better biomarkers for predicting overall survival of patients with advanced gastric cancer, Onco Targets Ther 10 (2017) 3145–3154.*
24. *Y. Jiang, Zang M, Li S. Serum PLR and LMR in Behçet's disease: can they show the disease activity? Medicine (Baltimore) 2017 May; 96(21): e6981.*
25. *Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005;45: 1638–43.*
26. *Fan Z, Ji H, Li Y, Jian X, Li L, Liu T. Relationship between monocyte-to-lymphocyte ratio and coronary plaque vulnerability in patients with stable angina. Biomark Med 2017; 11: 979-990.*
27. *Kiris T, Çelik A, Variş E, Akan E, Akyildiz ZI, Karaca M, et al. Association of lymphocyte-to-monocyte ratio with the mortality in patients with ST-elevation myocardial infarction who underwent primary percutaneous coronary intervention. Angiology 2017; 68: 707-715.*