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Evaluation of monocyte to high-density lipoprotein cholesterol ratio and other inflammatory markers in hidradenitis suppurativa: a case-control study

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ABSTRACT

Aims: Hidradenitis suppurativa (HS) is an inflammatory disease whose pathophysiology is not yet clearly known, but inflammatory parameters have been used for many years in the diagnosis and follow-up. The aim of this study is to evaluate NLR, PLR, MHR, and hemogram parameters in patients diagnosed with HS without comorbidities and compare them with healthy controls.

Methods: This study include 105 HS patients and 100 healthy volunteers. The medical records and laboratory findings of the participants were reviewed retrospectively. Patients and control group neutrophils, lymphocytes, monocytes, platelets, mean platelet volume (MPV), platelet distribution width (PDW), red cell distribution width coefficient of variation (RDW-CV), high-density lipoprotein cholesterol (HDL-C), C-reactive protein (CRP), Neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), platelet-lymphocyte ratio (PLR), and MHR were compared.

Results: A total of 105 patients [43 (41%) women and 62 (59%) men] and one hundred healthy volunteers [52 (52%) women and 48 (48%) men] participated in the study. The mean of neutrophil count (patient group=5.84±2.27, control group=4.29±1.81, p=0.001), lymphocyte count (patient group=2.78±0.90, control group=2.31±0.63, p=0.001), monocyte count (patient group=0.74±0.39, control group=0.55±0.16, p=0.001), platelet count (patient group=295.63±65.84, control group=274.45±59.06, p=0.007), CRP (patient group=12.71±24.38, control group=2.61±2.21, p=0.039), and MHR (patient group=0.0203±0.0135, control group=0.0114±0.0056, p=0.001) were higher in the patient whereas the mean of HDL-C (patient group=39.02±11.06, control group=52.85±16.46, p=0.001) and PLR (patient group=118.82±60.82, control group=126.07±39.13, p=0.028) were significantly higher in control individuals. The adjusted effect of MHR, NLR, and PLR was re-examined to eliminate the effect that may arise from the difference in age between patients and controls. It was observed that when MHR increased by 0.01 unit, the risk of disease increased significantly by 4.07 times. When NLR increases by 1 unit, the disease increased. significantly by 1.37 times. Both adjusted and unadjusted effects of MHR were significant. When the sensitivity and specificity of MHR, and NLR in differentiating patients were examined, the sensitivity of MHR was found to be 67.4% and its specificity was 72.5% (p=0.001), while the sensitivity of NLR was found to be 61.5% and its specificity was 74.0% (p=0.038).

Conclusions: Our study showed that MHR was more effective in distinguishing HS patients than other inflammatory markers. MHR can be used as a new marker to investigate the inflammatory effect of HS.

Keywords: Hidradenitis suppurativa, hematologic tests, monocytes, cholesterol HDL

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, inflammatory disease that progresses with abscesses, fistulas, and scar formation.[1] Although etiopathogenesis is not clearly known, the principal pathophysiological mechanism of HS is folliculosebaceous units' occlusion and rupturation and excessive immune reaction.[2] HS can occur with many important comorbidities, including metabolic, cardiovascular, endocrine, gastrointestinal, rheumatological, and psychiatric disorders.[3]

Diagnosis is made based on the clinical morphology of the lesions (nodules, abscesses, tunnels and scars), location (axilla, inframammary folds, groin, perigenital or perineal) and progression of the lesion (2 recurrences within 6 months or chronic or permanent lesions lasting ≥3 months).[4]

Counts of leukocytes, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) are well-known markers of inflammation and have been used in the diagnosis and follow-up of HS for years.[5]

Recent studies suggested that neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), mean platelet volume (MPV), and plateletcrit (PCT) are used as indicators of inflammation and severity of inflammatory diseases such as HS, psoriasis, psoriatic

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arthritis.[6,7] Monocytes are sources of oxidative stress and proinflammatory cytokines. High-density lipoprotein cholesterol (HDL-C) has protective activities against inflammation and oxidation by preventing low-density lipoprotein cholesterol's (LDL-C) oxidation and endothelium damage. Many studies have reported that the monocyte/HDL-C ratio (MHR) may be an effective biomarker of systemic inflammation and oxidative stress. Therefore, monocyte-lymphocyte ratio (MLR) has been found to be an indicator of inflammation and prognosis in autoimmune diseases. These markers are used as an inflammatory and prognostic marker in many autoimmunity, metabolic syndrome, cardiovascular diseases, and cancer.[8,9] There are only a few studies investigating the relationship between MHR and HS.[10]

In this research, we aimed to investigate the interrelation of HS with CBC parameters and inflammatory indicator parameters NLR, PLR, and MHR.

METHODS

The study was carried out with the permission of Erzurum Regional Training and Research Hospital Clinical Researches Ethics Committee (Date: 06.06.2022, Decision No: 2022/07-88). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients with HS who were consulted at Erzurum Regional Training and Research Hospital Dermatology outpatient clinic between January 2019 and January 2021 were included in our retrospective study. All patients who presented to our clinic were diagnosed with HS and were retrospectively reviewed. In total, 105 patients satisfying the following inclusion criteria were included: diagnosed with HS by a dermatologist, had complete blood count analysis results during follow-up, did not have any systemic and/or chronic inflammatory diseases (e.g., cardiac diseases, diabetes mellitus, hypertension, hyperlipidemia, and rheumatoid arthritis). The control group consisted of 100 completely healthy volunteers (without known systemic and/or inflammatory disease, non-smoker, acne vulgaris or chronic dermatological disease, and not using regular medication). The participant's hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width coefficient of variation (RDW-CV), white blood cells (WBCs), neutrophils, lymphocytes, monocyte, platelet distribution width (PDW), platelets, MPV, HDL-C, and CRP were recorded. NLR, PLR, MLR, and MHR were determined. In addition, the comparison results of the two groups in terms of hemogram measurements and measurements calculated with formulas are given, and unadjusted effects are without adjusting for the age difference of the groups.

Statistical Analysis

Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA, v21.0) software was used in all procedures. Normality distribution of scale variables was calculated using Kolmogorov-Smirnov test and continuous parameters were compared with Kruskal-Wallis H and/or Mann-Whitney U tests. Independent categorical variables were compared with Pearson chi-square or Fisher tests. If significant results were found in more than two comparisons, Bonferroni correction was applied post-hoc. The success of measurements that showed significant differences between the two groups in separating the groups was examined with the ROC (Receiver Operating Characteristic) curve and a cutoff for these measurements was determined. $P < 0.05$ was considered significant.

RESULTS

One hundred five patients [43 (41%) women and 62 (59%) men] and one hundred healthy volunteers [52 (52%) women and 48 (48%) men] participated in this study. The gender distribution of healthy participants was similar to the patients (p=0.113). The mean age of the patients was 33.25±11.84, and the mean age of the control group was 26.53±5.81. The mean age of the patient group was significantly higher (p=0.001).

As shown in Table 1, the mean of neutrophil count (patient group=5.84±2.27, control group=4.29±1.81, p=0.001), lymphocyte count (patient group=2.78±0.90, control group=2.31±0.63, p=0.001), monocyte count (patient group=0.74±0.39, control group=0.55±0.16, p=0.001), platelet count (patient group=295.63±65.84, control group=274.45±59.06, p=0.007), CRP (patient group=12.71±24.38, control group=2.61±2.21, p=0.039), and MHR (patient group=0.0203±0.0135, control group=0.0114±0.0056, p=0.001) were higher in the patient whereas the mean of HDL-C (patient group=39.02±11.06, control group=52.85±16.46, p=0.001) and PLR (patient group=118.82±60.82, control group=126.07±39.13, p=0.028) were significantly higher in control individuals.

According to Table 1, when the success of MHR, and PLR, which had a significant adjusted effect, in separating patients, was examined; the appropriate cutoff value for MHR was found to be 0.0139, and when those greater than this value were classified as patients, the sensitivity was 71.0% and the specificity was 74%. The ROC curve of MHR is observed in Figure 1.

The appropriate cutoff value for PLR was found to be 112.5, and when those greater than this value were classified as control, the sensitivity was 57% and the specificity was 63%. The ROC curve of the PLR is observed in Figure 2.

Table 1: Comparison of laboratory parameters HS patients separately with the healthy control group

	Grup	N	Mean	SD	Percentiles			P*
					25	Median	75	
Hb (g/dl)	Control Patients	100 104	14.74 15.05	1.42 1.65	13.70 14.00	14.70 15.00	15.90 16.00	0.112
MPV (fl)	Control Patients	99 103	10.15 10.12	1.14 0.83	9.40 9.60	10.20 10.00	10.90 10.80	0.568
Neutrophil (10^9/l)	Control Patients	100 104	4.29 5.84	1.81 2.27	3.31 3.97	3.90 5.55	4.86 6.69	0.001
Lymphocyte (10^9/l)	Control Patients	100 104	2.31 2.78	0.63 0.90	1.88 2.10	2.19 2.70	2.70 3.37	0.001
Monocytes (10^9/l)	Control Patients	100 104	0.55 0.74	0.16 0.39	0.43 0.53	0.54 0.70	0.63 0.89	0.001
Platelet (10^9/l)	Control Patients	100 104	274.45 295.63	59.06 65.84	231.00 252.75	265.50 292.50	314.75 338.75	0.007
CRP (mg/l)	Control Patients	42 55	2.61 12.71	2.21 24.38	0.50 1.20	3.00 3.00	3.16 8.00	0.039
HDL (mg/dl)	Control Patients	46 62	52.85 39.02	16.46 11.06	39.25 30.75	50.50 36..0	62.25 46.00	0.001
MHR	Control Patients	46 62	0.0114 0.0203	0.0056 0.0135	0.0071 0.0130	0.0103 0.0172	0.0152 0.0248	0.001
NLR	Control Patients	100 104	1.94 2.42	0.81 2.03	1.39 1.43	1.75 1.95	2.31 2.62	0.082
PLR	Control Patients	100 104	126.07 118.82	39.13 60.82	93.80 85.48	124.52 107.63	147.78 138.39	0.028

*: Mann-Whitney U test was used. Significant values were shown in bold. MPV: Mean platelet volume; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio; CRP: C-reactive protein; MHR:monocyte-high-density lipoprotein ratio

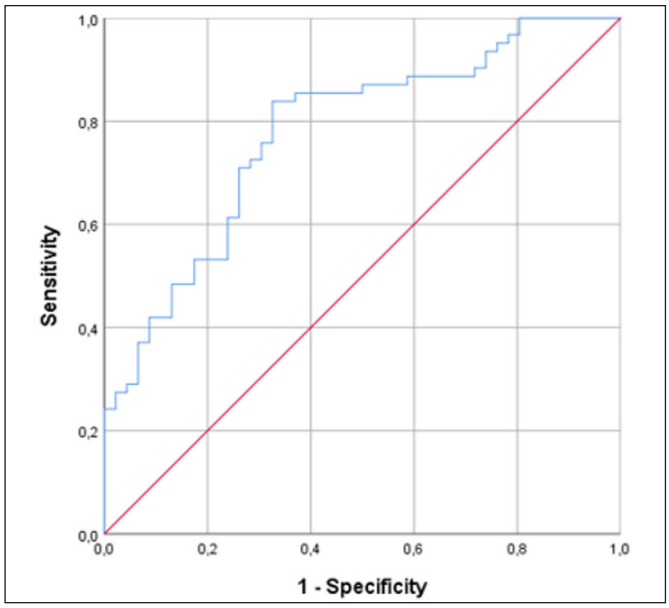

Figure 1. The ROC curve of MHR

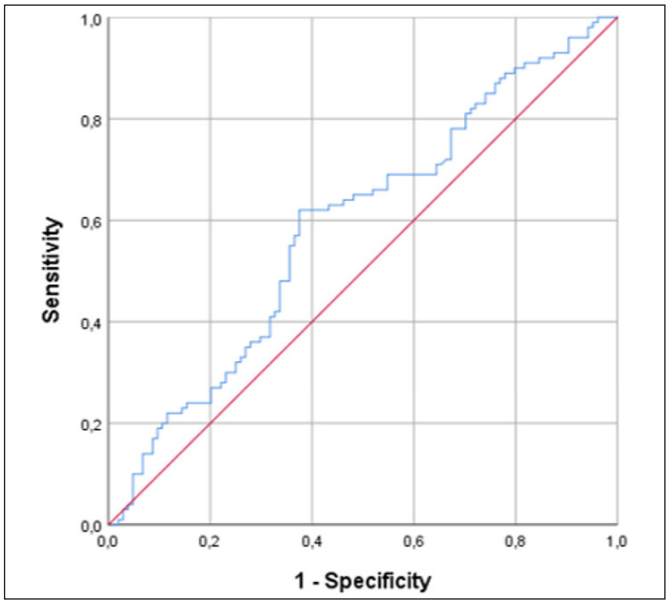

Figure 2. The ROC curve of PLR

Table 2 examined; when MHR increase by 0.01 units, it is seen that the risk of disease rise significantly by 4.07 times. (p=0.001) When NLR increase by 1 unit, the risk of rises increase significantly by 1.37 times. (p=0.038)

On the other hand, the unadjusted effect of the PLR given in Table 1 was significant, but it was not significant when the effect of age difference was eliminated (p=0.784).

While the adjusted effect of NLR was not significant (Table 1), it was significant when the effect of the age difference was removed. Both adjusted and unadjusted effects of MHR were significant. The success of the variables in Table 2 in separating patient and control individuals are given as sensitivity and specificity.

Table 2. Adjusted effects

	OR	95% C.I.for OR		P*	Sensitivite (%)	Spesifite (%)
		Lower	Upper			
MHR	4.070	1.887	8.777	0.001	67.4	72.5
NLR	1.370	1.017	1.845	0.038	61.5	74.0
PLR	0.999	0.993	1.005	0.784	---	---

*: Binary logistic regression model was used. MHR: monocyte-high-density lipoprotein ratio ; NLR: Neutrophil / lymphocyte ratio; PLR: Platelet/lymphocyte ratio

DISCUSSION

In recent years, it has been shown in many studies that biomarkers such as MPV, NLR, and PLR, derived from the complete blood cell count (CBC), can be prognostic indicators in evaluating various inflammatory diseases' activity and in the survival of malignancies.[6,11,12]

There are conflicting data regarding NLR and PLR.[10,13] Although It has been reported in some researches that NLR are higher in patients with HS.[13,14] Çetinarslan et al.[10] showed no significant differences in terms of NLR and PLR between HS patient group and control group. Gambichler et al.[7] suggested that PLR is lower in HS patients. They reported that PLR may not be an appropriate biomarker for disease activity or severity. In our study, while neutrophil, lymphocyte, monocyte, and platelet counts were higher in HS patients than in control group. When the effect of age difference is ignored, the the elevation of NLR was not statistically significant (p=0.082), but when the adjusted impact of of NLR was examined, it was found to be statistically significant higher compared to the control group (p=0.038). Results in the literature and our results indicate that NLR and PLR do not appear to be suitable biomarkers for HS disease.

The main role of platelets is maintaining homeostasis, however, they also play crucial roles in acute and chronic inflammatory reactions. They release large amounts of inflammatory cytokines and help recruit other inflammatory cells to the inflammation site. MPV and PDW are known as platelet activation biomarkers and represent platelet production rate and stimulation.[15-17] It has been shown in previous studies that MPV is a marker of increased platelets' activation and aggregation in inflammatory diseases such as psoriasis, recurrent aphthous stomatitis, and Behçet's disease.[11,18] However, MPV was not found to be related to disease and/or disease activity in some of the inflammatory diseases.[19,20] In the present study, platelet counts were higher in patients, however, MPV values were similar in patients and controls. We think that the fact that our patients consisted of HS patients without comorbidities led to these results. Literature data and our findings suggest that MPV may be more effective in detecting the risk of thrombosis rather than detecting inflammation.

Monocytes and macrophages are the main factors in inflammation development, which leads the development and progression of atherosclerosis. Monocytes that migrate from the circulation to the subendothelial space of the arterial wall are called macrophages and form foam cells by internalizing low density lipoprotein (LDL), very low density lipoprotein (VLDL), and oxidized lipoproteins. Foam cells cause the activation of T lymphocytes, platelets, and other monocytes by synthesizing pro-inflammatory cytokines.[21,22] Moreover, HDL-C inhibits the proinflammatory and pro-oxidant effects of macrophages and the migration of monocytes in addition to eliminating cholesterol from these cells, which exhibits antiatherosclerotic effects. Therefore, the ratio of these two parameters MHR may be a better inflammation marker. Recent studies showed that increased MHR levels may be a predictor biomarker of cardiovascular disease.[17,21,23] In the literature, it has been shown in many previous studies that the frequency of subclinical atherosclerosis and cardiovascular events is increased in patients with HS.[24-26] MHR has been found to be an effective biomarker in diseases in which chronic inflammation plays a role in etiopathogenesis, such as diabetes mellitus and metabolic syndrome.[6,27]

This study revealed that only MHR, an inflammation biomarker, was significantly increased in patients with HS without comorbidities. We found that MHR was a measure to discriminate activation patterns of patients from controls the MHR distinguished HS patients from controls with 71.0% sensitivity and 74% specificity. As shown in **Table 2**, after adjusting age we found that the risk of disease increased by 4.07 times when MHR increased by 0.01 units. Our results suggest that MHR may be an appropriate inflammatory biomarker in HS patients.

The fact that our patient group was selected from HS patients who did not have a chronic disease and did not use systemic medications eliminated additional factors that could affect MHR and other inflammatory markers. This is a factor that adds value to our research.

The fact that our study was retrospective and ESR values could not be evaluated is one of the most important limitations. In addition, since HS could not be staged, its relationship with the stage of the disease could not be determined with biomarkers.

CONCLUSION

As a result, this study makes remarkable contributions to the comprehension of the relationship between MHR and HS disease, which is limited in the literature. Excluding HS patients with comorbidities in our study eliminated additional factors that would affect MHR and other inflammatory markers (NLR, MPV, PLR) revealed that MHR discriminates inflammation in HS more effectively than other markers. MHR should be considered a promising value in distinguishing HS, a chronic inflammatory disease. However, there is a need for prospective studies, with a greater number of patients, to determine whether MHR can be used as an inflammatory or a prognostic marker in patients with HS.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Erzurum Regional Training and Research Hospital Clinical Researches Ethics Committee (Date: 06.06.2022, Decision No: 2022/07-88).

Informed consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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