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Original Article

The Relationship Between the Monocyte-to-High-Density Lipoprotein-Cholesterol Ratio and Disease Activity in Patients with Psoriatic Arthritis

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Abstract

Background: The aim of this cross-sectional study was to analyze the monocyte-tohigh-density lipoprotein ratio (MHR) as an inflammatory marker in patients with psoriatic arthritis (PsA) and healthy controls (HCs), as well as to determine the association between MHR and PsA severity.

Methods: This cross-sectional study included patients with PsA (n=66) and age and sex-matched HCs (n=68). Sociodemographic data and laboratory parameters were recorded in the study group. Disease Activity in PSoriatic Arthritis (DAPSA) was used to assess disease activity, while the Health Assessment Questionnaire (HAQ) was used for general health assessments. Disease Activity in PSoriatic Arthritis and HAQ were evaluated in the patient group. We compared sociodemographic, laboratory parameters, and the MHR between patients with PsA and HCs. Factors influencing MHR were assessed by regression analysis.

Results: Patients with PsA revealed increased MHR compared to HCs ($P=.025$). In regression analysis, a DAPSA score of 15 or higher results in a 3.08 unit rise in the MHR, compared to a DAPSA score of 14 or below. In individuals with coronary artery disease (CAD), MHR increases by 7.56 units. Patients with moderate–severe PsA (DAPSA ≥ 15) had significantly elevated levels of C-reactive protein, erythrocyte sedimentation rate, and MHR compared to patients with remission-mild PsA (DAPSA ≤ 14) ($P < .001$, <.001, .026, respectively).

Conclusions: Monocyte-to-high-density lipoprotein ratio can be used as an inflammatory marker in the follow-up of patients with PsA. Patients with PsA without evidence of active disease should also be evaluated for CAD in the presence of a high MHR value.

Keywords: Disease severity, monocyte-HDL ratio, psoriatic arthritis

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Introduction

Psoriatic arthritis (PsA) is a type of arthritis that causes inflammation and is linked to psoriasis. The general population has an overall prevalence rate of PsA ranging from 0.02% to 0.1%. However, among patients with psoriasis, the incidence rate of PsA varies between 7% and 40%.[1,2]

Macrophages and monocytes play a crucial role in releasing proinflammatory and pro-oxidant cytokines at the site of inflammation. High-density lipoprotein cholesterol (HDL-C) has been shown to protect endothelial tissue against the adverse effects of low-density lipoprotein cholesterol (LDL-C) and inhibit the oxidation of LDL molecules.[3] Recent studies have demonstrated that the monocyte-to-high-density lipoprotein ratio (MHR) is a novel prognostic indicator.[4,5] Elevated monocyte count and reduced HDL-C levels are potentially linked to inflammation and oxidative stress.[6]

Activity assessment in PsA is difficult due to axial and peripheral joint involvement, as well as skin involvement, nail involvement, and enthesitis. Disease Activity in PSoriatic Arthritis (DAPSA) is an effective activity assessment index.[7] The currently used inflammatory markers may not always be helpful for disease activity.[8] C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may be normal when the disease is active.[9]

However, while there has been research examining the association between MHR and psoriasis, no studies have specifically investigated the relationship between MHR and PsA in patients. We hypothesized

that MHR would be higher in patients than in healthy controls (HC) and would increase with disease severity. The aim of this study was to compare MHR in patients with PsA with the control group. It also aimed to investigate the factors affecting the MHR, including disease activity, in patients with PsA.

Material and Methods

This single-center, cross-sectional study included patients diagnosed with PsA using the classification criteria for PsA (CASPAR) criteria.[10] Patients over the age of 18 years with PsA who applied to our rheumatology outpatient clinic between June 2023 and April 2024 and agreed to participate in the trial were enrolled. Exclusion criteria included heart failure, moderate to severe valvular heart disease, renal and hepatic failure, active hepatobiliary illness, active infectious disease, hematologic diseases, cancer, rheumatologic, and immunologic diseases other than PsA. The healthy control group (HCG) consisted of healthcare workers who were of similar age and gender to the patient group and had a complete blood count and lipid profile. Patients who were part of the study were given a written consent form to fill out. The study protocol was approved by the Cukurova University Faculty of Medicine Ethics Committee (Date: May 13, 2022, Approval No.: 122/12).

The study collected data on height, weight, body mass index (BMI), smoking history, comorbidities, disease duration, and disease severity. Disease Activity in PSoriatic Arthritis was used as a measure of disease activity.[5] Health Assessment Questionnaire (HAQ) was also filled out.[11]

Turkish validation of the HAQ was used to test the patients. For each patient, we collected answers to questionnaires in face-to-face interviews assessing functional capacity, as measured with the HAQ scores.[12]

DAPSA score <4 is remission; >4 to ≤14 is low disease activity; >14 to ≤28 is moderate disease activity; score >28 is high disease activity.

Main Points

- Monocyte-to-high-density lipoprotein ratio could be a good indicator of systemic inflammation for patients with psoriatic arthritis.
- Patients with high MHR values but no disease activation should be examined for coronary artery disease.

Patients were classified into 2 distinct groups based on their DAPSA score: those with remission and low disease activity (score ≤14 points), and those with intermediate and high disease activity (score ≥15 points).[13]

Routine tests included recording of a complete blood count, lipid panel, CRP, and ESR. Monocyte-to-high-density lipoprotein ratio was calculated using monocyte and HDL tests.

Patients were categorized into different weight classifications based on their BMI, including underweight (<18.4 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-30 kg/m^2), obese (30-44.9 kg/m^2), and dangerously obese (>45 kg/m^2).[14]

Statistical Analysis

The G*Power® software (Heinrich-Heine-Universitat Düsseldorf, Düsseldorf, Germany) was used to calculate the sample size. Based on the values obtained from a previously conducted study,[15] accepting MHR as the primary assessment tool in the literature, the minimum sample size to be reached with 5% error and 80% power was found to be 64 for each group and 128 in total when two-sided hypothesis testing was taken as reference. A total of 134 patients were reached.

Data analyses were performed using the 20.0 version of IBM SPSS (IBM SPSS Corp.; Armonk, NY, USA) statistical software. The Shapiro–Wilk test was employed as a normal distribution test. Numbers, percentages, means, and standard deviations present the data. The study utilized the *t*-test, chi-square analysis, one-way ANOVA, and multivariable linear regression analysis. A value of $P < .05$ was considered statistically significant.

Multivariate linear regression analysis created to estimate the MHR was found to be significant. The dependent variables of the model are the presence of diabetes mellitus (DM) (reference category: no DM), hypertension (HT) (reference category: no HT), coronary artery disease (CAD) (reference category: no CAD), smoking (reference category: no smoking), and DAPSA (reference category: DAPSA ≤14 points).

Results

Sixty-six patients with PsA (mean age 49.97 ± 11.9 years) and 68 HCG (mean age 46.76 ± 9.93 years) were included in the study. Table 1 lists the features of the patients with PsA.

Table 2 summarizes the comparison of features of patients with PsA and HCG. Forty-nine of PsA patients were females, 47 of the HCG were female. Healthy control group and patients with PsA were comparable in terms of age and gender. Although the distribution based on BMI did not change significantly between the groups, the proportion of obese patients was higher in the PsA group ($P = .062$). Smoking rates are higher in patients with PsA than in HCG ($P = .035$). The patients with PsA exhibited increased MHR levels compared to HCG ($P = .025$).

Table 1. Socio-Demographic and Clinical Characteristics of Patients with PsA

Patients, n	66
Age (years) mean ± SD	49.97 ± 11.9
Female, n (%)	49 (74.2)
Duration of illness mean ± SD	8 ± 7.28
Comorbidities, n (%)	
Diabetes mellitus	16 (24.2)
Hypertension	25 (37.9)
Coronary artery disease	5 (7.6)
DAPSA score, n (%)	
≤14 points	34 (51.5)
≥15 points	32 (48.5)
HAQ score mean ± SD	0.29 ± 0.44
Smoker, n (%)	30 (45.5)
Smoking history (pack-years)	9.35 ± 10.7
Treatment, n (%)	
NSAID	2 (3)
DMARD	33 (50)
Biological treatment ± DMARD	31 (47)
CRP level (mg/liter), mean ± SD	10.88 ± 14
ESR (mm/hour), mean ± SD	18.29 ± 12.54

CRP, C-reactive protein; DAPSA, the disease activity index for psoriatic arthritis; DMARD, disease-modifying anti-rheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NSAID, non-steroidal anti-inflammatory drug.

Factors affecting MHR in patients with PsA are shown in Table 3 using regression analysis. A DAPSA score of 15 or higher results in a 3.08 unit rise in the MHR, in contrast to a DAPSA score of 14 or below. In individuals with CAD, MHR increases by 7.56 units.

Patients with moderate–severe PsA (DAPSA ≥15) had significantly elevated levels of CRP, ESR, and MHR compared to patients with remission-mild PsA (DAPSA ≤14) (*P* value <.001, <.001, .026, respectively).

No statistically significant difference was observed when the mean MHR values of the

Table 2. Comparison of Socio-Demographic and Laboratory Data of Patients with PsA and the Control Group

	PsA (n = 66)	Control Group (n = 68)	*P*
Age (mean ± SD)	49.97 ± 11.9	46.76 ± 9.93	.079
Female, n (%)	49 (74.2)	47 (69.1)	.641
BMI, n (%)			
Underweight	2 (3)	1 (1.5)	.062
Normal weight	15 (22.7)	26 (38.2)	
Overweight	20 (30.3)	26 (38.2)	
Obese	28 (42.4)	15 (22.1)	
Dangerously obese	1 (1.5)	0 (0)	
Smoker, n (%)	30 (45.5)	18 (26.5)	.035
Leukocyte ($\times 10^9$/L) mean ± SD	7.8 ± 2.23	6.34 ± 1.63	<.001
Neutrophil ($\times 10^9$/L) mean ± SD	4.8 ± 2.0	3.71 ± 1.36	<.001
Lymphocyte ($\times 10^9$/L) mean ± SD	2.06 ± 0.83	1.90 ± 0.67	.21
Monocyte ($\times 10^9$/L) mean ± SD	0.59 ± 0.24	0.50 ± 0.16	.011
Triglyceride (mmol/L) mean ± SD	8.07 ± 3.43	6.52 ± 3.30	.009
LDL (mmol/L), mean ± SD	6.81 ± 1.57	3.72 ± 1.83	.75
HDL (mmol/L), mean ± SD	3.08 ± 0.77	3.12 ± 0.76	.73
MHR, mean ± SD	0.20 ± 0.10	0.17 ± 0.083	.025

BMI, body mass index, HDL, high-density lipoprotein; LDL, low-density lipoprotein; MHR, monocyte-to-high-density lipoprotein ratio.

Table 3. Regression Analysis of Monocyte-HDL Ratio in Patients with PsA

	β	Standard Error	*P*	Collinearity Statistics Tolerance VIF
DM	-0.639	1.79	.72	0.70 1.42
HT	2.71	1.62	.10	0.66 1.50
CAD	7.56	2.58	.005	0.88 1.13
DAPSA	3.08	1.32	.024	0.93 1.0
Smoker	0.076	1.91	.96	0.45 2.1

CAD, coronary artery disease; DAPSA, the disease activity index for psoriatic arthritis; DM, diabetes mellitus; HT, hypertension.

patient group were compared based on the treatment type (Table 4).

Discussion

The results of the current study showed that patients with PsA had higher MHR compared to HCs, that MHR increased as disease severity increased, and that the presence of CAD increased MHR. Researchers have examined the relationship between MHR and many diseases, but to our knowledge, there has been no study on patients with PsA.

Although the distribution of BMI was similar between the PsA and HCGs, the PsA group had more obese patients.

Table 4. MHR in Patients with PsA According to Current Treatments

	n	MHR, Mean ± SD	*P*
DMARD	33	0.18 ± 0.10	
TNF blocker	9	0.21 ± 0.12	
TNFblocker + leflunomide/methotrexate	4	0.22 ± 0.079	.580
IL-17 antagonist	10	0.23 ± 0.11	
IL17antagonist + leflunomide/ methotrexate	8	0.23 ± 0.11	
Total	64	0.20 ± 0.10	

DMARD, disease-modifying anti-rheumatic drug; TNF, tumor necrosis factor.

Monocyte-to-high-density lipoprotein ratio was higher in the patient group compared to HCG. There was a positive relationship between ESR, CRP, and MHR, and these values were significantly higher in patients with high disease activity.

Upon evaluating the features of the patient group in our study, it becomes evident that the prevalence of obesity is increased. Indeed, studies on PsA demonstrate that a higher BMI raises the chance of developing PsA in psoriatic patients, supporting the relationship between fat-mediated inflammation and joint involvement.[16] In addition, the presence of obesity negatively affects PsA management.[17] Obesity is known to increase in the patients with the PsA group.[18] As expected, our patients with PsA were more obese than the control group.

The majority of research to date has focused on MHR in cardiovascular disease. Monocyte-to-high-density lipoprotein ratio is significantly associated with cardiovascular mortality.[19] In studies, MHR has been shown to be a parameter that can be used to predict individuals predisposed to cardiovascular disease and determine the severity of CAD.[20] In a study conducted by Ci et al,[21] MHR was observed to be higher in Takayasu arteritis patients with coronary artery involvement than in individuals without coronary artery involvement. This study shows MHR as a basic, easily measured index for coronary involvement. It is known that CAD increases in PsA disease. Similar to the literature, CAD was found to be the most important factor affecting MHR in our study.

Monocyte-to-high-density lipoprotein ratio has been studied as an inflammation marker in a variety of disorders, both rheumatologic and non-rheumatologic, in which inflammation occurs. Monocyte-to-high-density lipoprotein ratio has been demonstrated to be helpful as an indicator of inflammation in individuals with Behçet's disease.[3] Previous studies have shown that MHR is high in correlation with acute phase reactants in scleroderma, infective endocarditis, polycystic ovary syndrome, acute coronary syndrome, and Takayasu arteritis.[22-25] In a study by Kılınç et al on patients with Takayasu arteritis, MHR was found to be an essential inflammatory measure in both diagnosis and patient follow-up.[25] Monocyte-high-density lipoprotein ratio was significantly higher in patients with digital ulcers or a high modified Rodnan skin score, according to a study conducted by Kim et al on patients with scleroderma. Inflammatory indicators have been associated in our study with MHR levels.

In contrast to our study, no difference in MHR was observed between the rheumatoid arthritis and control group in the study by Romo-Cordero et al.[26]

Karabay et al found that MHR was higher in psoriasis patients than in controls, and there was a positive correlation between MHR and the psoriasis area and severity index score.[5] Furthermore, in this investigation, MHR and CRP levels had a favorable connection. Our study found a positive association between MHR and the DAPSA score. Simultaneously, we observed a positive correlation between MHR and CRP levels. Monocyte-to-high-density lipoprotein ratio is clearly associated with inflammation as a close correlation exists with CRP in its prediction of measurements of monocytes and HDL cholesterol individually. In addition, acute phase reactants may be normal in some patients with PsA. To our knowledge, this is the first study to investigate the association between MHR and disease severity in patients with PsA.

The study has some limitations. The small number of patients in the study is the most important limitation. The relationship between clinical involvements and MHR was not examined separately in the patient group (axial involvement, peripheral involvement, enthesitis, or dactylitis). Erythrocyte sedimentation rate, CRP, and DAPSA were examined as disease activity indicators. Other limitations include not considering the severity index of skin involvement.

In conclusion, PsA disease has different domains, and there are difficulties in evaluating disease activity. In addition to the frequently used acute phase reactants, MHR can be an alternative in the follow-up of patients. It is also recommended that patients with high MHR levels, even though there is no disease activation should be evaluated for CAD. Monocyte-to-high-density lipoprotein ratio was observed to be elevated in patients with PsA exhibiting greater disease severity.

Data Availability Statement: The datasets gathered during the preparation of this manuscript ara available from the corresponding author upon reasonable request

Ethics Committee Approval: This study was approved by the Ethics Committee of Cukurova University (Approval no122-12 ; Date: May 13,2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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