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Are inflammatory parameters an independent predictor of hip osteoarthritis severity? A prospective cross-sectional study

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SUMMARY

OBJECTIVE: This study aimed to investigate the relationship between the presence of hip osteoarthritis and the neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, monocyte-lymphocyte ratio, and neutrophil-monocyte ratio.

METHODS: Participants with hip osteoarthritis and healthy controls aged 45–75 years were recruited in the study. The participants with hip osteoarthritis were divided into two groups: mild/moderate hip osteoarthritis and severe hip osteoarthritis. Complete blood parameters of the participants were recorded, and neutrophil-lymphocyte ratio, neutrophil-monocyte ratio, monocyte-lymphocyte ratio, and platelet-lymphocyte ratio were calculated. Pain severity was evaluated using a visual analog scale.

RESULTS: A total of 76 participants with hip osteoarthritis and 59 healthy controls were included in the study. The mean age of the participants was 57.6±6.11 years. Mean neutrophil-lymphocyte ratio and neutrophil-monocyte ratio values were statistically significantly different between the hip osteoarthritis group and healthy control group ($p<0.05$). Platelet-lymphocyte ratio, monocyte-lymphocyte ratio, erythrocyte sedimentation rate, and C-reactive protein values were not significantly different between the groups. Also, there was no difference between all inflammatory parameters and hip osteoarthritis severity ($p>0.05$).

CONCLUSIONS: Neutrophil-lymphocyte ratio and neutrophil-monocyte ratio values were higher in patients with hip osteoarthritis than in healthy controls. Mean platelet-lymphocyte ratio, monocyte-lymphocyte ratio, erythrocyte sedimentation rate, and C-reactive protein values did not change according to the presence of hip osteoarthritis. Not all hematological indices give valuable information regarding the severity of hip osteoarthritis.

KEYWORDS: Hip osteoarthritis. Inflammation. X-rays.

INTRODUCTION

The hip joint, one of the largest weight-bearing joints in the body, is most affected by osteoarthritis (OA), along with the knee joint[1]. Although the articular cartilage is damaged in the foreground in hip osteoarthritis (HOA), the entire joint is affected. Articular cartilage loss, subchondral cysts, osteophyte formation, periarticular ligament laxity, muscle weakness, and possible synovial inflammation are seen in the process of OA[2]. Synovial inflammation, age, genetic factors, trauma, joint dysplasia, sex, and obesity are included in the etiology of HOA[3]. Although there are often different causes in the pathophysiology of OA, similar culminating processes occur during the development of the disease, and this situation creates the typical progression of OA[4]. Studies have shown that inflammation and the immune system play important role in the development of OA[5]. Various studies investigating the role of inflammation in the pathogenesis of OA have shown the effects of cytokines on disease progression, duration, and severity[6].

The neutrophil-lymphocyte ratio (NLR), which shows the two main functions of the immune system, i.e., inflammation and adaptive immune balance in peripheral blood, has been used as an effective and inexpensive biomarker for the past 20 years[7]. In the literature, NLR has been associated with conditions such as ischemic stroke[8] and cardiovascular diseases[9].

In addition, the platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR) are also accepted as markers to show inflammation in different diseases[10,11]. Furthermore, the neutrophil-monocyte ratio (NMR) has also been indicated as a potential marker that can be used to identify diseases such as skin cancer, breast cancer, knee OA, or predict prognosis, similar to PLR[12].

This study aimed to investigate the relationship between the presence of HOA and NLR, PLR, MLR, and NMR, which was previously shown to be an independent predictor of knee OA severity[12,13]. Using the information obtained from this study, it was aimed to better understand the role of inflammation in the pathogenesis of HOA and determine the points that could be used in treatment.

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METHODS

This was a prospective, cross-sectional study. Ethical approval was granted by the Abant İzzet Baysal University Medical Faculty clinical research ethical committee (2020/329) in conformity with the Declaration of Helsinki. Participants invited to take part in the study were informed in writing and verbally about the aim of the study. A signed Informed Volunteer Consent Form was obtained from each participant before inclusion in the study.

Participants

A total of 415 consecutive outpatients with HOA who were admitted to the Physical Medicine and Rehabilitation Outpatient Clinic between February and December 2021 were evaluated.

The power analysis of the study was estimated using the G*Power 3.1.9.4 software package (Franz Faul, Christian-Albrechts University of Kiel, Germany). We calculated that to achieve $\alpha<0.05$, $\beta=80\%$; according to the PLR, the minimum sample size required to be included in the study is 71 for the patient group and 53 for the healthy control group in order to identify a statistically significant difference between the two groups in terms of repeated measurements according to Taşoğlu et al.[14].

The inclusion criteria were ages 45–75 years and the presence of a radiologic and clinical diagnosis of HOA. Patients with secondary HOA, avascular necrosis, rheumatologic or autoimmune disease, chronic inflammatory disease, corticosteroid use, malignancy, hematological disease, and active viral and bacterial infection were excluded. Clinical and demographic characteristics of the participants were recorded.

Assessment methods

Radiologic Assessment

Grading of HOA was performed radiologically according to the Kellgren-Lawrence (KL) classification. The KL classification system is a radiologic grading method in OA. According to this system, narrow joint space exists in grade 1, joint obliteration and possible osteophytic lipping occur in grade 2, definite osteophytes, sclerosis, and cyst formation are seen in grade 3, and gross loss in joint space with sclerosis, cysts, and large osteophytes are present in grade 4[15].

Pain measurement

Participants were asked about mean pain experienced during the day using a visual analog scale (VAS) in order to measure hip pain. The patient was asked to indicate the severity of pain on a 10-cm line marked from 1 to 10, with 0 indicating no pain and 10 the worst possible pain[16].

Laboratory parameters

Peripheral venous blood specimens were collected using standard surgical procedures during presentation and were investigated in the Abant İzzet Baysal University Medical Faculty central laboratory. Complete blood count parameters (i.e., hemoglobin, leukocytes, erythrocytes, platelets, and leukocyte subtypes) were analyzed using a Syxmex XN-1000 (Kobe, Japan) automatic analyzer. Biochemical parameters [C-reactive protein (CRP)] were measured on an automatic biochemical analyzer (Abbott Architect C8000, USA). In addition, NLR (absolute neutrophil count/absolute lymphocyte count), NMR (absolute neutrophil count/absolute monocyte count), MLR (absolute monocyte count/absolute lymphocyte count), and PLR (absolute platelet count/absolute lymphocyte count) were calculated.

Statistical analysis

Statistical analysis was performed using the SPSS software version 23.0 (MacOs, IBM Corp., Armonk, NY, USA). The normality of the distribution of the variables was examined using the Shapiro-Wilk test. Descriptive statistics are presented as mean (standard deviation), median, and minimum and maximum values. For intergroup comparisons, the Mann-Whitney U test was used for nonparametric variables, and independent t-test was used for parametric variables. Spearman's correlation analysis was used to determine the relationship between the variables for ordinal or non-normally distributed variables.

RESULTS

A total of 76 participants with hip OA and 59 healthy controls aged 45–75 years were included in the study. Of these participants, 32 (23.7%) were male and 103 (76.3%) were female. The mean age of the participants was 57.6±6.11 years. The mean body mass index of the patients was 28.7±4.0. Demographic and clinical characteristics were similar between the HOA group and control group ($p>0.05$). Mild-to-moderate HOA was present in 37 (48.7%) patients, and 39 (51.3%) had severe HOA.

The mean NLR ($p=0.005$) and NMR ($p<0.001$) values were statistically significantly different between the hip OA group and healthy control group. In contrast, the mean PLR, MLR, erythrocyte sedimentation rate (ESR), and CRP values were not significantly different between the two groups (Table 1).

When the HOA group was separated into two groups – mild/moderate OA and severe OA, there was no significant

difference in terms of hemocytometric parameters between the two groups (Table 2).

According to the correlation analysis of the variables in HOA, there was no relationship between laboratory and hemocytometric parameters with the KL classification (severity of the HOA) and VAS (pain intensity) (Table 3).

Table 1. Intergroup analysis for HOA group and control group according to laboratory parameters.

	HOA group (n=76)	Control group (n=59)	p
NLR	2.1±1.3	1.7±0.7	0.005*
NMR	9.3±3.1	7.2±2.3	<0.001*
PLR	122.6±45.9	117.4±46.2	0.338
MLR	0.2±0.1	0.2±0.1	0.346
CRP (mg/L)	3.5±4.0	2.4±1.6	0.605
ESR (mm/L)	12.2±10.2	11.8±7.3	0.447

HOA: osteoarthritis; NLR: neutrophil-lymphocyte ratio; NMR: neutrophil-monocyte ratio; PLR: platelet-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate. *p<0.05 is considered significant for Mann-Whitney U test.

Table 2. Intergroup analysis for mild/moderate and severe osteoarthritis groups according to hemocytometric parameters.

	Mild-moderate HOA group (n=37)	Severe HOA group (n=39)	p
NLR	2.1±1.5	2.1±0.9	0.716
NMR	8.9±3.1	9.6±3.1	0.383
PLR	122.9±45.5	122.3±46.9	0.685
MLR	0.2±0.1	0.2±0.1	0.589
CRP (mg/L)	3.1±2.7	3.8±5.0	0.693
ESR (mm/L)	11.8±9.3	12.7±11.1	0.888
Neutrophil	1.8±2.9	1.6±0.2	0.697
Lymphocyte	2.2±0.8	2.2±0.7	0.647
Monocyte	0.2±0.0	0.1±0.0	0.693
Platelet	249.5±62.5	250.5±69.9	0.967
VAS	6.4±1.3	7±1.4	0.081

HOA: osteoarthritis; NLR: neutrophil-lymphocyte ratio; NMR: neutrophil-monocyte ratio; PLR: platelet-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analog scale. p<0.05 is considered significant for Mann-Whitney U test.

DISCUSSION

The relationship between the presence of HOA and inflammatory parameters has not yet been demonstrated[17]. In this study, the relationship between the presence of HOA and NLR, NMR, PLR, and MLR, which are indicators of inflammation, was evaluated. According to the results of the study, it was revealed that there is a relationship between NLR and NMR and the presence of HOA. Although there are few studies on this subject, it has been shown in recent studies that there is a relationship between hematologic indices and OA[12,18]. NLR, an inflammatory marker, was used to determine the prognosis of systemic inflammation[18,19]. Only one study has investigated the levels of NLR in HOA. Barbosa et al. found that NLR values were higher in unilateral coxarthrosis than that in the bilateral group[17]. Many studies investigated NLR levels in knee OA in the literature. In a retrospective, cross-sectional study, NLR was reported as an inflammatory marker that predicted the radiographic severity of knee OA[18]. In another study, a blood NLR cutoff value of ≥2.1 was reported as a predictor of knee OA by Tascioglu et al[14]. Similarly, in this study, the mean NLR value was significantly higher in participants with HOA than in healthy controls, with the mean value of 2.1. However, the mean value did not change significantly with respect to the severity of HOA. The aforementioned study reported a cut-off value for knee OA, and there is no cutoff value for HOA, which may have affected the results.

Similar to NLR, NMR is a biomarker for chronic inflammation in some diseases[19,20]. Shi et al. reported that NMR was correlated with KL grades in knee OA[12]. In this study, NMR was found to be significantly higher in participants with HOA than in healthy controls. In contrast, there was no relationship between disease severity and NMR in the HOA group.

Several studies reported that PLR and MLR levels were higher in systemic inflammatory processes such as rheumatologic disease[11,21]. A retrospective study reported that there was a relationship between PLR values and the radiographic severity of HOA[14]. Conflictingly, no relationship was found between PLR and the severity of HOA in this study. The mean age of our

Table 3. Correlation between the pain intensity, disease severity of hip osteoarthritis, and laboratory and hemocytometric parameters.

	NLR	NMR	MLR	PLR	Neutrophil	Lymphocyte	Monocyte	Platelets
VAS	r=-0.085 p=0.468	r=0.064 p=0.583	r=-0.145 p=0.211	r=0.092 p=0.429	r=-0.045 p=0.701	r=0.158 p=0.172	r=-0.145 p=0.211	r=0.041 p=0.727
KL grade	r=0.042 p=0.719	r=0.101 p=0.386	r=-0.0.62 p=0.592	r=-0.047 p=0.688	r=-0.045 p=0.699	r=0.053 p=0.650	r=-0.046 p=0.695	r=-0.005 p=0.967

NLR: neutrophil-lymphocyte ratio; NMR: neutrophil-monocyte ratio; MLR: monocyte-lymphocyte ratio; PLR: platelet-lymphocyte ratio; VAS: visual analog scale; KL: Kellgren-Lawrence. p<0.05 is considered significant.

participants was lower than that in the aforementioned study. It is known that the inflammatory process increases with age[22]. The nonsignificance of the PLR values may be related to the lower mean age of the participants in this study. In one study, MLR was found to be a reliable potential predictor for knee OA[23]. In this study, MLR values were not significantly different between the HOA group and healthy controls. However, no study has evaluated the level of MLR in HOA in the literature. Accordingly, it would be wrong to generalize the results of knee OA to HOA.

In several studies, elevated serum ESR and CRP levels were found in patients with knee OA[14,24]. No study has evaluated the relationship between these parameters and hip OA. In this study, there was no difference in ESR and CRP levels between participants with HOA and healthy controls. Additionally, no relationship was found between ESR and CRP levels and the severity of hip OA. ESR and CRP levels may increase in disease activity and correlate with clinical findings such as tenderness, patellar ballottement, and swelling[24]. The lack of difference between the groups in ESR and CRP levels may be related to the fact that some of the participants were not in an exacerbation period of OA.

The presence of inflammatory mediators in OA can cause a greater response to painful stimuli[25]. In this study, there was no correlation between pain intensity and inflammatory parameters. The exacerbation period in hip OA is not easy to detect through clinical examinations, so this situation can be explained by the fact that some of the participants were not in an exacerbation period. This is an important finding because this is the first study to evaluate the relationship between clinical findings such as pain intensity and inflammatory markers in HOA.

Being a prospective study and evaluating the relationship between most hematologic indices (NLR, NMR, PLR, MLR) and clinical findings, such as pain intensity, can be considered the strengths of the study. Additionally, this is the first study to compare inflammatory parameters of patients with HOA and healthy controls.

There are some limitations to the study. First, larger participant groups should be studied to determine the relationship between the severity of HOA and hematologic indices. Second, a cross-sectional design could be allowed for an instant evaluation.

CONCLUSION

This study showed that NLR and NMR values were higher in patients with HOA than in healthy controls. Mean PLR, MLR, ESR, and CRP values did not change according to the presence of HOA. Not all hematological indices give valuable information about the severity of HOA.

AUTHORS' CONTRIBUTIONS

MDK: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **AKM:** Conceptualization, Formal Analysis, Investigation, Supervision, Visualization, Writing – original draft, Writing – review & editing. **EY:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Visualization.

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