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Association of Neutrophil – to- Lymphocyte ratio as an inflammatory marker in patients with primary Osteoarthritis of the hands

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Abstract

Background and objectives: Hand osteoarthritis is a common joint disease that causes pain and functional impairment. Neutrophil to lymphocyte ratio is a novel marker, it can be used for evaluating inflammatory activity in chronic inflammatory disorders. The aim of the study is to evaluate the relationship of neutrophil to lymphocyte ratio in patients with primary osteoarthritis of the hands.

Patients and methods: This case-control research was carried out in the Rheumatology department of Rizgary Teaching Hospital from March 2022 to March 2023. It included fifty patients who fulfilled the American College of Rheumatology criteria for diagnosis of hand osteoarthritis and fifty healthy controls matched in sex, age, and body mass index. laboratory investigations including (CBC, ESR, CRP) were collected. Values of Neutrophil to Lymphocyte ratio were measured for both groups. Secondary causes of osteoarthritis were excluded.

Results: No significant difference was detected between the two groups in neutrophils (p= 0.495), lymphocytes (p=1.000), and CRP (p =1.000). The differences were significant (p=0.025) in ESR which was higher among patients in comparison to controls. The median of Neutrophil-lymphocyte ratio was higher in patients compared to control, but insignificantly (P=0.311). Moreover, seven patients had a high Neutrophil-Lymphocyte ratio as compared with only 3 individuals in the control group, again insignificantly (P = 0.182).

Conclusion: The current study did not find Neutrophil to lymphocyte ratio to be a reliable indicator of inflammation in the settings of primary osteoarthritis of the hands.

Keywords: Inflammatory markers, Neutrophil Lymphocyte Ratio, Primary Hand Osteoarthritis.

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Introduction

Osteoarthritis (OA) is the most frequent form of joint disease and affects 302 million people worldwide.[1] Primary and secondary OA are indistinguishable pathologically, although bilateral symmetrical involvement is frequently observed in primary osteoarthritis, especially when affecting hands.[2-3] Hand OA is a markedly frequent case with a wide range of clinical presentations.[4] Osteoarthritis (OA) of the hands occurs more frequently in middle-aged, particularly female, and elderly populations.[5] The etiology and pathogenesis of hand OA are not completely comprehended. Environmental factors, including stress from mechanical loading, particularly in frail joints [4], in addition to biomechanical and biological components, gender, age, and genetics, predispose individuals to develop OA.[6] The marked disability and diminished quality of life caused by the disease are similar to those caused by rheumatoid arthritis (RA).[7-8] Symptoms are normally bilateral, and there is a symmetric joint involvement. Bouchard's and/or Heberden nodes plus underlying interphalangeal OA constitute nodal OA.[9] Following interphalangeal joint osteoarthritis, thumb base OA seems to be the most common symptomatic type of hand OA. Older populations, mostly females, were observed to have erosive and widespread hand OA. Erosive OA tends to become more severe with time and may lead to most disabilities.[10] The American College of Rheumatology suggested applying clinical criteria for the diagnosis of hand OA, with a specificity of 98% and a sensitivity of 92%.[11] Inflammatory mechanisms have a significant function in the pathogenesis of OA; cytokines, microRNAs, and metabolites are subjected to these changes.[12] Inflammatory cytokines like interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α), might contribute to the degeneration of the articular cartilage matrix.[13] The ratio of absolute neutrophil count to lymphocyte count is the neutrophil to lymphocyte ratio (NLR). It's cheap and can be easily achieved with a regular test of complete blood count (CBC).[14] It has been successfully used as a parameter of general inflammation, predict malignancy and cardiovascular outcomes [15-16], as well as postoperative complications and infectious pathologies (including pediatric appendicitis).[17-18] Nevertheless, none of the above research looked at the association between NLR and hands primary OA. Therefore, this research was carried out to assess the possible association of NLR as an inflammatory marker in primary OA of the hands.

Patients and methods

This case-control research was conducted at Rizgary Teaching Hospital. Participants were recruited from the Rheumatology and Rehabilitation Department in Erbil City from March 2022 to March 2023. A total of 100 individuals were recruited. Out of them, fifty patients fulfilled the ACR criteria for diagnosing OA of the hand[11]. These criteria include (1) pain in the hand, aching, or stiffness; (2) hard tissue enlargement of 2/10 considered joints in the hand; (3) fewer than three swollen metacarpophalangeal (MCP) joints; (4) hard tissue enlargement of two or more distal interphalangeal joints (DIP); and (5) deformity in two or more of the 10 considered joints. The ten considered joints involve the 2nd and 3rd DIP, the 2nd and 3rd proximal interphalangeal joints (PIP), and carpometacarpal joint (CMC) 1 bilaterally[11]. Controls were fifty healthy individuals matched with the patient group in sex, age, and body mass index (BMI). Patients with diseases that were predisposed to secondary osteoarthritis, including infection, autoimmune diseases, malignancy, hematological disease, metabolic disease, and post-traumatic arthropathy, were excluded from the study. Data was gathered

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and recorded on a questionnaire, which was specially designed. Demographic data, such as gender, age, body weight, and height, were registered, and the body mass index (BMI) was measured. Clinical symptoms and signs; evidence of palpable nodes including Heberdens nodes (DIP joints), Boushards nodes (PIP joints), and clinical evidence of OA of the base thumb (CMC joint) confirmed by one of the researchers. Anticoagulated whole blood was drawn under an aseptic technique from patients and controls using a hematology analyzer (Nihon Kohden, Celltac Alpha, Japan). The absolute neutrophil is divided by the absolute lymphocyte count to calculate NRL. In an adult population in good health, normal NLR levels range from 0.78 to 3.53.[19] Utilizing the Westergren method, the erythrocyte sedimentation rate (ESR) was measured. ESR levels were considered elevated if they were greater than 25mm/h. C-reactive protein was also measured and regarded as elevated if it was greater than 5mg/ dl. The ethical approval was obtained from the Ethics and Scientific Committees of the Kurdistan Higher Council for Medical Specialties. The Statistical Package for Social Sciences (SPSS, version 26) was utilized for analyzing the data. Applying the chi-square test of association, the proportions of the two study groups were compared. Fisher's exact test was used as the predicted frequency (value) of more than 20% of the table's cells was less than 5. The NLR data was not distributed regularly, as shown by the Shapiro-Wilk test. To compare the mean rankings of the two groups, the Mann-Whitney test was used. Less than 0.05 is considered a statistically significant P value.

Results

The work involved 50 individuals with hand osteoarthritis (OA) and 50 healthy individuals with no OA. Around half (46%) of the patients and (38%) of controls were aged ≥ 60 years, but no significant difference between patients and controls (p = 0.59). The majority (92%) of the patients were female, compared with 88% of the controls (p = 0.50). More than two-thirds (72%) of the patients and (70%) of controls were housewives; however, the differences were not significant regarding the occupation (p = 0.62). The majority of the patients and controls were non-smokers, at 90% and 92% respectively (p = 0.18). No significant differences were detected between patients and controls regarding the body mass index (p = 0.921), as illustrated in Table (1).

Table (1): Basic Characteristics of the Study Groups.

	Patients No. (%)	Controls No. (%)	Total No. (%)	p value
Age (years)				
40-49	6 (12.0)	11 (22.0)	17 (17.0)	
50-59	21 (42.0)	20 (40.0)	41 (41.0)	
60-69	11 (22.0)	9 (18.0)	20 (20.0)	
≥ 70	12 (24.0)	10 (20.0)	22 (22.0)	0.598
Gender				
Male	4 (8.0)	6 (12.0)	10 (10.0)	
Female	46 (92.0)	44 (88.0)	90 (90.0)	0.505
Occupation				
Housewife	36 (72.0)	35 (70.0)	71 (71.0)	
Teacher	5 (10.0)	5 (10.0)	10 (10.0)	
Worker	1 (2.0)	0 (0.0)	1 (1.0)	
Retired	4 (8.0)	5 (10.0)	9 (9.0)	
Employee	1 (2.0)	4 (8.0)	5 (5.0)	

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Others	3 (6.0)	1 (2.0)	4 (4.0)	0.625
Smoking				
Smoker	2 (4.0)	4 (8.0)	6 (6.0)	
Non-smoker	45 (90.0)	46 (92.0)	91 (91.0)	
Ex-smoker	3 (6.0)	0 (0.0)	3 (3.0)	0.185
BMI (weight / height^2)				
< 25	6 (12.0)	4 (8.0)	10 (10.0)	
25-29	21 (42.0)	22 (44.0)	43 (43.0)	
30-34	16 (32.0)	16 (32.0)	32 (32.0)	
≥ 35	7 (14.0)	8 (16.0)	15 (15.0)	0.921
Total	50 (100.0)	50 (100.0)	100 (100.0)	

Table (2) shows that 28% of the OA patients had a family history of the disease. The duration of the disease was ≥ 36 months in 42% of the patients, and it was < 12 months in only 10% of the patients. The majority (94%) of the patients had morning stiffness lasting 0-30 minutes. More than one-third (34%) of the patients had 4-6 tender joints, 22% had 7 or more tender joints, and 22% had no tender joints.

Table (2): Disease Characteristics.

	No.	%
Family history		
Yes	14	28.0
No	36	72.0
Disease duration (months)		
< 12	5	10.0
12-23	10	20.0
24-35	14	28.0
≥ 36	21	42.0
Duration of morning stiffness (minutes)		
0-30 minutes	47	94.0
> 30 minutes	3	6.0
Number of tender joints		
None	11	22.0
1-3	11	22.0
4-6	17	34.0
≥ 7	11	22.0
Total	50	100.0

When the normal range of NLR was taken as 0.78-3.53 [19], it was observed as outlined in Table (3) that 14% of the patient group had a high NLR ratio compared to 6% of the controls, but the differences were insignificant (p = 0.182). The median (interquartile range) of the patient's group was 1.97 (1.46-2.69) compared to 1.80 (1.42-2.28) for controls (p = 0.311).

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Table (3): Distribution of NLR categories among patients and controls.

	patients No. (%)	Controls No. (%)	Total No. (%)
NLR			
Normal (0.78-3.53)	43 (86.0)	47 (94.0)	
High > 3.53	7 (14.0)	3 (6.0)	0.182
Total	50 (100.0)	50 (100.0)	
Mean (SD)	2.18 (0.93)	1.94 (0.69)	
Mean Rank of NLR	53.44	47.56	0.311
Meadin	1.97	1.80	
Interquartile rane	1.46-2.69	1.42-2.28	

Among laboratory studies, no significant differences were observed between patients and controls regarding the followings: neutrophils (p = 0.495), lymphocytes (p = 1.000), and CRP (p = 1.000). While the ESR was elevated in 18% of patients compared to 4% of the controls, the differences were significant (p = 0.025), as illustrated in Table (4).

Table (4): Laboratory Results of Patients and Controls.

	Patients No. (%)	Controls No. (%)	Total No. (%)	p value
Neutrophil (1.2-8.0) 10^9/L				
Low < 1.2	0 (0.0)	2 (4.0)	2 (2.0)	
Normal (1.2-8.0)	50 (100.0)	48 (96.0)	98 (98.0)	0.495
Lymphocyte (0.5-5.0) 10^9/L				
Normal (0.5-5.0)	50 (100.0)	49 (98.0)	99 (99.0)	
High >5.0	0 (0.0)	1 (2.0)	1 (1.0)	1.000
CRP				
Normal (0-5)	49 (98.0)	48 (96.0)	98 (98.0)	
High >5	1 (2.0)	2 (4.0)	2 (2.0)	1.000
ESR				
Normal (≤25)	41 (82.0)	48 (96.0)	89 (89.0)	
High (> 25)	9 (18.0)	2 (4.0)	11 (11.0)	0.025
Total	50 (100.0)	50 (100.0)	100 (100.0)	

Discussion

To the best of our knowledge, the relation between neutrophil to lymphocyte ratio as an inflammatory marker has not previously been recorded in patients with primary OA of the hands. This case-control research was designed to look for the possibility of this relationship. The main finding in our study was that there were no significant differences between patients and healthy controls in the median rank of NLR, with matched demographic data and BMI to avoid factors that can affect the results. As a result of severe joint pain, stiffness, and reduced mobility of hand joints, osteoarthritic patients are less productive and have a lower quality of life, as well as imposing a heavier socioeconomic burden on themselves and society.[20] Hand OA has a heterogeneous clinical burden ranging from mild (in the general population) to considerable, particularly in secondary care patients.[21] Our study shows more than one-half (56%) of the patients had tender four or more joints,

https://doi.org/10.56056/amj.2024.307

compared to 22% of patients without joint tenderness. A lack of balance between pro-inflammatory and anti-inflammatory mediators is largely responsible for OA's pathogenesis. This results in low-grade inflammation, which damages cartilage, changes bone structure and increases synovial tissue production.[22] In this research, it was revealed that in most patients with primary hand OA, the levels of CRP and ESR were within the normal range. However, 18% of patients had an unknown cause for ESR elevation compared to 4% of healthy controls, with significant differences among the two groups. Two individuals in the case group were anemic, and it is well known that low levels of hemoglobin (Hb) may lead to increased ESR.[23] Also, technical factors may have some effect, such as seasonal variations in room temperature, which may affect the results. We collected data from the patient group during a twelve-month period, which includes the four seasons of the year. There was a need for using a cooling system during hot weather for the first six months of the study, during which electricity was exposed to repeated daily power outages, which led to an increase in laboratory temperature to around mid-forties sometimes. Fifty percent of the patient group was collected during the first six (hot weather) months of the study, while the other fifty percent of patients and all healthy controls were collected during the last six months of the study, during which the weather was moderate too cold without the need for using a cooling system. The high laboratory temperature might explain, in part, the rise in the ESR in patients compared with controls. Reduced blood viscosity and perhaps greater ESR are caused by a higher room temperature.[24] Previous studies also have shown that several factors can impact the baseline CRP level and ESR, including sex differences, body mass index (BMI), comorbidities, intraarticular injection history, and smoking [25-27], The study has some limitations. First, In the numerical analysis, radiographic (Kellgren–Lawrence grading) was not included; however, it is an important part of the diagnosis of hand OA and should be considered in the evaluation of patients in the later stages of the disease since it wouldn't have been meaningful in the beginning. Clinical imaging can help detect underlying abnormalities and rule out alternative diagnoses when they are suspected. Second, the study included a small sample size of only fifty patients, making it difficult to draw any broad conclusions. To gain a broader understanding of the outcomes, it would be beneficial to conduct a study with a larger sample size.

Conclusion

Despite the small sample size in the current work, the outcomes suggest that there is no significant relationship between primary hand osteoarthritis and the neutrophil to lymphocyte ratio. To further investigate this relationship, a larger study group would be necessary to confirm this result.

Conflict of Interest:

In conducting this study, we hereby declare that there are no conflicts of interest.

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