Relationship of Platelet Lymphocyte Ratio and Neutrophil Monocyte Ratio with Disease Severity of Knee Osteoarthritis

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ABSTRACT:
BACKGROUND:
Osteoarthritis is a low-grade systemic inflammatory and degenerative disease in which many inflammatory mediators are known to be elevated in the peripheral blood. Platelet lymphocyte ratio and neutrophil monocyte ratio are novel markers in many systemic inflammatory disorders. Studies are limited on its link with knee osteoarthritis severity.
OBJECTIVE:
To evaluate the relationship of PLR and NMR with the Knee Osteoarthritis (KOA) severity
PATIENTS AND METHODS:
A total of 200 patients with KOA were diagnosed according to the American College of Rheumatology clinical criteria 2016. Demographic and clinical characteristics data were recorded. X-ray was taken for both knee joints in standing and lateral position view. Blood samples were collected PLR and NMR were calculated.
RESULTS:
Mean age was 62.3 ± 8.7 years, female to male ratio as 1.5:1. Mean BMI was 29.2 ± 6.3 kg/m^2, and knee OA duration 9.8 ± 7.8 years. Age, knee OA duration, menopausal duration, total WOMAC score and menopause were significantly correlated with increase knee OA severity (p<0,001), (p<0,001), (p<0,001), and (p=0,003) respectively while marital status was significantly inversely correlated with knee OA severity (P<0.001). Knee OA duration and total WOMAC score were the only independent predictors of knee OA severity (p<0.001), (p<0.001) respectively. PLR and NMR were not correlated with severity of KOA.
CONCLUSION:
PLR and NMR had no significant correlation with the KOA severity
KEYWORDS: Platelet lymphocyte ratio, Neutrophil Monocyte ratio, Osteoarthritis, Knee OA severity

INTRODUCTION:

Osteoarthritis (OA) is the most common joint disease with significant impact on quality of patient's life[1]. Knee OA (KOA) is one of the most common forms of the disease[2]. The literature reported an increasing evidence of inflammatory mechanisms play a role in the pathogenesis of OA. Macrophages and proinflammatory cytokines are recognized to have a part in the process. Moreover, OA also shares a similar inflammatory and biochemical profile with metabolic syndrome, and deserves attention as a systemic disease[3–6].

In clinical practice, the evaluation of knee OA is mainly based on clinical manifestation and radiographic changes.

The Kellgren-Lawrence (KL) grading scale was traditionally used to grade the severity of knee OA on radiographs[7]. A simple low-cost laboratory test that can be used as a marker of disease severity in OA has not been defined yet. It is important to identify an effective and easily accessible biomarker to monitor the progress of knee OA. Platelet lymphocyte ratio (PLR) and neutrophil monocyte ratio (NMR): Are cheap and simple useful tools for determining inflammation in various diseases, such as rheumatoid arthritis and systemic lupus erythematosus. The relationship of platelet to lymphocyte ratio and neutrophil to monocyte ratio to radiographic grades of knee osteoarthritis were reported by a previous study and concluded that PLR could reflect the inflammation response in knee OA while NMR

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emerged as an independent factor and could be used as a potential marker indicating the severity of knee OA [8].

Monocyte activation is elevated in women with knee-osteoarthritis and associated with inflammation, BMI and pain and they concluded that monocytes contribute to synovitis and disease pathogenesis in osteoarthritis[9].

Recently, PLR was considered as an available marker to determine inflammation in various diseases, such as rheumatoid arthritis[10], systemic lupus erythematosus[11], and epithelial ovarian cancer [12]. It has also been identified as an available marker for the prognostic prediction of diverse diseases [13–16]. Similar to PLR, NMR was also suggested as a potential index for identifying disease or predicting prognosis, such as skin cancer and breast cancer[17, 18]. However, there are few studies of the association of PLR and NMR with knee OA, for which the costs of laboratory tests are much lower and which are much more easily accessible.

Recognizing the limited research investigating the relationship between blood PLR and NMR and KOA severity, this study was undertaken to evaluate the relation between PLR and NMR with the severity of KOA.

PATIENTS AND METHODS:

Study design

This analytical cross-sectional study was conducted at the Rheumatology Unit in Baghdad Teaching Hospital, Medical City, (Baghdad) from January 2018 until August 2018. Ethical approval was obtained from the Department of Medicine, College of Medicine and Baghdad Teaching Hospital and patient informed consent was taken.

Patients selection

A total of 200 patients with KOA (121 females: 79 males) diagnosed according to the American College of Rheumatology criteria 2016 who attended the outpatient clinic of the Rheumatology Unit in Baghdad Teaching Hospital were included in the study[19]. Exclusion criteria were: Malignant diseases, Hematological diseases, recent history of blood transfusion, Chronic liver and kidney diseases, Infection and other autoimmune diseases, Steroid use, and post traumatic arthropathy.

Data collection: Data were collected using a pre-constructed data collection sheet which includes a (demographic data) and (clinical, laboratory and imaging) data.Patients were examined clinically and X-ray were taken for both knee joints for all patients and the radiographic grade calculated using Kellgren and Lawrence system [7].

Blood samples were collected under aseptic procedures. The NIHON KOHDEN® (Celltacα) which is a photometric pathway and The VITAL MICROSED-SYSTEM ® ESR analyzer (Europe) were used, both of which are automated analyzer for getting the final results of CBC and ESR respectively. Liver function test, renal function test, and fasting blood sugar was measured.

Statistical analysis

Anderson darling test was done to assess if continuous variables followed normal distribution. mean and standard deviation was used for normally distributed continuous variables. Discrete variables were presented by numbers and percentages. Ordinal logistic regression was used to assess the correlation of PLR and NMR with Knee OA severity. SPSS 22.0.0 (IBM, Chicago, IL), p value < 0.05 was considered statistically significant.

RESULTS:

The mean age was 62.3 ± 8.7 years, mean BMI was 29.2 ± 6.3, female to male ratio as 1.5:1, smoker 18%. Regarding knee OA severity, 37% had G2, 34.5% had G3 and 28.5% had G4. knee OA duration was 9.8 ± 7.8 years, and 22.5% used NSAIDs. The mean of PLR was 123.8 ± 40.6 and NMR was 18.6 ± 8.4 as illustrated in table 1.

Table 1: Baseline Characteristics of 200 patients with knee osteoarthritis

Variables	Value
Age (years), mean ± SD	62.3 ± 8.7
BMI (kg/m^2), mean ± SD	29.2 ± 6.3
Gender n (%)	
Female	121(60.5)
Male	79 (39.5)
Smoker n (%)	36 (18)
Knee OA severity n (%)	
G2	74 (37)
G3	69 (34.5)
G4	57 (28.5)
Knee OA duration (years), mean ± SD	9.8 ±7.8
Platelet/lymphocyte ratio	123.8 ± 40.6
Neutrophil/monocyte ratio	18.6 ± 8.4
NSAIDs n (%)	45(22.5)

SD: standard deviation, BMI: body mass index, OA: osteoarthritis, n: number, G: grade, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, NSAID: non-steroidal anti-inflammatory drug.

There was no statistical difference and correlation between PLR and NMR with Knee OA severity (PLR in G2 120.6 ± 33.9m in G3 123.4 ± 41.4, and G4 128.6 ± 47.2, P=0.271, And NMR was 19.1 ± 6.4 in G2, 19.1 ± 9.9 in G3, and 17.2 ± 8.8 in G4, p=0.254) as shown in Table 2

Table 2: ordinal logistic regression to assess correlation of Platelet Lymphocyte Ratio and Neutrophil Monocyte Ratio with Knee Osteoarthritis severity

	G2 n= 74	G3 n = 69	G4 n = 57	OR (95%CI)	p-value
PLR	120.6 ± 33.9	123.4 ± 41.4	128.6 ± 47.2	1.004 (0.997-1.010)	0.271
NMR	19.1 ± 6.4	19.1 ± 9.9	17.2 ± 8.8	0.983 (0.953-1.013)	0.254

p-value calculated and odd ratio (95% CI) using ordinal logistic regression. PLR: Platelet/lymphocyte ratio,
NMR: Neutrophil/monocyte ratio, n, number.

DISCUSSION:

The cross-sectional study assessed the relationship of PLR and NMR with Disease Severity of KOA and showed no significant correlation between PLR, NMR with KOA severity.

In literature, Shi et al[8] reported similar findings in which there was no significant correlation between PLR and KOA severity, however there was negatively significant correlation between NMR and KOA severity.

Other studies, Loukov D et al [9] concluded that monocytes contribute to low-grade inflammation occurs in OA and correlates with disease severity and progression.

Özler K (20) found that increased neutrophil leukocyte ratio is a risk factor for osteoarthritis severity. Tasoglu et al[1] reported Neutrophil lymphocyte ratio (NLR) was correlated with KOA severity.

Up to the best of our knowledge, this study may be the first study that looked for the association of PLR, NMR with the severity of KOA in a sample of Iraqi patients basic, inexpensive and easily available blood tests that may be used as markers to assess the radiographic severity of OA of the knee in the daily practice.

The current study has some limitations:

First: Small sample size was obtained.

Second: the blood sample was used one time and does not allow assessment of the stability of PLR, NMR over time. Finally, this study was a cross-sectional study and cannot assess the causation between PLR, NMR with KOA.

CONCLUSIONS:

PLR and NMR were not significantly correlated with the KOA severity. Further prospective case control studies with larger sample size, including other markers is recommended to generalize the results.

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