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Original Article

May neutrophil lymphocyte ratio and platelet lymphocyte ratio be used as inflammatory markers in patients with epicondylitis? Inflammatory markers in patients with epicondylitis

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Abstract

Aim: The aim of this study was to determine whether there is any correlation between neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and acute phase reactants such as C-reaktive protein (CRP), erythrocyte sedimentation rate (ESR) in patients with epicondylitis.

Material and Methods: Our study included 274 patients. 154 patients with epicondylitis constituted the epicondylitis group and 120 healthy individuals constituted the control group. Demographic data such as age, gender, and laboratory values such as NLR and PLR were analyzed retrospectively. Both groups were compared in terms of dermographic data, leukocyte, neutrophil, lymphocyte, platelet count, CRP, ESR, NLR and PLR.

Results: There was no significant differences between patient and control groups in term of demographic data such as height and weight, and laboratory values such as nuetrophil, lymphocyte, platelet, ESR and CRP ($p>0,05$ for all). Besides, no significant difference was found between the two groups in terms of NLR and PLR values ($p>0,05$ for both). There was a significant positive correlations between NLR or PLR and ESR or CRP values in the patient group ($p<0,001$ for all).

Conclusions: In our study, no significant difference was found between NLR, PLR and other blood paramaters in patients with epicondylitis compared to those of controls. As a result, we determined that it is not meaningful to use these rates to show the presence of inflammation in epicondylitis pathogenesis, and there is no correlation between the severity of epicondylitis and these rates. There is a need for further studies with more patient numbers and clinical evaluation parameters.

Keywords: Lateral epicondylitis; medial epicondylitis; neutrophil to lymphocyte ratio (NLR); platelet to neutrophil ratio (PLR)

INTRODUCTION

The term epicondylitis is mostly used to describe caused by overuse or stress at the muscle-tendon joints that adhere to the elbow area. The most common type is lateral epicondylitis and is also known as tennis elbow (1). Medial epicondylitis is less common than lateral epicondylitis, and is known as golfer's elbow (2). Epicondylitis is a tendinitis condition characterized by pain and tenderness in the elbow area and significant restrictions in daily life activities (1).

Although the cause and pathogenesis of epicondylitis have not been fully understood, it is thought to be caused by overloading, overuse, and repetitive movements in the elbow area (3). As a term, epicondylitis refers to an inflammatory status, although studies on this issue are limited. Although researchers have produced many theories regarding the pathophysiology of epicondylitis, authors have emphasized especially the view that micro-tears occur on the surface of the tendons around the epicondyle, particularly as a result of repeated and over loading, resulting in degeneration and tendinosis (4,5). Since histological studies could not demonstrate any inflammatory cell, the terms tendinosis or tendinopathy are used (6,7). A chemical inflammatory situation can not be mentioned in tendinosis or tendinopathy. These definitions indicate that this situation is a degeneration process. There is angiofibroblastic fibrosis developing due to the increased fibroblastic and vascular activity during this process. Vascular hyperplasia, collagen with impaired structure, and degeneration in tendons occur as a result of excessive hypovascular area (7-9).

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The most commonly used inflammatory markers in clinical practice are erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). When compatible with the clinic, high levels of ESH and CRP indicate that the disease is active, regardless of the diagnosis (10). Besides, in recent years blood values such as NLR and PLR are also used as markers of systemic inflammation in various diseases. It has been shown that these markers have been used especially in rheumatic diseases, diabetes mellitus, cardiovascular diseases, and some cancer cases (11-13). No study was found in the literature on this issue in epicondylitis. Parameters such as neutrophils, lymphocytes, and platelets are easy to examine laboratory findings that can be studied with complete blood count. Whereas NLR and PLR parameters are easily obtained by dividing neutrophil or platelet count by lymphocyte count (14-16).

In the light of this current knowledge, in this study, we aimed to investigate the relationship between NLR and PLR that are among complete blood count parameters and play a role in inflammatory events and epicondylitis and considering the importance of these parameters to evaluate whether these markers can be an indicator of disease activity and to contribute to the literature.

MATERIAL and METHODS

Files of the patients who presented to the physical therapy and rehabilitation outpatient clinic due to elbow pain and were diagnosed with epicondylitis based on clinical and MRI findings between January 1, 2018 and June 30, 2018. Files of the patients were retrospectively screened. According to the collected data, a total of 154 epicondylitis patients'records were included in the patient group, and a total of 120 age and gender- matched and had no chronic and systemic disease hospital staff's records were included in the control group. Demographic and laboratory data of the patient and control groups were recorded.

Inclusion criteria were being diagnosed with epicondylitis, being aged between 18-65, having normal laboratory values, not having had any physical therapy, not received injections, not having had elbow surgery and extracorporeal shock wave therapy. The participants with systemic infection, diabetes, rheumatological, neurological diseases, malignancy, pregnancy, non-cooperative and abnormal laboratory findings were excluded.

Laboratory outcomes of the patient and control groups were evaluated. CRP (mg/dL) and ESR (mm/hour) values were obtained from the biochemical analyses. Neutrophil (103/µL), lymphocyte (103/µL) and platelet (103/µL) counts were recorded from the hemograms. NLR value was calculated by dividing neutrophil count by the lymphocyte count. PLR value was calculated by dividing platelet count by the lymphocyte count. Laboratory and clinical evaluations were carried out from the same visit of the patients. Data of the patient and control groups were statistically compared. This study was conducted in accordance with the principles of the Declaration of Helsinki and the ethics approval was received from Aksaray University Ethics Committee (date: 26/09/208; no: 2018/179).

As a result of the power analysis conducted with the Gpower 3.1 program before the study, the minimum number of samples (with 95% confidence interval and 5% error margin) for each group was 58 people and the power of the study was 90%.

Statistical Analysis

Statistical analysis of the study was performed using SPSS 22.0 statistical package software. The normality of all data was determined with the Kolmogorov-Smirnov test. Data were expressed as a percentage (%) and mean±standard deviation (SD). A comparison of paired groups was made with Student-t or Mann-Whitney test. Correlations were determined with Spearman's analysis. $p<0.05$ values considered statistically significant.

RESULTS

The mean age was 55.31±2.30 in the patient group and 56.45±4.81 in the control groups. The majority of the patients with epicondylitis (54.5%) were female. The rate of lateral epicondylitis was 64.3%, while the rate of medial epicondylitis was 35.7%. No statistically significant difference was found between the groups in terms of sociodemographic characteristics ($p>0.05$). The sociodemographic features of the groups are shown in Table 1.

Table 1. Demographic data of the study groups

	Epicondylitis group (n:154)	Control group (n:120)	p
Age (years)	55.31±2.30	56.45±4.81	0.745
Gender (F/M), n	84/70	70/50	0.356
BMI (Kg/m^2)	30.61±4.37	31.92±3.81	0.623
Height (cm)	164.26±7.02	166.45±5.25	0.756
Epicondylitis type			
Medial	55(35.7)		
Lateral	99(64.3)		
Affected side			
Left elbow	70(% 45.5)		
Right elbow	84(% 54.5)		

BMI: Body mass index

When laboratory outcomes were compared between the patient and control groups; white cell, neutrophil, lymphocyte, and platelet counts, ESR and CRP levels were slightly higher in the patient group, although the difference was not statistically significant ($p>0.05$). The laboratory values of the groups are shown in Table 2.

Table 2. Laboratory findings of the study groups

	Epicondylitis group (n:154)	Control group (n:120)	p
Leukocytes (10^3/µl)	7.29 (4.49-9.9)	7.15 (4.4-9)	0.089
Hemoglobin (g/dL)	14.04±1.46	15.69±1.76	0.156
Neutrophils (10^3/µl)	4.22±0.87	4.12±1.24	0.067
Lymphocytes (10^3/µl)	2.27±0.60	2.26±0.71	0.359
Platelets (10^3/µl)	240.87 (175-450)	239.4 (145-355)	0.070
NLR	1.85 (0.84-4.56)	1.83 (0.67-2.86)	0.234
PLR	106.11(39-230)	105.92 (60-239)	0.267
ESR (mm/hour)	11.07±4.65	10.35±3.52	0.532
CRP (mg/L)	2.07 (0.08-4.49)	2.04 (0.18-4.90)	0.443

NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

NLR and PLR ratios were similar between the patient and control groups, and no statistically significant difference was observed between the groups (p>0.05). Significant positive correlations were found between NLR and PLR ratios and ESR (r:0.105; r:0.189) and CRP (r:0.113; r:0.255) levels in the patient group (p<0.05) (Figures 1,2,3,4).

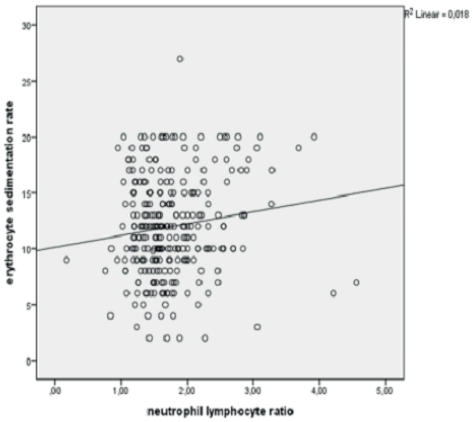

Figure 1. Correlation between NLR and ESR in the patients group

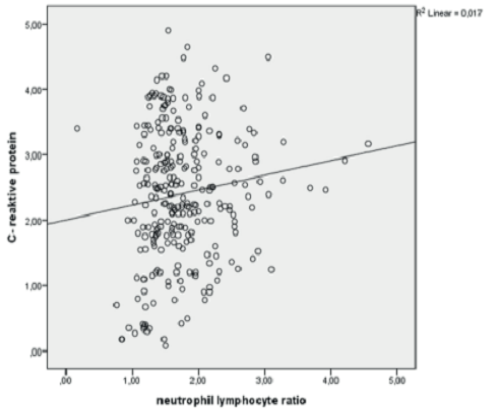

Figure 2. Correlation between NLR and CRP in the patients group

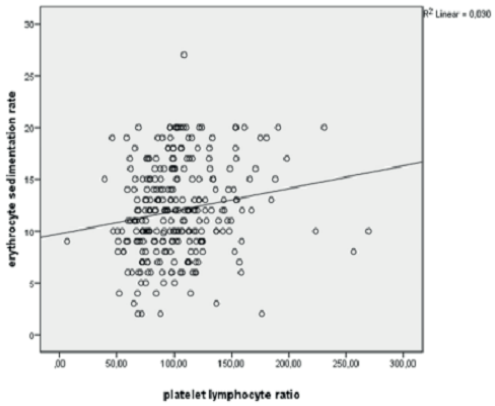

Figure 3. Correlation between PLR and ESR in the patients group

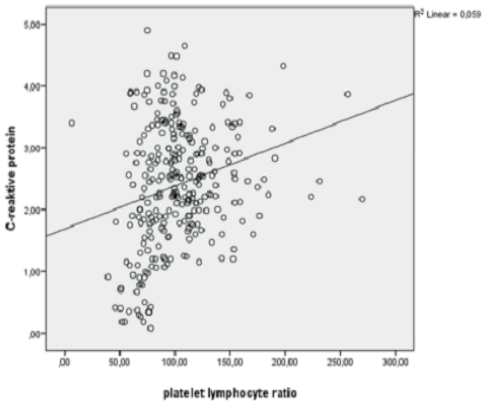

Figure 4. Correlation between PLR and CRP in the patients group

DISCUSSION

In this study, we aimed to determine whether there is any correlation between NLR, PLR and acute phase reactants such as CRP, ESR in patients with epicondylitis.

In our study, no significant difference was found between the patient and control groups in terms of NLR and PLR values. Although leukocyte, neutrophil, platelet, ESR and CRP levels were slightly higher in the patient group compared to the controls, the difference was not statistically significant. There was a significant positive correlation between NLR and PLR ratios and ESR and CRP levels in the patient group.

In recent years, blood parameters such as NLR and PLR have been used as the markers of systemic inflammation in various diseases. However, screening the literature we could not find a study performed with inflammatory markers in patients with epicondylitis. Therefore, our study is the first in the literature on this issue.

Although the term epicondylitis, in general, indicates an inflammatory condition, many studies could not find cells regarding inflammation in the elbow area. This is why the term tendinosis or tendinopathy is used. These definitions show that there is a degeneration process (17,18).

Researchers have produced numerous theories about the pathophysiology of epicondylitis, the authors have reported that especially repeating micro- traumas occur on the surface of the tendons surrounding epicondyle rather than an inflammatory process, resulting in angiofibroblastic degeneration and structural disruptions in tendons (tendinosis) (19-21). It should be remembered that angiofibroblastic hyperplasia should be present and cells forming inflammation should be absent to mention tendinosis (21,22).

Neutrophils and lymphocytes are precursor cells of the immune systems and are produced in the bone marrow. These cells have the property of initiating and increasing cytokine release that causes inflammation to begin (23). Similar to neutrophils, platelets increase cytokine release in inflammatory events, supporting increase of inflammation. Besides, neutrophil and platelet counts increase, while lymphocyte count decreases especially in inflammatory conditions (24,25).

In a retrospective study by Kılıç et al. in 2016 with 77 rheumatoid arthritis (RA) patients and 97 healthy individuals investigating the relationship with inflammatory markers; neutrophil and platelet counts were found to be higher and lymphocyte count significantly lower in the patient group compared to the controls (26). These results are expected as RA is a systemic inflammatory event. In a study by Karabaş et al. in 2018 with 25 fibromyalgia patients and 25 healthy controls, the relationship with inflammatory markers was examined and neutrophil count was found to be lower in the patient group. In the same study, lymphocyte and platelet counts were similar between the two groups and no statistically significant difference was found (27). In a study by Atar et al. with patients having knee osteoarthritis, no significant difference was observed between the patient and control groups in terms of neutrophil, lymphocyte and platelet counts (28). Similar to above- mentioned studies, also in our study we could not find a statistically significant difference between the patient and control groups in terms of neutrophil, lymphocyte, and platelet counts. Unlike RA, epicondylitis is not a systemic inflammatory event like fibromyalgia and knee osteoarthritis.

Recently, NLR and PLR values have been used in order to assess inflammation in various diseases such as various malignancies, cardiovascular diseases, cerebrovascular diseases, kidney diseases, hypertension, diabetes mellitus and inflammatory diseases (ankylosing spondylitis, rheumatoid arthritis, appendicitis, ulcerative colitis etc.) and high levels of these parameters have been shown to be an indicator of poor prognosis in various studies (11-13,29).

NLR and PLR parameters are accepted as markers of systemic inflammatory response. NLR and PLR are defined as the ratio of neutrophil and platelet counts to lymphocyte count (27). As the most important advantages, these ratios can be obtained from complete blood count without any additional cost and there for their use is increasing. In a study by Uslu et al., NLR and PLR ratios were studied in patients with rheumatoid arthritis, and were found to be statistically significantly higher compared to the control group (30). In another study, it was claimed that NLR may be an important marker in determining subclinical inflammation and the risk of developing amyloidosis in patients with familial Mediterranean fever (FMF) (31).

Ata et al. and Karabas et al. found no statistically significant difference in terms of NLR and PLR values in their study comparing patients with fibromyalgia and healthy persons (27,32). In a study by Turgay et al. with patients having fibromyalgia, no statistically significant difference was found between the healthy and patient groups in NLR and PLR values, and no correlation was found with disease activity (33).

Similar to these studies, also in our study no statistically significant difference was found between the patient and control groups in terms of NLR and PLR values. Besides, these results also indicates that epicondylitis is not a systemic inflammatory condition In the literature screening, we could not find a study to compare these ratios with disease pathogenesis or clinical symptoms in epicondylitis and to show a possible link between them. Therefore, our study is the first in the literature on this issue.

ESR and CRP are the most commonly used laboratory findings in routine clinical practice and not specific to the disease (34). Balbaloğlu et al. found significantly higher CRP levels in knee osteoarthritis patients with synovitis compared to the control group (35). Atar et al. found higher ESR and CRP levels in patients with knee osteoarthritis compared to the controls and at the same time a significant correlation between CRP level and osteoarthritis stage. This was attributed to synovitis, which is a local inflammation that plays a role in the development and progression of osteoarthritis, and not to systemic inflammation (28). In our study, no significant difference was found between the patients with epicondylitis and the control group in terms of CRP and ESR values, while a significant positive correlation was found between ESR and CRP levels and NLR and PLR ratios. We think this might be a result of the local inflammation which emerged in the cute period before angiofibroblastic degeneration and tendinosis periods, as specified by some authors for the pathogenesis of epicondylitis (4,5).

This study has some limitations. Among these, data were obtained from a single center and the numbers of participants in the patient and control groups were relatively small. Besides, the retrospective design of the study might hinder clinical evaluation of the presence of inflammation in the patients. In this respect, further studies including clinical parameters may contribute significantly to the literature. Another limitation, we had no knowledge about drug use of retrospectively screened patients. This lack of information might have led to a limitation in assessing possible drug effects on hematological parameters.

CONCLUSION

It was shown that there was a positive correlation between NLR, PLR and ESR, CRP and NLR, PLR had no significance in patients with epicondylitis compared to the control group. Further studies with a larger series of patients and clinical evaluation parameters are needed on this issue.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: A total of 154 patients diagnosed with epicondylitis based on clinical and MRI findings and 120 age and gender matched hospital staff's who had no chronic and systemic disease in our clinic between January 1, 2018 and June 30, 2018 were retrospectively evaluated. Institutional review board (IRB) approval was acquired from Aksaray University Ethics Committee.

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