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Evaluation of red blood cell distribution width in patients with fibromyalgia

Fibromiyalji hastalarında kırmızı kan hücresi dağılım genişliğinin değerlendirilmesi

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SUMMARY

Objective: In the present study we investigate the level of subclinical inflammatory markers neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and red blood cell distribution width (RDW) in FMS
Method: Included in the study were 98 patients who had been newly diagnosed with FMS according to the 2010 American College of Rheumatology (ACR) criteria and 38 healthy controls. The age, Body Mass Index (BMI), White Blood Cell (WBC), neutrophil, lymphocyte, platelet, high-sensitivity C-reactive protein (hsCRP) and Erythrocyte Sedimentation Rate (ESR) values of the participants in both groups were recorded, and also the Visual Analogue Scale (VAS) and Fibromyalgia Impact Questionnaire (FIQ) scores of the patients
Results : There was no statistically significant difference between Groups 1 and 2 with respect to NLR, PLR, and RDW values ($p>0.05$).
Conclusions: Blood NLR, PLR, and RDW values in patients with FMS have no significance in an investigation of subclinical inflammation.
Keywords: Fibromyalgia syndrome, red blood cell distribution, neutrophil, lymphocyte, platelet

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ÖZET

Amaç: Bu çalışmada Fibromiyalji sendromunda (FMS) subklinik inflamasyon belirteçleri olan nötrofil/lenfosit oranı (NLO), platelet/lenfosit oranı (PLO) ve eritrosit dağılım genişliği (RDW) seviyesini incelemeyi amaçladık.
Yöntem: Çalışmaya 2010 Amerikan Romatoloji Koleji (ACR) kriterlerine göre FMS tanısı alan 98 FMS'li hasta (Grup 1) ve 38 sağlıklı kontrol (Grup 2) alındı. Her iki grubun yaş, vücut kitle indeksi (VKİ), sigara kullanımı, beyaz küre (BK), yüksek duyarlılıklı C-reaktif protein (hsCRP) ve eritrosit sedimantasyon hızı (ESR) değerleri kaydedildi ve ayrıca Grup 1'de ek olarak hastaların görsel analog skala (GAS) ve fibromiyalji etki anketi (FEA) skorlarıda kaydedildi.
Bulgular: Grup 1 ve Grup 2'nin NLR, PLR ve RDW değerleri arasında istatiksel olarak anlamlı fark yoktu ($p>0.05$).
Sonuç: FMS'li hastalarda serum NLR, PLR ve RDW değerleri subklinik inflamasyonun göstermede herhangi bir önemi yoktur.
Anahtar sözcükler: Fibromiyalji sendromu, eritrosit dağılım genişliği, nötrofil, lenfosit, platelet

INTRODUCTION

FMS is a clinical condition that is characterized by widespread chronic pain, fatigue, sleep disturbance, and cognitive dysfunction [1]. Previous clinical studies have suggested that genetic, environmental, and immunological factors and peripheral and central mechanisms could play a role in the etiology of FMS, the pathology of which remains unknown [2,3]. FMS is defined as a non-inflammatory disease, although some clinical studies have argued that inflammatory mechanisms could play a role in the pathogenesis of FMS [4].

NLR and PLR are calculated from a complete blood count (CBC) with a blood differential test, as an inexpensive and easily obtainable marker of inflammation. Recent studies have shown that NLR and PLR may be used to measure the severity of inflammation, particularly in cardiovascular diseases, malignancies, and diabetes [5]. RDW is a parameter that is routinely reported in CBC analyses, expressing variations in the size of red blood cells [6], and recent studies of RDW have suggested its use as an inflammatory marker in rheumatoid arthritis and psoriasis [7,8]. In addition to studies suggesting that high RDW values could be a finding in favor of inflammation, recent clinical studies have shown that NLR and PLR values could also be markers of subclinical inflammation in certain rheumatic diseases [9,10].

A number of recent clinical studies have shown that systemic inflammatory mechanisms and neuro-inflammation could play a role in the etiology of FMS [11]. Investigating NLR, PLR, and RDW showing subclinical inflammation in patients with FMS may contribute to our understanding of FMS. There have to date been only limited studies evaluating PLR and RDW in patients with FMS, and these studies are often retrospective in design and include a small number of patients. In the present study, we prospectively evaluate the markers of subclinical inflammation, including NLR, PLR, and RDW, in patients newly diagnosed with FMS. Furthermore, the study evaluates the relationship between NLR, PLR, and RDW values and pain, and the quality of life in patients with FMS.

MATERIAL AND METHODS

Included in the study were 98 patients newly diagnosed with FMS, according to ACR 2010 [12], along with 38 healthy volunteers as controls.

The criteria for inclusion were: female patient aged between 18 and 65 years, newly diagnosed with FMS according to the ACR 2010 diagnosis criteria, willingness to participate in the study, under no drug treatments for the last a month, or prior to the study, and no known acute or chronic inflammatory disorders, acute or subacute infections, neurological or psychiatric disorders, malignancy, a propensity for thrombotic or bleeding disorders or undergoing anticoagulant therapy. The control group consisted of volunteers were determined as healthy, with inclusion criteria of aged 18–65 years, female, willingness to participate in the study, and no known psychiatric or metabolic disorders.

Patients with FMS were assigned to Group 1, and the healthy volunteers were assigned to Group 2. The age, height, and weight of the patients in the two groups were recorded.

Approval of the local ethics committee was obtained for the study, which was carried out in accordance with the Helsinki Declaration.

Fibromyalgia Impact Questionnaire (FIQ): An FIQ comprising 20 questions was used to assess the patients' physical function, occupational status, depression, anxiety, sleep, pain, rigidity, fatigue, and healthiness in order to evaluate the functional status of the patients, as well as the progression and results of the disease [13]. The validity and reliability of the Turkish version of the study were carried out previously by Sarmer et al. [14].

Visual Analogue Scale (VAS): The VAS was used to examine pain levels in patients. On a 10 cm long scale on which 0 means no pain and 10 means the most severe pain, the patients were requested to mark the point corresponding to their level of pain.

Blood Sample

Venous blood samples were collected into tubes with and without an anticoagulant substance from all participants on the morning following an overnight fasting period, and an automated blood cell counter (BC-6800; Mindray, Shenzhen, People's Republic of China) was used for complete blood count tests. hsCRP concentrations were measured using nephelometry (Beckman Coulter, California, USA), and ESR was determined using the Westergren method.

Statistical methods

All data analyses were carried out using SPSS (version 22.0) software (SPSS Inc., Chicago, IL, USA). Continuous data were expressed as mean±standard deviation (SD), and categorical data were expressed as a percentage (%). The

normal distribution of the data was analyzed using visual (histogram) and analytical methods (Kolmogorov-Smirnov/Shapiro Wilk tests). The Student's t-test and Pearson correlation test were used in the data analysis when the parametric test assumptions were met, a Mann-Whitney U-test was used when the parametric test assumptions could not be met, and a Chi-square test was used to evaluate the categorical data. A p-value <0.05 was accepted as statistically significant.

RESULTS

The study included 98 patients with FMS (Group 1) and 38 healthy controls (Group 2), and there was no statistically significant difference between the groups in terms of age, BMI, WBC, hsCPR or ESR (p>0.05). The sociodemographic data of the groups and their WBC, CRP, and ESR values are presented in Table 1. There was no statistically significant difference identified between the NLR, PLR, and RDW values of Groups 1 and 2 (p>0.05). The NLR, PLR, and RDW values of the two groups are shown in Table 2. Furthermore, there was no significant correlation between the NLR, PLR, and RDW values of Group 1 and the VAS and FIQ scores (p>0.05).

Table 1: Sociodemographic data of groups, and ESR, hsCRP and WBC values of groups

		Grup 1(n=98) Mean±SD	Grup 2 (n=38) Mean±SD	*p value
Age (years)		49.13±11.33	47.57±12.47	0.506
BMI (kg/m^2)		29.06±5.96	28.41±5.49	0.545
WBC (10^9/ml)		6.7±1.7	7.2±1.5	0.058
hsCRP (mg/dl)		4.43±2.71	5.24±2.84	0.333
ESR (mm/h)		15.14±8.97	13.29±6.79	0.197
Tobacco use	Positive,n(%)	14 (15.3)	9 (23.7)	0.208
	Negative,n(%)	84 (85.7)	29 (76.3)	

Statistically significant(p<0,05) when compared with the control group. BMI: Body Mass Index; ESR: erythrocyte sedimentation rate; hsCRP: High-sensitivity C-reactive protein; WBC: White blood cell

Table 2: NLR, PLR and RDW values of groups

	Group 1 (n=98) Mean±SD	Group 2 (n=38) Mean±SD	*p value
NLR	2.07±1.06	1.84±0.59	0.107
PLR	131.47±51.87	118.31±31.10	0.073
RDW (%)	13.93±1.19	14.36±3.64	0.485

*Statistically significant(p<0,05) when compared with control group; NLR: neutrophil / lymphocyte ratio; PLR: platelet / lymphocyte ratio; RDW :Red blood cell distribution width

DISCUSSION

The present study identified no significant difference in the serum NLR, PLR, and RDW values of the patients with FMS and the healthy volunteers, and these findings are consistent with those in previous literature[15,16]. Furthermore, the study also found no significant relationship between the serum NLR, PLR and RDW values and VAS and FIQ scores of patients with FMS. The present study is the first to identify a lack of a relationship between VAS scores and RDW values, as well as a lack of a relationship between FIQ score and the markers of subclinical inflammation.

NLR is used as a marker in viral and bacterial infections, and also of subclinical inflammation in some diseases [17]. It is particularly important in demonstrating inflammation in the diagnosis of

such diseases like coronary artery disease, diabetes mellitus, ulcerative colitis, and inflammatory arthritis [18,19]. On the other hand, there have been studies reporting that PLR may also be used as an inflammatory parameter in demonstrating subclinical inflammation [20]. High PLR values are thought to be of particular prognostic importance in breast cancer, ovarian cancer, and colorectal cancer [21]. Furthermore, various clinical studies have shown higher NLR and/or PLR values in patients with such rheumatic diseases as rheumatoid arthritis, systemic lupus erythematosus, Behçet's disease, and familial Mediterranean fever than in healthy individuals [22,23]. In a retrospective study, Boyraz et al. found no significant difference in the NLR and PLR values of patients with FMS and healthy individuals [16], and concurring with their findings, the present study found no statistically significant difference between patients with FMS and healthy individuals in terms of NLR and PLR values. In their study, Aktürk et al.[24] reported higher NLR values in patients with FMS than in healthy individuals , while İlgün et al.[25] found higher serum PLR values in patients with FMS than in the healthy controls. The findings of the latter two studies reporting higher NLR and PLR values in patients with FMS differ from the findings of the present study.

A high RDW value is a poor prognosis marker in cardiovascular diseases [26], and elevated RDW values have also been reported in liver disease, inflammatory bowel disease, and colon cancer, among others [27]. In addition to high NLR and PLR values, a high RDW value is also related to chronic subclinical inflammation [7]. In their study, Uslu et al. [28] showed higher RDW values in patients with FMF than in healthy subjects. A review of the literature revealed only two clinical studies investigating RDW values in patients with FMS, the first of which found no significant difference in the RDW values of patients with FMS and healthy individuals [15]. In another study, Alves et al. [29] found no significant difference between the RDW values of patients with FMS and healthy individuals. In the present study, no significant difference was noted in the RDW values of patients with FMS and healthy individuals.

The present study can be considered limited in terms of its cross-sectional study design, the small number of subjects in the patient and control groups, the inclusion of only recently diagnosed patients with FMS, the inclusion of no male patients with FMS, and the lack of evaluations of other factors, that could affect pain and quality of life.

In conclusion, NLR, PLR, and RDW are unsuitable for the evaluation of subclinical inflammation in patients with FMS, and they are not useful in the diagnosis of FMS. Furthermore, there is no relationship between the NLR, PLR and RDW values of patients with FMS and VAS and FIQ scores, although there is a need for further clinical studies investigating NLR, PLR and RDW values involving a larger group of patients with FMS.

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