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Association of Mean Platelet Volume with Bone Mineral Density in Fibromyalgia

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BACKGROUND/AIMS
We aimed to evaluate the mean platelet volume levels in patients with fibromyalgia and to determine whether there is a relationship between mean platelet volume and bone mineral density.

MATERIAL and METHODS
One hundred female patients with the diagnosis of fibromyalgia included in the study. The age, gender, weight, height, body mass index, mean platelet volume, fibromyalgia impact questionnaire score, bone mineral density (g/cm^2), and T- score of LI-4, femoral neck, and femur total were recorded.

RESULTS
The mean age of the patients was 48.29±10.53 years. The mean platelet volume level and fibromyalgia impact questionnaire score were 10, 45±1.87 fL and 61.71±17.16, respectively. The mean LI-L4 T-score was -1.52±1.26, mean femoral neck T-score was -0.89±0.99, BMD was 0.86±0.13 for LI-4, 0.89±0.13 for the total femur, and 0.75±0.09 for femoral neck. We found increases in the BMD, total, and femoral neck score when MPV decreased. MPV was found higher in osteoporotic fibromyalgia patients compared to normal BMD. No significant correlation was found between MPV and these parameters.

CONCLUSION
The mean platelet volume is meaningful for osteoporosis in fibromyalgia patients. Higher MPV may be related to the reason that osteoporosis is affected by inflammatory processes in fibromyalgia patients.

Keywords: Fibromyalgia, bone mineral density, mean platelet volume

INTRODUCTION

Fibromyalgia is a multi-symptom disorder, characterized mainly by chronic widespread musculoskeletal pain, chronic widespread pain, fatigue, sleep disturbances, and many other symptoms that impair the quality of life (QoL) (1). It is found in 2–4% of the population. Pain is the predominant symptom with allodynia and hyperalgesia being common signs (2). On physical examination of soft tissue tenderness, the presence of at least 11 of 18 defined tender points is observed (3). There are no specific laboratory abnormalities and they have a limited role in the evaluation of fibromyalgia (4). The multidisciplinary approach and patient self-management are important keys for the treatment of fibromyalgia. Successful management of fibromyalgia includes patient education, cognitive behavioral therapy, exercise, and drug therapy. Tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, gabapentin, pregabalin, pramipexole, tramadol, or other opioids are some of the pharmacological therapies effective in fibromyalgia (2). Somatic and psychological symptoms lead to poor health-QoL (5). Therefore, the approach to treating fibromyalgia should focus on maintaining or improving function, improving QoL, and managing symptoms (3).

With the aging population and longer life span, osteoporosis (OP) has become an epidemic, making this a major public health problem (6). Primary OP is most often related to either postmenopausal estrogen loss or age. Glucocorticoids, diabetes mellitus, rheumatoid arthritis, liver diseases, and hematological malignancies such as multiple myeloma are some of the etiological factors of secondary OP (7). OP is often called a "silent disease" or "silent thief" without warning signs or symptoms. Falls, fractures, and functional decline are important complications of OP, affecting QoL in patients (6, 8). OP in fibromyalgia has

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been investigated in various studies (9, 10). The related factors for OP in fibromyalgia patients are as follows: reduced daily activities, reduced sun exposure, and vitamin D deficiency (10). Erdal et al. (9) evaluated bone mineral density (BMD) in 38 fibromyalgia patients and 20 healthy controls. They found that BMD was lower in the fibromyalgia group compared to the control group (9). Moreover, Jensen et al. (10) analyzed BMD in 31 women with fibromyalgia and 41 healthy women. However, they found no differences in BMD in both the lumbar spine and the femoral neck.

Mean platelet volume (MPV) is one of the most widely used markers of platelet function and activation. It reflects the inflammatory burden in inflammatory disorders (11). It was found to increase with aging, a well-known risk factor for OP (12). Also, megakaryocytes can increase osteoblast proliferation in vivo and in vitro (13). The association between MPV and BMD is still the subject of research (14-16). Li et al. (14) found a significant negative correlation between MPV and femoral neck-lumbar BMD. According to Resorlu et al. (15), MPV was higher in osteopenic patients and a significant negative correlation was found between MPV and femoral neck T-score. In another study, a significant positive correlation was found between MPV and femoral neck BMD in a normal weight osteoporotic group (16).

To the best of our knowledge, the association between MPV and BMD has not been investigated in fibromyalgia. Our study aimed to assess the association between MPV and BMD in fibromyalgia patients. Also, we evaluated the fibromyalgia impact questionnaire (FIQ) score and body mass index (BMI) in fibromyalgia patients and their association with MPV.

MATERIAL and METHODS

In this retrospective study, a total of 100 patients with fibromyalgia who were admitted to Physical Medicine and Rehabilitation, Division of Rheumatology were enrolled in the study. Our study was conducted according to the criteria set by the declaration of Helsinki. All participants signed the informed consent form. All fibromyalgia patients were diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria (17). We recorded patients' age, body weight, height, BMI, MPV, FIQ scores, BMD (g/cm2) of the lumbar vertebrae LI-L4 and femoral neck, and total femur T-score.

OP is defined as a BMD with 2.5 standard deviations (SD) or more below the average value for young healthy women (a T-score of <-2.5 SD) (18). The health status of fibromyalgia patients was determined by the FIQ score 1991 version. It consists of 10 items. The physical impairment items are rated on a 4-point Likert type scale. Responses range from 0 (always) to 3 (never). The "Feel Good" item response includes the number of days of the past week. The "Work Missed" item response includes the number of workdays in the past week. The other symptom-based items use a 100-mm anchored visual analog scale. The final score ranges from 0 to 80 (19).

Main Points:

- Osteoporosis is affected by inflammatory processes in fibromyalgia patients.
- Mean platelet volume is a simple and available blood parameter to evaluate activated platelets.
- Mean platelet volume elevation may be related to osteoporosis in fibromyalgia patients.

The inclusion criteria were age over 18 years and a diagnosis of fibromyalgia according to the ACR/EULAR 2010 criteria. Exclusion criteria were the presence ofa spinal implant, pregnancy, lactation, use of drugs which may cause OP and affect inflammation/MPV, and additional comorbidities (especially diseases affecting thrombocytes).

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences version 19.0. Descriptive statistics were given as number (n), frequency (%), mean±standard deviation, and median [25-75p] according to the distribution analysis. The Kolmogorov-Smirnov test was used to determine whether the quantitative variables were normally distributed or not. One-Way ANOVA test was used to determine differences between independent groups. Pearson's and Spearman's correlation tests were used to determine the relationship between variables according to the normality distribution. A p-value of less than 0.05 was considered statistically significant.

RESULTS

One hundred fibromyalgia patients were enrolled in our study. Allpatients were female. The mean age of the patients was 48.29±10.53 years. The patients included in our study were divided into 3 groups based on DEXA as follows: normal, osteopenic, and OP. Among these patients, 49% were osteopenic and 16% were osteoporotic. There were no significant differences in age and gender between groups. The mean LI-4 T-score was -1.52±1.26 in all patients. The median T-score of total femur and femoral neck was -0.5 [-1.1–0.3] and -0.9 [-1.5–0.1], respectively. The mean BMD was 0.86±0.13 for LI-4, 0.89±0.13 for total femur, and 0.75±0.09 for femoral neck.

The mean MPV level was 10.45±1.87 fL in patients with fibromyalgia. It was 10.57±1.93 in osteopenic, 10.43±0.83 in osteoporotic, and 10.29±2.14 in normal patients with fibromyalgia. MPV was higher in osteopenic and osteoporotic patients compared with normal patients. However, no significant differences in MPV were found between groups. We found an increase in the BMD, total, and femoral neck score when MPV decreased. However, there was no significant correlation between MPV and these

TABLE I. The demographic features and laboratory findings of the patients with fibromyalgia

Age (years)	48.29±10.53
Gender (Female/Male)	100/0
Body Mass Index (kg/m^2)	31.47±7.12
Mean Platelet Volume (fL)	10.45±1.87
T-score/Lomber	
• LI-L4	-1.52±1.26
• T-Score/Femur*	
• Neck	-0.9 [-1.5-0.1]
• Total	-0.5 [-1.1-0.3]
Bone Mineral Density (g/cm^2)	
• LI-4	0.86±0.13
• Total Femur	0.89±0.13
• Femur Neck	0.75±0.09
Fibromyalgia Impact Questionnaire	61.71±17.16

*median [25-75p]

TABLE 2. The correlation analyses between mean platelet volume, fibromyalgia impact questionnaire and T-scores, bone mineral density in patients with fibromyalgia

Parameter (value)	Mean Platelet Volume (10.45±1.87)	FIQ (61.71±17.16)
T-score/Lomber		
• LI-L4 (-1.52±1.26)	p=0.997, r=0.000	p=0. 469, r=-0.073
T-Score/Femur*		
Neck (-0.9 [-1.5--0.1])	p=0.615, r=-0.051	p=0. 346, r=0.095
• Total (-0.5 [-1.1-0.3])	p=0.141, r=-0.162	p=0. 666, r=0.048
Bone Mineral Density (g/cm²)		
LI-4 (0.86±0.13)	p=0.151, r=-0.161	p=0. 431, r=-0.089
Total Femur (0.89±0.13)	p=0.196, r=-0.143	p=0. 959, r=0.006
Femoral Neck (0.75±0.09)	p=0.291, r=-0.117	p=0. 912, r=0.012

*median [25-75p], FIQ: Fibromyalgia Impact Questionnaire

parameters. The mean FIQ score was 61.71±17.16. The demographic features and laboratory findings of the patients with fibromyalgia are shown in Table I.

The correlation between T-scores of LI-4, femoral neck, total femur, and BMD of the same regions and MPV were calculated. There was no correlation between MPV and T-scores of femoral neck (p=0.615, r=–0.051), total femur (p=0.141, r=–0.162), and LI-4 (p=0.997, r=0.00). The distribution of correlation analyses between T-scores, BMD, MPV, and FIQ score is shown in Table 2.

When the BMI of patients was evaluated, 14%had a normal weight and 86% were above normal weight. There was no correlation between MPV and LI-4, total femur, and femoral neckT-score in patients with normal BMI. Moreover, no significant difference was found between BMI and these parameters. The results were similar in the group with BMI above normal limits. Patient age showed a negative correlation with LI-4 T-score and femoral neck T-score (r=0.231, p=0.02, r=0.253, p=0.01, respectively).

DISCUSSION

The pathogenesis of fibromyalgia includes central and autonomic nervous system dysfunctions, neurotransmitters, hormones, external stressors, and psychiatric aspects (20). Also, reports show that the immune system and inflammatory mechanisms play roles in this pathogenesis (21). Mast cells, dendritic cells, and T-lymphocytes have a role in the inflammatory processes of fibromyalgia (22). The upregulation of pro-inflammatory cytokines, including TNF-α, IL-1, and IL-6, are related to several disease-related comorbidities in fibromyalgia. All these processes are defined as "neuro-inflammation" (21).

In a study, higher neutrophil-lymphocyte ratio (NLR), MPV, and lower platelet distribution width (PDW) were reported in fibromyalgia patients compared to the control group (23). Akaltun et al. (24) evaluated MPV, NLR, and PDW values in 91 fibromyalgia patients and 33 healthy volunteers. They found higher MPV, CRP, and lower PDW in the fibromyalgia group. Also, they found a significant difference between the groups in terms of NLR (24). Haliloğlu et al. (25) reported higher MPV levels in fibromyalgia patients than in the control group (8.09±0.84 fl vs 7.73±0.65 fl). Also, higher NLR and MPV, and a lower PDW were reported in fibromyalgia patients in another study with 197 fibromyalgia patients and 53 healthy controls (23). The mean MPV of patients in our study was 10.45±1.87 fL. It was 10.57±1.93 in osteopenic, 10.43±0.83 in osteoporotic, and 10.29±2.14 in normal patients with fibromyalgia. The mean MPV was 10.29±2.14 in normal patients with fibromyalgia. The mean MPV was higher in osteopenic and osteoporotic patients compared to patients with normal BMD. However, there were no significant differences in MPV between groups. There are many factors such as adenosine diphosphate, thromboxane A2, platelet-activating factor, and pro-inflammatory cytokines that affect platelet activation (26). Serotonin has an important role in the pathogenesis of fibromyalgia and activates platelets (27). Significantly lower serum serotonin levels were reported in fibromyalgia patients compared to healthy individuals and a non-significant correlation was found between serum serotonin levels and platelet indices (27). However, we could not evaluate serotonin levels in patients with fibromyalgia.

The association between MPV and OP was reported in 175 Turkish postmenopausal women (16). In this study, 20 patients were normal, 37 patients were osteopenic, and 126 patients were osteoporotic. They found a positive correlation between MPV and femoral neck BMD in the normal weight osteoporotic group, and a significant negative correlation in the overweight-obese osteoporotic group. In our study, we evaluated 100 fibromyalgia patients. All the patients were female, with 49% of osteopenic and 16% of osteoporotic patients. With regards to BMI, there was no correlation between MPV and both femoral and LI-4 T-score in patients with normal BMI. The results were similar in the group with BMI above normal. Also, the association between MPV and BMD (30 normal vs 20 osteopenic) has been investigated in ankylosing spondylitis patients (15).

In a study, MPV was high in osteopenic patients than the normal group (16). The T-score of LI-4, femoral neck, total femur, and BMD(g/cm2) of the femur and lumbar vertebrae were evaluated in all patients included in our study. The mean BMD was 0.86±0, 13 for LI-4, 0.89±0.13 for total femur, and 0.75±0.09 for femoral neck. The mean total lumbar T-scorewas-1.52±1.26. The median T-score of total femur and femoral neck was -0.5 [-1.1–0.3] and -0.9 [-1.5–0.1], respectively in all patients.

The mean MPV was 10.57±1.93 in osteopenic and 10.43±0.83 in osteoporotic patients. We found an increase in the BMD ofLI-4 and femoral neck score when MPV decreased. However, there was no significant correlation between MPV and T-scores and BMD of these regions (Table 2).

OP in fibromyalgia has (9, 10). Aging is a well-known risk factor for OP. Also, MPV was found to been investigated in various studies increase with aging (1). Moreover, megakaryocytes in the bone marrow increase with age, leading to an imbalance between osteoblastic and osteoclastic functions (13). There was a statistically significant correlation between age and both LI-4 and femoral neck T-score. There were 5 geriatric patients in our study. Psychological factors, physical, and emotional distress have been frequently identified in fibromyalgia (28). Fibromyalgia has a greater impact on daily life; patients have more difficulties adjusting to the disease and generally use poor strategies to cope with pain (29). Erdal et al. (9) evaluated depression with the Beck scale and its correlation with BMD in fibromyalgia. They found a negative correlation between Beck's scale and BMD (9). In another study, pain and degree of physical activity in daily life were evaluated in premenopausal fibromyalgia (10). It

showed that self-reported pain and FIQ-activities of daily living among fibromyalgia patients were correlated with BMD. In our study, the mean FIQ score was 61.71±17.16. MPV increased with the FIQ score. No significant correlation was found between MPV and FIQ score (p>0.05). To the best of our knowledge, the association between FIQ score and BMD in fibromyalgia has not been previously investigated. In our study, the FIQ score was higher in osteopenic patients compared to patients with normal BMD (65.32±16.69 vs 59.18±17.98). However, there were no significant differences between groups and correlation for FIQ scores. This result shows that bone mass affects the health status of fibromyalgia patients. Also, no correlation was found between FIQ score and T-scores and BMD of the areas (Table 2). The limitations of our study were that we evaluated the association between MPV and BMD in a small number of fibromyalgia patients. Also, the study was designed as a cross-sectional-retrospective study. However, to the best of our knowledge, our study was the first to assess the association between MPV, FIQ score, and BMD in fibromyalgia.

Consequently, MPV is a simple and available blood parameter to evaluate activated platelets. According to our study, MPV was higher in osteoporotic fibromyalgia patients compared to normal BMD. This may be related to the fact that OP is affected by inflammatory processes in fibromyalgia patients. However, the difference was not significant. If there is no other condition to explain MPV elevation, it may be thought that this condition may be related to OP in the differential diagnosis for patients with fibromyalgia. More studies with more patients are warranted to elucidate the association between MPV and BMD in fibromyalgia.

Ethics Committee Approval: N/A

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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