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Research Article

# The relationship between bone mineral density and hematological parameters in the geriatric age group

Geriatrik yaş grubunda kemik mineral dansitesinin hematolojik parametrelerle ilişkisi

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## ABSTRACT

**Introduction:** As populations gradually become older, osteoporosis manifests itself as an important public health problem. Studies have shown that inflammation plays a critical role in the pathogenesis of osteoporosis. NLR (neutrophil to lymphocyte ratio) and PLR (platelet to lymphocyte ratio) are simple, non-invasive, and inexpensive markers of inflammation in malignancies and inflammatory diseases. This study aims to compare osteopenic, osteoporotic, and control subjects, who do not have other known diseases or a history of medication use, in terms of their NLR and PLR levels and evaluate the relationship between NLR, PLR levels and BMD.

**Methods:** This cross-sectional study included a total of 308 patients aged 65 or above. Total bone mineral density (BMD) was measured using dual energy X-ray absorptiometry (DEXA). Complete blood count (CBC), biomarkers of inflammation (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), glucose/lipid metabolism, and thyroid function test results were recorded.

**Results:** The osteoporosis group demonstrated higher NLR levels compared to the osteopenic and control groups (respectively 3.58 ± 4.22, 2.64 ± 1.99, and 2.36 ± 1.39), and this relationship between the groups was found to be statistically significant (p=0.025). Our data revealed higher sedimentation values for the osteoporosis group than for the osteopenic and healthy control groups with statistical significance (p=0.011).

**Conclusions:** The fact that individuals with geriatric osteoporosis demonstrate elevated NLR levels and that this elevation is also seen in sedimentation suggests that inflammation plays an important role in bone remodelling.

**Keywords:** Bone mineral density, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, inflammation

## ÖZ

**Giriş:** Toplumların giderek yaşlanması sonucu osteoporoz önemli bir halk sağlığı sorunu olarak karşımıza çıkmaktadır. Yapılan çalışmalarda inflamasyonun osteoporozun patogenezinde kritik bir rol oynadığı gösterilmiştir. NLR (neutrophil to lyphocyte *ratio* ) ve PLR (platelet to lyphocyte *ratio* ) maligniteler ve inflamatuar hastalıklarda basit, invazif olmayan ve uygun maliyetli bir inflamasyon belirtecidir. Bu çalışmanın amacı bilinen başka ek hastalığı ve ilaç kullanım öyküsü olmayan osteopenik, osteoporotik ve kontrol deneklerinde NLR ve PLR düzeylerini karşılaştırmak ve NLR, PLR düzeyleri ile KMY arasındaki ilişkiyi değerlendirmektir.

**Yöntem:** Bu kesitsel çalışmaya 65 yaş ve üzeri toplam 308 hasta dahil edildi. Tüm vücut BMD (bone mineral densıty) çift enerjili X ışını absorpsiyometrisi (DEXA) ile ölçülmüştür. Tam kan sayımı (CBC), inflamasyonun biyobelirteçleri C-reaktif protein (CRP), eritrosit sedimantasyon hızı (ESR), glukoz / lipid metabolizması, tiroid fonksiyon testleri kayıt altına alınmıştır.

**Bulgular:** Osteoporoz grubunda, NLR düzeylerinin osteopenik ve kontrol grubuna göre yüksek olduğu bulundu (sırasıyla 3,58 ± 4,22, 2,64 ± 1,99 ve 2,36 ± 1,39) ve gruplar arasındaki bu ilişki istatistiksel olarak anlamlı saptandı ( p = 0,025). Elde ettiğimiz verilerde sedimantasyon değerleri osteoporoz grubunda osteopenik ve sağlıklı kontrol grubuna göre yüksek saptanmış olup istatistiksel olarakta anlamlıydı (p=0,011).

**Sonuç:** Yaşlı osteoporozu olan bireylerde NLR seviyelerinin yükselmesi ve bu yüksekliğin sedimantasyonda da olması kemik remodellinginde iltihaplanmanın önemli bir rol oynayabileceğini düşündürmektedir.

**Anahtar kelimeler:** Kemik mineral dansitesi, nötrofil/lenfosit oranı, trombosit/lenfosit oranı, inflamasyon

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## Introduction

Osteoporosis is a bone disease that increases the risk of fractures as a result of decreased bone strength due to low bone mineral density and distorted bone mineralization micro-architecture. This asymptomatic condition is usually not diagnosed until a fracture of the hipbone, spine, proximal humerus, pelvis and/or wrist is encountered due to a fall trauma and the patients are usually hospitalized [1,2]. The prevalence of osteoporosis in the United States of America is currently 10 million people and it is estimated to exceed 14 million until 2020. Although osteoporosis is typically associated with women, one of every five Americans diagnosed with osteoporosis or low BMD is male [3]. Besides being the main cause of fractures in the geriatric population, osteoporosis is also strongly connected to serious complications and a bedridden state [4]. Bones protect the organs of the body from trauma and allow the storage of minerals such as calcium and phosphorus, which are required for bone development and stability. Individuals continue to produce bones after they are born, reach the highest bone mass around the age of 30, and then start to experience a gradual decrease in bone mass. Although peak bone mass is largely dependent on genetics, many variable factors such as nutrition, exercise, and certain diseases and/or medications may affect bone mass [5].

The relationship between osteoblasts, osteoclasts, and proinflammatory cytokines shows that inflammation plays a role in the pathogenesis of osteoporosis [6-8]. Certain in vitro and rodent studies determined a significant correlation between BMD and levels of inflammatory markers such as interleukin-1 (IL-1), interleukin-6 (IL-6), CRP, and tumour necrosis factor-alpha (TNF-a) [9, 10]. Furthermore, Barbour et al. have recently shown that high levels of inflammatory markers were connected to an increased hipbone fracture risk in older women [11]. NLR emerged as a simple, inexpensive, and practical inflammation marker associated with certain inflammatory, cardiovascular, and neoplastic diseases. Moreover, NLR was shown to be superior to the white blood cell count in patients with cardiovascular diseases and malignancies [12, 13]. Considering that there are no studies that have investigated the relationship of NLR and PLR with osteoporosis, we conducted this study to investigate whether or not NLR and PLR levels are different in osteoporotic patients and to evaluate their correlations with other laboratory parameters in the geriatric population

## Methods

This cross-sectional study included 308 patients aged 65 or above who had presented to the outpatient clinic of interneal medicine between March 2015-September 2018. All patients underwent a complete geriatric evaluation and were questioned for a history of co-morbidities. The control group was composed of individuals who presented to the hospital for routine controls and had normal BMD. Both groups were tested for the presence of osteoporosis by performing a total body BMD measurement using dual energy X-ray absorptiometry (DEXA). BMD results were divided into three groups according to the World Health Organization criteria as normal (T -score $\geq$ -1.0 SD), osteopenia (T -score between -1.0 and -2.5 SD), and osteoporosis (T -score $\leq$ -2.5 SD). CBC, fasting plasma glucose (FPG), ESR, CRP, blood urea nitrogen (BUN), creatinine, calcium (Ca), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein albumin, vitamin D, total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) cholesterol, triglyceride (TG), and thyroid stimulating hormone (TSH) values of the patients were accessed through the patient file system. NLR was computed by dividing the neutrophil count with the absolute lymphocyte count and PLR by dividing the absolute platelet count with the absolute lymphocyte count.

Patients with malignant diseases, liver failure, kidney failure, active infectious diseases, secondary osteoporosis, type 2 diabetes, coronary artery disease and history of medication use with effects on bone metabolism were excluded from the study. This study was conducted in accordance with Helsinki Declaration guidelines.

### Ethical Approval

Fırat University ethics committee granted approval for this study (No:07, date: 28.03.2019).

### Statistical Analysis

All statistical analyses were performed using a computer packaged program (SPSS-22). In addition to descriptive statistical methods [Mean ( $\bar{X}$ ), Standard deviation (SD)]; quantitative data was analyzed using the Student's t-test in testing parameters that show normal distribution and one-way variance analysis in comparisons across groups (One-way ANOVA). The Wilcoxon matched pairs test, which assesses the significance of the difference between pairs was utilized and the chi-square test was used for the comparison of qualitative data. The results were evaluated with a 95% confidence interval and a $p<0.05$ level of significance.

## Results

This study included a total of 308 individuals, of which 169 were in the osteoporosis group, 93 in the osteopenia group, and 46 in the healthy control group. Mean ages and associated standard deviations were determined as 73.6±6.1 years for the osteoporosis group, 73.4±6 years for the osteopenia group, and 74.2±7.3 years for the healthy control group. Female patients comprised 86.9% of the osteoporosis group, 75.2% of the osteopenia group, and 65.2% of the healthy control group

NLR levels were higher in the osteoporosis group (3.5±4.2) compared to the osteopenia group (2.6±1.9) and the control group (2.3±1.3), and this difference was statistically significant (p=0.025) (Fig.1). As another parameter, PLR was higher in the osteoporosis group (179.1±130.7) compared to the osteopenic (163.5±109.9) and control groups (153.5±88.2) but this relationship was not statistically significant (p=0.34). Sedimentation values of the osteoporosis group were also higher compared to the other two groups with statistical significance (respectively, 27±18.5; 26.2±17.6; 20.2±18.2), (p=0.01). Osteoporosis, osteopenia, and control groups did not demonstrate any statistically significant differences in terms of the tested biochemical parameters, thyroid function tests, and vitamin D levels. NLR levels did not show a notable difference between male and female

sexes (respectively 3.2±2.6 and 3±3.5) and there was no statistical significance (p=0.72). PLR levels did not show a notable difference between male and female sexes (respectively 183.3±129.6 and 167.4±116.6) and there was no statistical significance (p=0.35).

**Table 1.** Demographics and laboratory parameters of study population.

| Parameters | Osteoporosis(n=169) | Osteopenia(n=93) | Healthy Control (n=46) | p value |
|---|---|---|---|---|
| **Age (years)** | 73.6±6.1 | 73.4±6 | 74.2±7.3 | 0.76 |
| **Gender, female(%)** | 147(%86.9)[a] | 70(%75.2) | 30(%65.2) | 0.02* |
| **NLR** | 3.5±4.2[a] | 2.6±1.9 | 2.3±1.3 | 0.02* |
| **PLR** | 179.1±130.7 | 163.5±109.9 | 153.5±88.2 | 0.34 |
| **ESR (mm/h)** | 29.3±18.6[a] | 26.2±17.6 | 20.2±18.2 | 0.01* |
| **CRP (mg/dl)** | 10.1±20.3 | 13.9±30.8 | 10.9±20.1 | 0.46 |
| **HGB (g/dl)** | 13.5±9.2 | 12.9±1.7 | 12.8±1.3 | 0.74 |
| **WBC (k/µL)** | 7.3±3 | 7.9±2.6 | 7.6±2.5 | 0.25 |
| **BUN (mg/dl)** | 19.9±11 | 20.7±14.1 | 20.8±10.4 | 0,82 |
| **Creatinine (mg/dl)** | 0.8±0.4 | 0.7±0.4 | 0.8±0.3 | 0.24 |
| **Ca (mg/dl)** | 9.1±0.7 | 9.1±0.7 | 9.1±0.6 | 0.96 |
| **Total protein (g/dl)** | 6.9±0.7 | 7±0.6 | 6.9±0.4 | 0.58 |
| **Albumin (g/dl)** | 4±0.5 | 4±0.4 | 4±0.3 | 0.84 |
| **TSH (mlU/ml)** | 1.8±2.8 | 1.6±1.2 | 1.7±1.3 | 0.85 |
| **FT4 (mlU/ml)** | 1.2±0.6 | 1.2±1 | 1.2±0.2 | 0.89 |
| **VitaminD (mg/l)** | 18.4±10.3 | 16.7±9.8 | 16.5±8 | 0.31 |
| **ALT (U/l)** | 18.4±19.4 | 20.7±15.4 | 21.4±14.7 | 0.71 |
| **AST (U/l)** | 25.4±26.3 | 22.7±11.4 | 23.6±13.2 | 0.60 |
| **Platelet (k/µL)** | 267.4±89.9 | 277.8±95.6 | 260.5±73.6 | 0.51 |
| **Neutrophil (k/µL)** | 4.7±2.8 | 4.9±2.1 | 4.5±1.7 | 0.73 |
| **Lymphocyte (k/µL)** | 1.7±0.8[b] | 2.1±0.9 | 2.3±1.3 | <0.001* |
| **MPV**(fl) | 8±0.2 | 8±0.2 | 7.9±0.2 | 0.71 |
| **RDW(%)** | 14.4±0.8 | 14.3±0.7 | 14.4±0.8 | 0.55 |

**ESR:** erythroid sedimentation rate; **CRP:** C-reactive protein; **ALT:** alanine aminotransferase; **AST:** aspartate aminotransferase; **FT4:** Free thyroxine; **TSH:** Thyroid-stimulating hormone; **MPV:** Mean platelet volume; **RDW:** Red Cell Distribution Width; When compared to the healthy control group: [a]p <0.05, [b]p <0.001; * Statistically significant differences

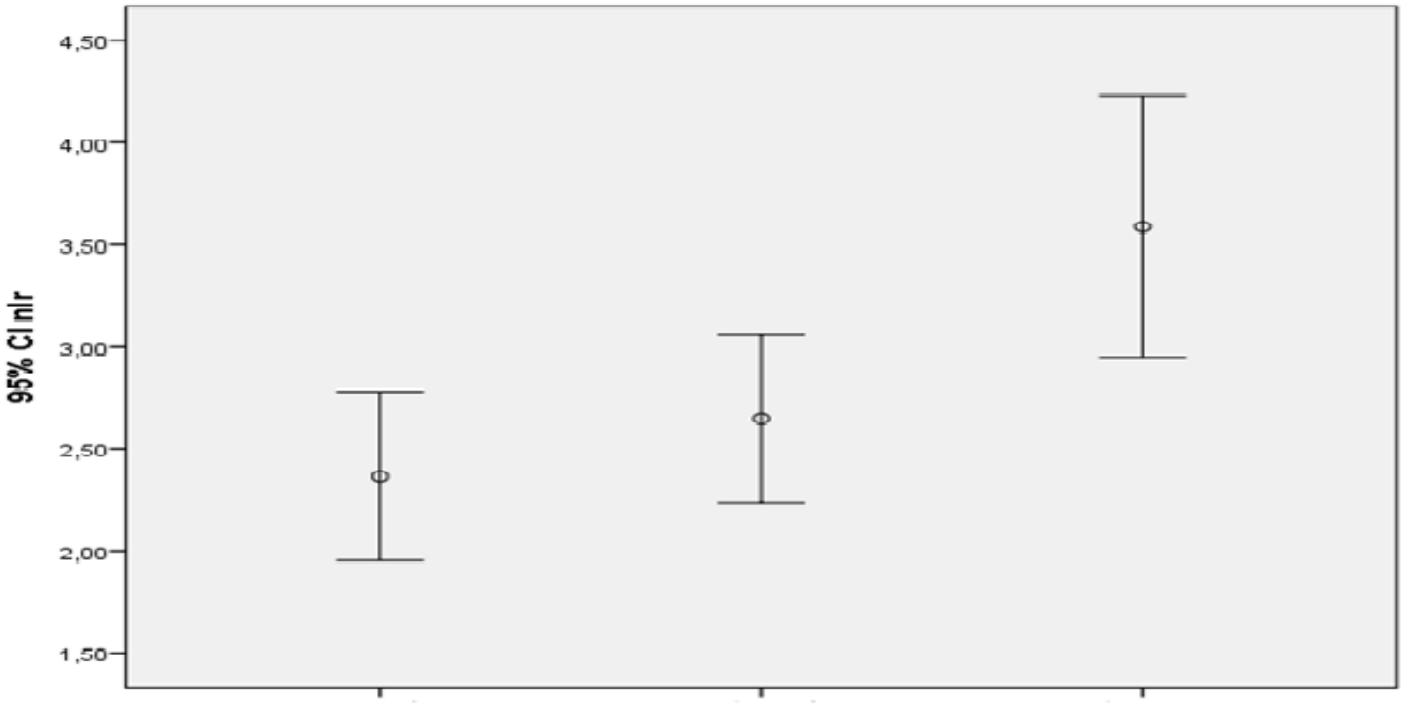


**Figure 1.** Comparison of NLR in patients with osteoporosis, osteopenia and controls.

## Discussion

Considering that there are no studies that have investigated the relationship of NLR and PLR with osteoporosis, we aimed to investigate in this study whether or not NLR and PLR levels are altered in osteoporotic patients and to evaluate their correlations with other laboratory parameters in the geriatric population.

Osteoporosis is a bone disease that increases the risk of fractures as a result of decreased bone strength due to low bone mineral density and distorted bone mineralization micro-architecture. This asymptomatic condition is usually not diagnosed until a fracture of the hipbone, spine, proximal humerus, pelvis and/or wrist is encountered due to a fall trauma and the patients are usually hospitalized [1, 2]. Certain in vitro and rodent studies determined a significant correlation between BMD and levels of inflammatory markers such as interleukin-1 (IL-1), interleukin-6 (IL-6), CRP, and tumour necrosis factor-alpha (TNF-a) [9, 10]. NLR emerged as a simple, inexpensive, and practical inflammation marker that was associated with certain inflammatory, cardiovascular, and neoplastic diseases. Moreover, NLR was shown to be superior to the white blood cell count in patients with cardiovascular diseases and malignancies [12, 13]. Neutrophil and lymphocyte counts undergo temporary changes under inflammatory conditions. Neutrophil/lymphocyte ratio (NLR) is obtained by dividing the absolute neutrophil count with the absolute lymphocyte count. As an index of systemic inflammation, NLR was determined to be a useful index for the differential diagnosis or prognostic prediction of diseases [14, 15]. NLR is also an available marker that can convey important information about the inflammatory activity of the patient. Some epidemiologic studies have shown that chronic inflammation indicated by NLR is correlated with other conventional risk factors such as obesity and hypertension. Latest studies have demonstrated that an abnormal NLR level is linked to autoimmune diseases [16].

Platelet/lymphocyte ratio is calculated by dividing the absolute thrombocyte count with the absolute lymphocyte count and is recommended as a potential marker for determining inflammation. Similar to NLR, PLR is also used as an index for the differential diagnosis and prognostic prediction of diseases such as cancer and inflammatory diseases [17]. In this study, NLR levels were found to be higher in the osteoporosis group (3.5±4.2) compared to the osteopenic group (2.6±1.9) and the control group (2.3±1.3) with statistical significance. As another parameter, PLR was higher in the osteoporosis group (179.1±130.7) compared to the osteopenic group (163.5±109.9) and the control group (153.5±88.2) but a statistically significant relationship was not determined. The osteoporosis group also manifested higher sedimentation values compared to the other two groups with statistical significance.

It is known to be an inflammatory component in the pathogenesis of osteoporosis [9, 10]. In our study, we can say that the amount of sedimentation increases as bone mineral density decreases. The correlation between these laboratory data suggests that there may be a relationship between osteoporosis and hematological markers.

In a study conducted by Ozturk Z.A. and colleagues, NLR values were determined to be significantly elevated in osteoporotic patients and to be negatively correlated with BMD (bone mineral density) scores. They suggested that this finding could be an indicator of the relationship between bone loss and inflammation [18]. In our study, the number of PLR and lymphocytes was significantly higher in the osteoporosis group than in the previous study. Previous studies showed that these values increased in inflammation. These findings reinforce the relationship between osteoporosis and inflammatory process.

By detecting higher NLR and PLR values in osteoporosis patients compared to the osteopenic and healthy control groups and determining that the difference in NLR values were statistically significant, our study may prove that NLR and PLR can be utilized as useful indices in detecting osteoporosis as well as in certain autoimmune disorders, malignancies, coronary artery disease, and other diseases that progress with inflammation

## Limitations

Our study should be evaluated in the light of several limitations. The presented study was conducted on a retrospective basis and represented single-center experience.

## Conclusion

In conclusion, we believe that NLR and PLR values, which can be obtained via an easily accessible and inexpensive routine hemogram, can become practical and valuable markers in the diagnosis and follow-up of osteoporosis based on prospective and more comprehensive studies that will be conducted.

**Recommendations:** Prospective and comprehensive studies that will include a larger number of patients are needed to conclude our study with definitive results.

**Conflict of interest:** None.
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