Journal of Orthopedics Research and Rehabilitation

Original Article

DOI: 10.51271/JORR-0023

The relationship between neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), hemoglobin albumin lymphocyte and platelet (HALP) score and bone mineral density in Hemodialysis Patients

Ülkem Şen Uzeli, Murat Doğan

Department of Internal Medicine, Hitit University Erol Olçok Training and Research Hospital, Çorum, Turkiye

Received: 01/01/2024 ◆ **Accepted**: 23/01/2024 ◆ **Published**: 29/01/2024

Corresponding Author: Murat Doğan, murat404040@hotmail.com

ABSTRACT

Aims: The aim of this study is to develop new indices from hemogram and biochemical parameters to evaluate bone mineral density in hemodialysis patients.

Methods: 49 patients who had been receiving hemodialysis for at least 6 months were included in the study. The patients were divided into three groups according to bone mineral density (BMD). Neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and hemoglobin albumin lymphocyte and platelet (HALP) score were compared between all three groups. The correlation between all three indices and lumbar and femur BMD scores was examined.

Results: No correlation was found between NLR, PLR and HALP score and lumbar and femur BMD.

Conclusion: As a result, we concluded that NLR, PLR and HALP score cannot be used as an auxiliary marker to detect osteoporosis in hemodialysis patients.

Keywords: Bone mineral density, NLR, PLR, HALP score

INTRODUCTION

Chronic kidney disease (CKD) is an important public health problem all over the world and in our country.[1] Bone mineral density (BMD), an indicator of bone mass and mineralization, is one of the main determinants of bone strength. In chronic kidney disease patients, BMD is lower than in the general population and the prevalence of osteoporosis is more common.[2] Hemodialysis (HD) is the most important renal replacement therapy for patients with end-stage renal disease. As the survival time of HD patients increases, complications such as phosphorus-calcium metabolism disorder, energy and protein consumption and sarcopenia occur due to the combined effect of various factors. This condition predisposes patients to osteoporosis, which causes increased fragility. Osteoporosis causes increased rates of fractures, falls, hospitalizations and deaths.[3]

Microinflammation is common in HD patients. Inflammation has been shown to be one of the causes of osteoporosis in HD patients.[4,5] As new inflammatory indices, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and hemoglobin (g/L) x albumin (g/L) x lymphocyte count (/L)/platelet count (/L) (HALP score) plays an important role in the prognosis of diseases such as coronary heart disease, myocardial infarction and neoplastic diseases.[6-8] Considering that studies on the effect of NLR, PLR and HALP score on bone mineral density in HD patients are very limited, this study will be the first study to address the HALP score in predicting osteoporosis in HD patients. The aim of this study is to examine the relationship between bone mineral density and simple, inexpensive parameters such as NLR, PLR and HALP score, which do not have any risk of complications, in the diagnosis of osteoporosis and osteopenia in HD patients.

Cite this article: Şen Uzeli Ü, Doğan M. The relationship between neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), hemoglobin albumin lymphocyte and platelet (HALP) score and bone mineral density in Hemodialysis Patients. *J Orthop Res Rehabil.* 2024;2(1):5-8.

METHODS

In this cross-sectional study, 49 HD patients were included in the study between September and December 2023 at Hitit University Erol Olçok Training and Research Hospital. Approval for the study was received from Hitit University Clinical Researches Ethics Committee (Date: 01.11.2023, Decision No: 2023-78). Informed written consent was obtained from all participants in accordance with the principles of the Declaration of Helsinki. The inclusion criteria of the study are being between the ages of 19-74 and having received hemodialysis treatment for at least 6 months. Exclusion criteria were determined as cardiac arrhythmia such as atrial fibrillation, aortic stenosis, myocardial infarction or unstable angina in the last 6 months, uncontrolled hypertension (>180/100 mmHg), history of acute respiratory failure, history of thromboembolism, autoimmune diseases and malignancy.

49 patients who received hemodialysis treatment for at least 6 months and were followed up in our internal medicine clinic were included. In pre-dialysis blood tests, hemogram, biochemistry parameters such as urea, creatinine, lipid parameters and serum albumin levels were examined. The patients' age, gender, height, weight, smoking history, presence of diabetes mellitus, hypertension and the medications they used, if any, presence of hypothyroidism and hyperparathyroidism were recorded. Blood tests and bone densitometry (BMD) were requested from patients who met the inclusion criteria by internal medicine doctors. According to the total lumbar T score obtained from the BMD score, the patients were divided into 3 groups: normal, osteopenia and osteoporosis. All parameters were compared between groups.

Statistical Analysis

The data were evaluated in the statistical package program IBM SPSS Statistics Standard Concurrent User V 29 (IBM Corp., Armonk, New York, USA). Descriptive statistics were given as number of units (n), percentage (%), mean ± standard deviation, median, minimum and maximum values. Normal distribution of the data of numerical variables was evaluated with the Shapiro Wilk normality test. Homogeneity of variance of the groups was analyzed with the Levene test. When comparing numerical variables according to osteoporosis, osteopenia and normal patient groups, one-way analysis of variance was used if the data showed a normal distribution, and Kruskal-Wallis analysis was used if the data did not show a normal distribution. As a multiple comparison test, the Duncan test was used in one-way analysis of variance and the Dunn-Bonferroni test was used in Kruskal Wallis analysis. The relationship between Log-HALP scores and other numerical variables was first evaluated by single linear regression analysis. Variables with a p value of <0.10 in univariate analyzes were included in the multiple linear regression model. Multiple backward stepwise regression analysis was used to determine the final factors affecting log-HALP scores. A value of $p<0.05$ was considered statistically significant.

RESULTS

In the study, 16 (32.7%) in the osteoporosis group. A total of 49 patients were included, 18 (36.7%) in the osteopenia group and 15 (30.6%) in the normal group. The average age of the patients is 58.9±11.8 years. 26 (53.1%) of the patients are male. Additional diseases included hypertension in 40 (81.6%), diabetes in 29 (59.2%), and coronary artery disease in 4 (8.2%) (Table 1).

Table 1. Descriptive and clinical characteristics of patients (n=49)

Parameters	Statistics
Group *n (%)*	
Osteoporosis	16 (32.7)
Osteopenia	18 (36.7)
Normal	15 (30.6)
Age	58.9±11.8
Gender *n (%)*	
Male	26 (53.1)
Female	23 (46.9)
BMI	28.76±6.67
Comorbid Diseases* n (%)	
Hypertension	40 (81.6)
Diabetes Mellitus	29 (59.2)
Coronary artery disease	4 (8.2)
Hyperlipidemia	2 (4.1)

n: Number of patients %: Percentage value Numerical variables are summarized as mean±standard deviation. *: A patient may have more than one comorbid disease. BMI: Body mass index

In Table 2, hemogram and biochemical parameters are compared according to groups. According to Table 2, the uric acid values of the groups differ statistically. Uric acid levels of osteoporosis patients are statistically higher than osteopenia and normal patients. Uric acid values of patients in the osteopenia and normal groups are not statistically different.

According to Table 3, no statistically significant relationship was found between NLR, PLR, log-HALP scores and lumbar and femur BMD.

Table 3. Correlation of NLR, PLR and HALP score with bone mineral density

Parameters		
	r	*p*
NLR		
L1-L4 Total T score	0.167	0.252
L1-L4 Total Z score	0.164	0.261
Femur Neck T score	0.219	0.131
Femur Neck Z score	0.186	0.201
PLR		
L1-L4 Total T score	0.271	0.059
L1-L4 Total Z score	0.076	0.603
Femur Neck T score	0.017	0.908
Femur Neck Z score	0.004	0.977
HALP score		
L1-L4 Total T score	0.205	0.157
L1-L4 Total Z score	0.262	0.070
Femur Neck T score	0.149	0.306
Femur Neck Z score	0.159	0.276

*: Since the data showed a skewed distribution, log transformation was applied before analysis. rho: Spearman correlation coefficient

Table 2. Comparison of hemogram and biochemical parameters by groups

	Groups			Statistics	
Parameters	Osteoporosis	Osteopenia	Normal	Test value	p value
Glucose	125.5 (76.0-517.0)	144.0 (80.0-375.0)	184.0 (98.0-309.0)	1.134	0.567[&]
BUN	38.0 (11.0-71.0)	41.50 (26.0-71.0)	52.0 (30.0-69.0)	3.68	0.159[&]
Urea	81.00 (23.00-152.00)	88.5 (27.0-152.0)	112.0 (63.0-147.0)	3.586	0.166[&]
Creatinine	5.20 (3.40-12.80)	6.90 (1.10-8.90)	6.90 (3.60-10.80)	2.778	0.249[&]
Total protein	66.13±5.41	64.94±5.90	66.60±7.76	0.299	0.743[†]
Albumin	3.0.00±6.13	3.3.11±3.77	3.3.73±4.95	2.549	0.089[†]
Phosphorus	4.28±1.04	4.25±0.78	4.62±1.20	0.659	0.522[†]
Calcium	8.68±1.25	8.66±1.36	8.95±0.87	0.299	0.743[†]
Uric acid	8.68±2.04a	6.22±1.24b	5.17±1.02b	22.671	<0.001[†]
Triglyceride	181.5 (58.0-431.0)	122.5 (33.0-326.0)	156.0 (70.0-756.0)	0.555	0.758[&]
Total-C	180.0 (112.0-225.0)	163.0 (85.0-224.0)	179.0 (107.0-308.0)	1.563	0.458[&]
HDL-C	47.0 (32.0-97.0)	44.5 (20.0-68.0)	49.0 (26.0-81.0)	0.842	0.656[&]
LDL-C	102.5 (20.0-188.0)	87.0 (20.0-141.0)	96.0 (55.0-188.0)	2.090	0.352[&]
White blood cell	7.70±2.98	7.01±2.03	8.35±2.06	1.297	0.283[†]
Hemoglobin	11.13±1.41	11.11±1.75	11.42±1.58	0.182	0.834[†]
MCV	87.11±4.01	88.95±6.19	87.07±4.87	0.74	0.483[†]
Neutrophil	4.54 (2.32-11.50)	4.62 (2.32-8.14)	5.70 (3.40-9.43)	2.536	0.281[&]
Lymphocite	1.57 (0.92-2.60)	1.34 (0.57-3.43)	1.66 (0.65-2.80)	0.047	0.977[&]
Monocyte	0.72 (0.28-0.98)	0.54 (0.27-3.62)	0.71 (0.26-1.23)	3.456	0.178[&]
Platelet	244.5 (45.0-522.0)	247.5 (45. 0-368. 0)	242.0 (135. 0-360. 0)	0.397	0.820[&]
NLR	3.19 (2.17-6.25)	3.20 (2.29-7.19)	3.51 (1.78-9.17)	2.026	0.363[&]
PLR	177.99 (48.91-375.54)	172.78 (48.91-340.35)	166.67 (49.09-348.19)	0.151	0.927[&]
Ferritin	421.5 (41.0-1011.0)	496.5 (85.0-3285.0)	387.0 (52.0-1005.0)	2.149	0.342[&]
Parathormone	310.5 (70.0-877.0)	268.5 (40.0-823.0)	198.0 (50.0-639.0)	2.961	0.228[&]
CRP	7.45 (3.19-53.40)	9.15 (3.19-81.00)	17.90 (3.19-77.10)	4.064	0.131[&]
L1-L4 Total T score	-2.91±0.78[a]	-1.47±0.42[b]	0.71±1.05[c]	85.868	<0.001[†]
L1-L4 Total Z score	-1.63±1.40[a]	-0.55±0.74[b]	1.56±1.32[c]	29.458	<0.001[†]
Femur Neck T score	-2.15±1.30[a]	-1.41±0.97[b]	-0.31±0.77[c]	12.315	<0.001[†]
Femur Neck Z score	-1.08±1.25[a]	-0.40±0.85[a]	0.17±0.93[b]	5.730	0.006[†]
HALP Score	1.98 (0.74-6.21)	2.14 (1.05-6.21)	2.23 (0.91-8.82)	0.409	0.671[&]

Data are summarized as mean±standard deviation or median (minimum-maximum) value. [†]: One-way analysis of variance, [&]: Kruskal Wallis Analysis, superscripts a, b and c indicate differences between groups on the same line. There is no statistically significant difference between groups with the same superscripts.

DISCUSSION

49 HD patients were included in this study. It was performed to determine the predictive role of NLR, PLR and HALP score in BMD evaluation of chronic kidney failure (CKD) patients who have been on hemodialysis for at least 6 months. It was concluded that all three values do not have an index that will give an idea about the prognosis of bone mineral density in HD patients.

Osteoporosis is the most common metabolic bone disease characterized by low bone mass, deterioration of bone tissue and bone architecture, decreased bone strength and increased risk of fracture.[9] Studies have shown that bone mineral disorders are an important health problem in CKD patients and that fractures caused by osteoporosis significantly increase morbidity and mortality rates. While osteoporosis due to CKD was detected in approximately 53% of patients with CKD in the study of Festuccia et al.[10] this rate was found to be 43% in the study of Aslan et al.[11] In our study, the osteoporosis rate in CKD patients was found to be 32.7% and the osteopenia rate was 36.7%. Persistent chronic systemic inflammation in individuals with CKD can lead to various negative consequences such as cardiovascular disease, malnutrition, anemia, atherosclerosis, morbidity and mortality, as well as negative effects on bone metabolism.[12,13] Neutrophils stimulated by inflammatory cytokines such as IL-4 and TNF-α increase the stimulation of NF-kappa B-ligand (RANKL), which is transferred to their cell membranes. It has been shown that bone resorption increases in inflammatory conditions due to increased osteoclast activity.[14]

NLR and PLR are hemogram parameters and increase in inflammatory conditions. A cross-sectional study examining the relationship between NLR and bone density reported that NLR was an independent predictor of osteoporosis, negatively correlated with the lumbar spine and femoral neck. High NLR levels in elderly people with osteoporosis suggest that inflammation may play an important role in bone remodeling.[15]

In a study by Lee et al.[16] a negative correlation was found between NLR and lumbar BMD in postmenopausal women, while no relationship was found between femoral neck BMD. While Koseoglu et al.[17] study found that BMD values were inversely proportional to PLR but did not have a significant relationship with NLR, Yolaçan et al.[18] showed that NLR, as well as PLR, had an inverse relationship with BMD. In the study conducted by Ban et al.[19] in dialysis patients, NLR rates were independent of BMD. In our study, NLR and PLR values did not change according to BMD values.

Recently, there are studies showing that the HALP score reflects systemic inflammation and nutritional status. It has been proven to be a useful prognostic factor in patients with stomach, prostate, bladder and kidney malignancies and acute ischemic attack.[20] We did not find any study in the literature comparing bone mineral density and HALP score. Low BMI, which is among the risk factors for bone mineral density and exists in hemodialysis patients, may increase the susceptibility to osteoporosis in CKD patients. In addition, although it is considered that the presence of increased inflammation in CKD patients may contribute to low bone mass, no relationship was found between HALP score and BMD in this study.

Study Limitations

The limitation of this study is that there are many underlying mechanisms in the pathogenesis of osteoporosis in CKD patients and the small number of patients. In addition, the uncertainty of the effect of HALP score on prognosis in patients with independent CKD and low BMD compared to the healthy population is another limitation of this study.

CONCLUSION

As a result, no relationship was found between low BMD and NLR, PLR and HALP score in CKD patients.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the Hitit University Medical Faculty Clinical Researches Ethics Committee (Date: 01.11.2023, Decision No: 2023-78).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Aguilar A, Gifre L, Ureña-Torres P, et al. Pathophysiology of bone disease in chronic kidney disease: from basics to renal osteodystrophy and osteoporosis. *Front Physiol*. 2023;14:1177829.
2. Klibanski A, Adams-Campbell L, Bassford T, et al. Osteoporosis prevention, diagnosis, and therapy. *J Am Med Assoc*. 2001;285(6):785-795.
3. Abdalbary M, Sobh M, Elnagar S, et al. Management of osteoporosis in patients with chronic kidney disease. *Osteopor Int*. 2022;33(11):2259-2274.
4. Panuccio V, Enia G, Tripepi R, et al. Pro-inflammatory cytokines and bone fractures in CKD patients. An exploratory single centre study. *BMC Nephrol*. 2012;13(1):1-6.
5. Meuwese CL, Snaedal S, Halbesma N, et al. Trimestral variations of C-reactive protein, interleukin-6 and tumour necrosis factor-α are similarly associated with survival in haemodialysis patients. *Nephrol Dial Transplant*. 2011;26(4):1313-1318.
6. Mosca M, Nigro MC, Pagani R, De Giglio A, Di Federico A. Neutrophil-to-lymphocyte ratio (NLR) in NSCLC, gastrointestinal, and other solid tumors: immunotherapy and beyond. *Biomolecules*. 2023;13(12):1803.
7. Ekinci F, Balcik OY, Oktay E, Erdogan AP. HALP Score as a new prognostic index in metastatic renal cell cancer. *J Coll Physicians Surg Pakistan*. 2022;32(3):313-318.
8. Kocaoğlu S, Alatlı T. The efficiency of the HALP score and the modified HALP score in predicting mortality in patients with acute heart failure presenting to the emergency department. *J Coll Physicians Surg Pakistan*. 2022;32(06):706-711.
9. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteopor Int*. 2014;25(10):2359-2381.
10. Festuccia F, Jafari MT, Moioli A, et al. Safety and efficacy of denosumab in osteoporotic hemodialysed patients. *J Nephrol*. 2017;30(2):271-279.
11. Aslan B, Funda Sarı. Hemodiyaliz ve periton diyalizi yapan hastalarda osteoporoz sıklığı ve osteoporoz gelişmesini etkileyen faktörler. *Akdeniz Tıp Derg*. 2021;7(2):277-282.
12. Akchurin OM, Kaskel F. Update on inflammation in chronic kidney disease. *Blood Purif*. 2015;39(1-3):84-92.
13. Duarte MP, Ribeiro HS, Neri SG, et al. Prevalence of low bone mineral density (T-score≤− 2.5) in the whole spectrum of chronic kidney disease: a systematic review and meta-analysis. *Osteopor Int*. 2023;34(3):467-477.
14. Poubelle PE, Chakravarti A, Fernandes MJ, Doiron K, Marceau AA. Differential expression of RANK, RANK-L, and osteoprotegerin by synovial fluid neutrophils from patients with rheumatoid arthritis and by healthy human blood neutrophils. *Arthritis Res Ther*. 2007;9(2):R25.
15. Öztürk ZA, Yesil Y, Kuyumcu ME, et al. Inverse relationship between neutrophil lymphocyte ratio (NLR) and bone mineral density (BMD) in elderly people. *Arch Gerontol Geriatr*. 2013;57(1):81-85.
16. Lee SH, Ryu SY, Park J, Shin MH, Han MA, Choi SW. The relationship of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio with bone mineral density in Korean postmenopausal women. *Chonnam Med J*. 2019;55(3):150-155.
17. Koseoglu SB. Bone loss and platelet-to-lymphocyte ratio. *Biomark Med*. 2017;11(1):5-10.
18. Yolaçan H, Guler, S. Inverse correlation between bone mineral density and systemic immune inflammation index in postmenopausal Turkish women. *Cureus*. 2023;15(4):e37463.
19. Ban TH, Choi BS, Yoon SA, et al. Clinical significance of neutrophil-to-lymphocyte ratio on the risk of abdominal aortic calcification and decreased bone mineral density in patients with end-stage kidney disease. *Plos One*. 2023;18(10):0286612.
20. Pan H, Lin S. Association of hemoglobin, albumin, lymphocyte, and platelet score with risk of cerebrovascular, cardiovascular, and all-cause mortality in the general population: results from the NHANES 1999-2018. *Front Endocrinol*. 2023;14: 1173399.