ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ)* 2021, Volume 10, Number 3: 1002-1005
P-ISSN.2089-1180, E-ISSN: 2302-2914

Bali Medical Journal
www.BaliMedicalJournal.org
Published by Bali Medical Journal

Correlation between Bone Mineral Density (BMD) with blood phosphorus levels in elderly women: study using Dual Energy X-ray Absorptiometry (DXA)

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Received: 2021-10-26
Accepted: 2021-12-05
Published:2021-12-28

ABSTRACT

Background: The main constituent of Bone Mineral Density (BMD) is bone mineral, with the main composition of the *hydroxyapatite* complex, a combination of calcium and phosphorus. In the aging process, the mineral content in the bones will decrease, resulting in lower BMD than normal levels (osteopenia) or leading to the most common musculoskeletal disorder as well as morbidity in the elderly population. This study aims to determine the correlation between BMD and blood phosphorus levels in elderly women.
Methods: This cross-sectional study was based on data from several geriatric health centers in Semarang from March until June 2019. There were 29 female respondents aged ≥ 60 years who participated and signed informed consent of this study. The study performed laboratory tests to assess blood phosphorus levels and BMD examination with Dual Energy X-ray Absorption (DXA). BMD is categorized based on World Health Organization (WHO) criteria into normal, osteopenia, and osteoporosis categories. Data were analyzed using SPSS version 17 for Windows.
Results: Most of the subjects were 60-69 years old group (69.0%), followed by osteoporosis in the BMD category (62.0%) and normal blood phosphorus levels (83.0%). There was no significant correlation between BMD and blood phosphorus levels ($p > 0.05$), but there was a tendency for a negative correlation between BMD and blood phosphorus levels ($r = -0.096$).
Conclusion: The result shows no correlation between blood phosphorus level and BMD.

Keywords: Bone Mineral Density, Phosphorus, Elderly, DXA.
Cite This Article: Aripriandari, A., Sukmaningtyas, H., Ngestiningsih, D., Batubara, L. 2021. Correlation between Bone Mineral Density (BMD) with blood phosphorus levels in elderly women: study using Dual Energy X-ray Absorptiometry (DXA). *Bali Medical Journal* 10(3): 1002-1005. DOI: 10.15562/bmj.v10i3.2848

INTRODUCTION

In the aging process, the mineral content in the bones decreases, so that bone mass density (BMD) is lower than normal levels (osteopenia) and can progress to osteoporosis, which is the most common musculoskeletal disorder in the elderly population, especially women.[1] In the elderly, various changes also occur, including changes in body composition and nutritional intake. BMD is composed mostly of bone minerals with the most composition: calcium (± 99%) and phosphorus (± 85%), which will form hydroxyapatite crystals.[1,2] Phosphorus itself is known to induce osteoclastic activity and its homeostasis is very closely related to calcium, so it can affect BMD both directly and indirectly.[2,3] The gold standard check for assessing BMD is examining Dual Energy X-Ray Absorption (DXA).[4]

Bone is formed by bone cells, bone matrix, and mineral salts. Mineral salt is a crystallization complex consisting of calcium and phosphate called hydroxyapatite and includes a large part of BMD. In the aging process, minerals in the bones will decrease. BMD decreases from around 50 years of age. In addition, bone turnover will increase with age, driven by increased bone resorption, continuing as osteopenia and osteoporosis. Women can lose up to 20% of bone mass within 5-7 years post-menopause, and after that, loss of bone mass will continue approximately 0.5-1% per year (unless other conditions can cause bone loss to progress faster). WHO divides BMD into 4 categories: normal, osteopenia, osteoporosis and advanced osteoporosis.[5,6] Osteoporosis occurs due to a disruption in bone remodeling, which is a disturbance of the balance between the process of resorption and bone formation, where the number and activity of osteoclast cells exceed the number and activity of osteoblast cells. This situation can cause a decrease in bone mass. Loss of bone density is a natural thing that occurs due to age development. However, it has not been known with

certainty the cause of decreased osteoblast function in the elderly, presumably due to a decrease in estrogen levels and Insulin-like Growth Factor-1 (IGF-1). Calcium and vitamin D deficiency are also often found in older people. Besides calcium, phosphorus also has an important role in forming bone tissue in the form of hydroxyapatite.[7-9] However, it is suspected that there is a potential for a negative effect from excessive phosphorus intake on bone health. This negative effect is caused by an imbalance in calcium-phosphorus homeostasis when excess phosphorus intake in the body. Short-term experimental studies in humans show that excess phosphorus intake and low calcium intake can be associated with increased serum PTH concentrations and/or bone turnover damage and loss of Fibroblast Growth Factor-23 (FGF-23) from bones.[2,3,10]

DXA is a quantitative radiological procedure for measuring BMD, a major bone strength determinant. DXA measurements are used to diagnose osteoporosis, monitor BMD changes over time, and estimate fracture risk. According to the International Society of Clinical Densitometry in adult patients, there are various indications of bone densitometry (ISCD), one of which is recommended for women aged 65 years and over. DXA measurements in adult patients are recommended using concentrations in the proximal vertebrae and femur. If the two areas cannot be evaluated, measurements can be made on the forearm (antebrachial) area.[4] Based on those mentioned above, this study aims to assess the correlation between Bone Mineral Density (BMD) with blood phosphorus levels in elderly women by using Dual Energy X-ray Absorptiometry (DXA).

METHODS

A cross-sectional study was conducted to evaluate elderly women in several geriatric health centers in Semarang. There are 29 elderly women aged ≥ 60 years as research respondents, selected by consecutive sampling, have met the inclusion criteria, and are willing to sign informed consent. Bone Mineral Density (BMD) examination using Dual Energy X-ray Absorptiometry (DXA) and examination of phosphorus levels in the blood were carried out at Semarang Medical Center Telogorejo Hospital. The independent variable in this study is blood phosphorus levels. The measured phosphorus level is inorganic phosphate in blood serum, expressed in mg/dl—examination method by taking blood samples from participants in the afternoon.

The dependent variable is BMD, defined as bone mineral mass or density per unit area, expressed in mg/cm^2. The examination method uses DXA, with centrifuge of the vertebrae, proximal femur, and antebrachial (2 selected Region of Interest (ROI) are eligible for BMD analysis). BMD values are categorized based on WHO categories as follows (5): 1) Normal (T-Score between -1 or greater); 2) Osteopenia (T-Score -1 and -2.5); 3) Osteoporosis (T-Score -2.5 or less (without fracture)); and 4) Advanced osteoporosis (T-score -2.5 or less and fragility fracture).

Samples were categorized based on WHO categories such as normal BMD, osteopenia, and osteoporosis, shown as a tabulation of data. At the same time, blood phosphorus levels were shown as numerical data (mean, median, standard deviation, maximum and minimum value). Analytical data were shown as tables and graphs. The non-parametric statistical test used is the Rank-Spearman correlation test to identify the associative hypothesis of two variables in the form of an ordinal scale. P-value ≤ 0.05 indicates a significant correlation between variables. Statistical analyses were performed using SPSS version 17.0 for Windows.

RESULTS

This study involved 29 subjects consisting of elderly women aged ≥ 60 years. Sixty-nine percent of subjects aged 60-69 years old, 24.1% were 70-79 years old, and 6.9% were aged ≥ 80 years old. All subjects had experienced menopause. In this study, the highest frequency of BMD was obtained in the osteoporosis category (62.5%), while the others were categorized as osteopenia (34.5%) and normal category (3.5%) (Table 1).

From this study, in the 60-69 years age group, 50% of the study subjects were in the osteoporosis category (n = 10), 45% were in the osteopenia category (n = 9), and 5% were in the normal category (n = 1). Subjects who are categorized into the normal BMD category are 60 years old. In the age group of subjects > 70 years, 89% were categorized as osteoporosis (n = 8) and 11% were categorized as osteopenia (n = 1). There was a significant correlation between the age group and BMD (p <0.05) (Figure 1).

From all 29 subjects, 24 samples (83%) showed phosphorus levels were within normal limits (i.e., 2.5-4.5 mg/dl), while the other 5 samples (17%) showed phosphorus levels in the blood were more than the normal limit. In the 60-69 year age group, the lowest phosphorus level is 3.00 mg/dl and the highest phosphorus level is 5.07 mg/dl, while in the > 70 year age group, the lowest phosphorus level is 3.06 mg/dl and phosphorus levels the highest was 4.49 mg/dl. The mean value of phosphorus levels in the blood in the 60-69 years age group was 3.92 mg/dl and in

Table 1. Baseline characteristics of study subjects.

Variables	Total (%)
Age (years old)	
60-69	20 (69.0)
>70	9 (31.0)
Bone Mineral Density (BMD) Category	
Normal	1 (3.5)
Osteopenia	10 (34.5)
Osteoporosis	18 (62.0)
Blood Phosphorus Levels (mg/dL)	
Normal (2.5-4.5)	24 (83.0)
>4.5	5 (17.0)

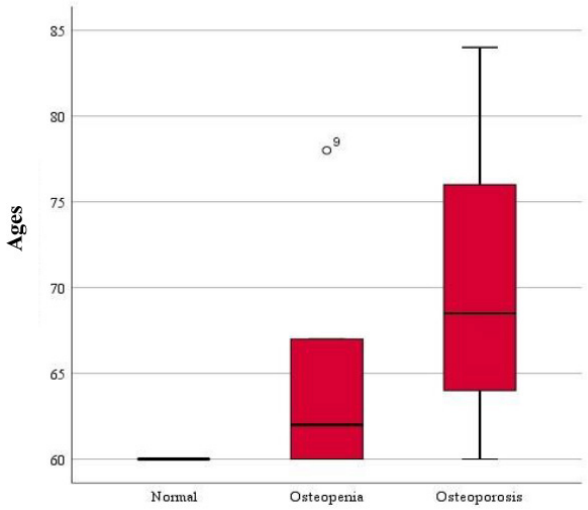

Figure 1. Distribution of BMD category according to ages.

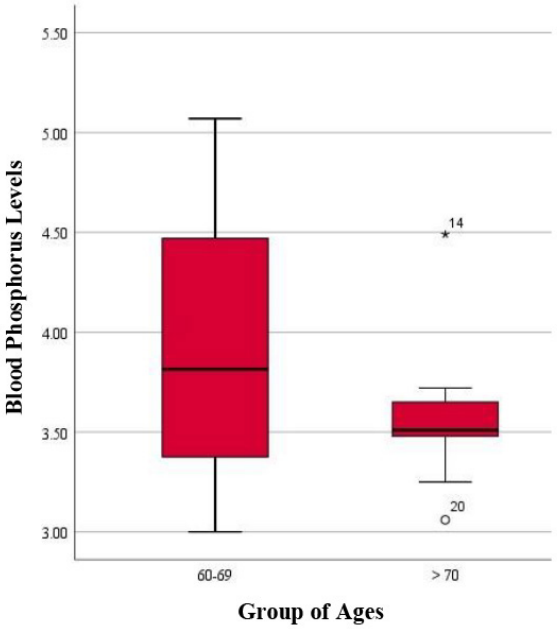

Figure 2. Distribution of blood phosphorus levels according to ages.

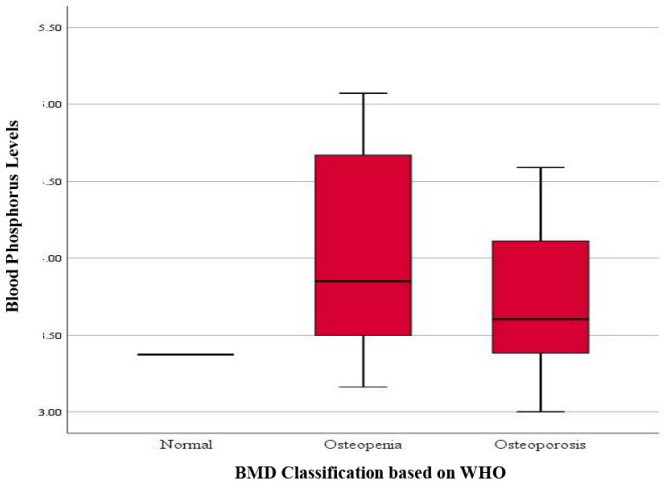

Figure 3. Distribution of BMD category according to blood phosphorus levels.

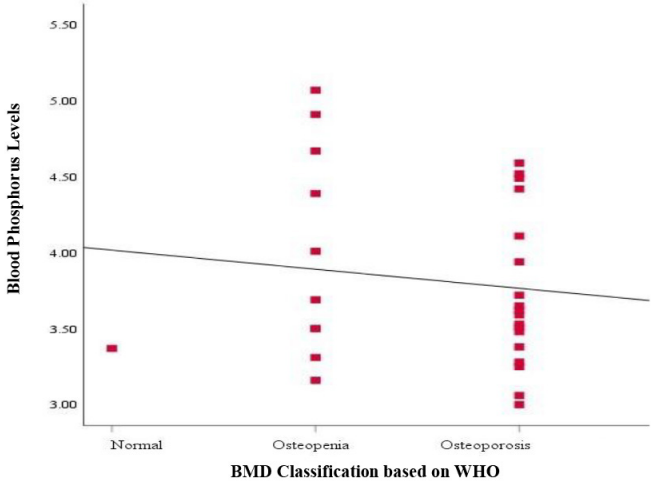

Figure 4. Correlation Diagram between BMD and Blood phosphorus Levels.

the > 70 years age group, the mean value was 3.59 mg/dl. There was no significant correlation between age groups and blood phosphorus levels (p> 0.05) (Figure 2).

The phosphorus level in the blood in the normal BMD category was 3.37. In contrast, in the osteopenia category, it had a mean value of 4.02 (with a range of 3.16-5.07 mg/dl) and in the osteoporosis category, a mean value of 3.73 (with a range of 3.00-4.49mg/dl) (Figure 3).

Based on the *Rank-Spearman* correlation test, there was no significant correlation between BMD and blood phosphorus levels (p> 0.05). However, the scattered graph shows a decreasing curve, which means that there is a tendency for a negative correlation between BMD and phosphorus levels in the blood (r=-0.096) (Figure 4).

DISCUSSION

This study aims to determine the correlation between BMD and phosphorus levels in the blood. No significant correlation was found between BMD and phosphorus levels in the blood. This is probably because most phosphorus is in the bones and only 1% is in the blood. Almost all the phosphorus found in the Extracellular Fluid (ECF) is inorganic phosphate.[11] Although the form of inorganic phosphate is easier to measure and can describe the phosphorus levels in the body, inorganic phosphate in serum only reflects a very small percentage of total phosphorus in the body. In addition, phosphorus levels in the blood are regulated by various hormones, including Parathyroid Hormone (PTH), Fibroblast Growth Factor-23 (FGF-23), and 1,25-dihydroxy

vitamin D. Phosphorous homeostasis is also very closely related to calcium in the form of calcium-phosphorus (Ca-P ratio), resulting in an imbalance the Ca-P ratio can further disrupt the process of bone mineralization.[12,13]

Although there is no significant correlation between BMD and phosphorus levels in the blood, there is a tendency for a negative correlation due to the coefficient correlation (r) was -0.096, which means that when phosphorus levels in the blood are high, BMD will decrease. High phosphorus levels in the blood can cause the impaired formation of the active structure of vitamin D in the kidneys, reduce blood calcium levels, and increase PTH released by the parathyroid gland, which disrupts bone mineralization that can progress to osteoporosis.[14]

Various limitations in this study that can be a confounding factor include the absence of data on phosphorus intake in respondents either through information on food intake, frequency or content of these foods. In addition, the examination of phosphorus levels in the blood only represents 1% of the total phosphorus in the body, so it cannot describe the amount of phosphorus that forms a bone mass. As a suggestion for further research, it can compare phosphorus and calcium levels concerning the Ca-P ratio that plays an important role in the process of bone mineralization, evaluating other indicators of phosphorus metabolism such as calcium, PTH, FGF-23, and 1,25-dihydroxy vitamin D and considered about food intake in the study subjects so that it can monitor the intake of phosphorus which can affect the levels of phosphorus in the blood.

CONCLUSION

There was no significant correlation between bone mass density and blood phosphorus levels in elderly women. In addition, there is a tendency to have a negative correlation between bone mass density and blood phosphorus levels in elderly women.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

ETHICAL APPROVAL

The research ethics committee of the Faculty of Medicine, Diponegoro University (Undip), Semarang, has approved this study with the Ethical Clearance number 70/EC/FK-UNDIP/ III/ 2019 prior to the study being conducted.

FUNDING

No specific funding was provided for this article

AUTHOR CONTRIBUTIONS

Adhikarmika Aripriandari is conceived the presented idea, developed the theory and performed the computations, processed the experimental data, performed the analysis, and drafted the manuscript. Hermina Sukmaningtyas, Dwi Ngestiningsih, and Lusiana Batubara supported and supervised this study and contributed to the research's design and implementation. All authors provided critical feedback and helped shape the research, analysis and manuscript.

ACKNOWLEDGMENTS

The first author wishes to acknowledge the support and assistance of her family, without their support, this project could not have been initiated. The first author also would like to thank other authors Dr. Hermina Sukmaningtyas, Dr. Dwi Ngestiningsih and Dr. Lusiana Batubara, for their support and assistance during the writing of this article. All of the authors would like to thank Dr. Lukas Sarjono, radiologist in Radiology Installation of Semarang Medical Centre - Telogorejo Hospital, for his contribution in helping this study. Last, we would like to thank all the medical staff of the Radiology Department, Medical Faculty of Universitas Diponegoro for supporting this study.

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