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Short Communication

Correlation between serum vitamin D levels and bone mass density evaluated by radiofrequency echographic multi-spectrometry technology (REMS) in menopausal women

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Abstract

Osteoporosis is a common condition associated with an increased risk of bone fractures due to fragility. Bone mineral density (BMD) is lower in menopausal women due to estrogen deficiency, age-related decline in osteoblast function, decreased calcium absorption, and reduced synthesis of vitamin D, which lead to osteoporosis. The aim of this study was to determine the correlation between serum vitamin D levels and BMD assessed using radiofrequency echographic multi-spectrometry technology (REMS) in menopausal women. A cross-sectional study was conducted at Prof. Dr. Chairuddin P. Lubis Hospital of Universitas Sumatera Utara, Medan, Indonesia, from May 2023 to August 2023. Consecutive sampling method was employed to sample menopausal women with no history of hysterectomy or oophorectomy (unilateral or bilateral), and no history of hormone replacement therapy or vitamin D supplementation. Interviews and physical examinations were conducted to obtain the characteristics of the subjects (age, duration of menopause, and body mass index). The 25(OH)D level was measured using immunoassay and REMS examination was conducted to assess BMD. The Spearman correlation test was used to assess the correlation between serum vitamin D levels and BMD. A total of 32 menopausal women were included in this study with the average vitamin D level was 18.05±5.81 ng/mL, and the mean BMD level was -2.13±1.23. The data showed a significant positive correlation between serum vitamin D levels and BMD in menopausal women (r=0.710; p=0.020). This study highlights that REMS could be useful as an alternative to dual-energy x-ray absorptiometry (DXA) to assess DMD in postmenopausal women.

Keywords: Menopause, vitamin D, bone mineral density, radiofrequency echographic multi-spectrometry technology, diagnostic method

Introduction

Osteoporosis is characterized by bone resorption leading to a decrease in bone mass, disrupted microarchitecture, and structural damage that increases the likelihood of fractures. These

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fragility fractures disproportionately contribute to high mortality rates and significant reductions in quality of life [1,2]. In 2019, 22–55% of elderly women in Indonesia were reported to have osteoporosis, and approximately 8.5 million elderly individuals are affected by osteoporosis [3]. Osteoporosis affects more than 30% of women between the ages of 60–70, with the incidence increasing to 70% in those aged 80 years and above [4]. This is associated with estrogen deficiency during menopause (type 1 primary osteoporosis), the cessation of menstruation for 12 consecutive months in women and typically occurs between the ages of 45–55, and the decrease in bone mass due age-related decline in osteoblast function (type 2 primary osteoporosis) [3,4]. Other associated factors contributing to the significant decrease in bone mineral density (BMD) among women with menopause and post-menopause include decreased calcium absorption, and diminished ability to synthesize Vitamin D.

Vitamin D is essential for maintaining calcium levels in bones, stimulating bone resorption by increasing the number of osteoblasts, and regulating parathyroid hormone levels to stabilize serum calcium [5-7]. Vitamin D is a lipid-soluble vitamin and is mostly found in milk, meats, egg yolk, fish oil, fish and the synthesis of vitamin D requires various organs such as the liver, kidneys, skin and intestines [8-10]. Ultraviolet-B (UVB) radiation aids in the transformation of vitamin D into its active form [8-12]. Post-menopausal women have low estradiol levels which are more vulnerable to vitamin D deficiency [13-16]. Based on the data, there is a 0.2% annual bone loss from the spine in pre-menopause, and this rate escalates to 0.75% in postmenopausal individuals [17]. Low vitamin D is associated with osteoporosis, osteoarthritis, osteopenia, bone tissue frailty and increased risk of fractures [6,18,19].

Bone densitometry assessment utilizing radiofrequency echographic multi-spectrometry (REMS) is a novel ultrasound-based technique that provides reliable evaluations of BMD in the lumbar spine, femoral neck, and hip. The use of REMS has been validated in postmenopausal osteoporosis and has been recognized as a potential alternative to bone density scan by dual-energy x-ray absorptiometry (DXA) [20]. A study compared DXA and REMS in assessing BMD and found that both DXA and REMS had specificity and sensitivity rates over 90% and a diagnostic concordance of about 86% for both the lumbar spine and proximal femur [21]. Another study of five years of follow-up with 1370 women found that T-scores obtained by REMS were effective in predicting the fragility of fractures and representing a further promising parameter for improving the diagnosis of osteoporosis in clinical practices [22]. Another study also found REMS is effective in discrete osteoporotic and non-osteoporotic patients using the lumbar spine (sensitivity 91.7% and specificity 92.0%) and femoral neck (sensitivity 91.5%, and specificity 91.8%) [23]. Since the use of REMS in evaluating BMD in Indonesia is limited, the aim of this study was to determine the correlation between serum vitamin D levels and BMD assessed using REMS in menopausal Indonesian women.

Methods

Study design, setting and sampling method

A cross-sectional study with a case series approach was conducted at Prof. Dr. Chairuddin P. Lubis Hospital of Universitas Sumatera Utara, Medan, Indonesia, from May until August 2023. A consecutive sampling method was employed in this study with a minimum sample size of 32 calculated by using the numerical-numerical correlational analytical formula.

Participants

This study included menopausal women with the following criteria: (1) having a spontaneous cessation of menstruation for at least 12 consecutive months; (2) no history of hysterectomy or oophorectomy (unilateral or bilateral); and (3) no history of hormone replacement therapy or vitamin D supplementation. Patients with a history of endocrine, cardiovascular, and malignancy diseases, and obesity were excluded from the study.

Data collection

Interviews and physical examinations were conducted to obtain the characteristics of the patients (age, duration of menopause, and body mass index). To obtain the serum vitamin D levels, 10 mL

venous blood sample was collected from the median cubital vein of the participants and tested using the immunoassay method conducted at the Gatot Subroto Clinical Laboratory, Pematang Siantar, Indonesia. Vitamin D level was considered normal if vitamin D: >20 ng/mL; insufficiency: 12–20 ng/mL; and deficiency: <12 ng/mL. The BMD assessment of the participants was conducted at Prof. Dr. Chairuddin P. Lubis Hospital of Universitas Sumatera Utara utilizing REMS. The lumbar spine was used to measure the BMD. BMD was defined using T-scores and considered as normal: >1; osteopenia: -1 to -2.5; and osteoporosis <-2.5.

Statistical analysis

The data were analyzed descriptively to present the frequency distribution of the participants based on the characteristics. The Spearman correlation test was used to assess the correlation between D levels and BMD since the data did not distribute normally. The result was considered significant at $p<0.05$ with a confidence level of 95%. All statistical analyses were performed on SPSS ver.25 (IBM, New York, USA).

Results

Characteristics of participants

A total of 32 menopausal women were included in this study, as presented in (**Table 1**). The mean age of participants was 58.06±5.0 years old with a mean duration of menopause of 7.50±4.25 years, and a body mass index of 22.64±1.61 kg/m^2. The mean serum vitamin D levels were 18.05±5.81 ng/mL and the mean T-score for lumbar BMD was -2.13±1.23 (**Table 1**).

Table 1. Basic characteristics of menopausal women included in the study (n=32)

Characteristics	Mean±SD
Age (years)	58.06±5.00
Duration of menopause (years)	7.50±4.25
Body mass index (kg/m^2)	22.64±1.61
Serum vitamin D levels (ng/mL)	18.05±5.81
T-score of lumbar bone mass density (BMD)	-2.13±1.23

Out of 32 women, 23 (71.9%) had insufficient serum vitamin D levels, while eight women (25%) had normal vitamin D, and one woman (3.1%) had a deficiency (**Table 2**). The REMS evaluation of BMD in the women revealed osteoporosis in 17 patients (53.1%), while 15 patients (46.9%) had osteopenia. None of the samples had normal BMD (**Table 2**).

Table 2. Serum vitamin D level and BMD of women included in the study (n=32)

Variable	Classification	Frequency	(%)
Serum vitamin D level	Normal	8	25.0
	Insufficiency	23	71.9
	Deficiency	1	3.1
Bone mass density (BMD)	Normal	0	0.0
	Osteopenia	15	46.9
	Osteoporosis	17	53.1

The Spearman correlation test showed a significant positive correlation between serum vitamin D level and BMD assessed in menopausal women (r= 0.710; p=0.020) (**Table 3**). This indicated that the higher the serum vitamin D level, the higher the BMD in menopausal women.

Table 3. Correlation between serum vitamin D levels and BMD assessed by REMS

Variables	Mean±SD	Spearman correlation coefficient*	p-value
Serum vitamin D level	18.05±5.81	0.710	0.020
Bone mass density (BMD)	-2.13±1.23		

Discussion

Natural menopause is associated with endocrinological changes and alterations in bone and mineral metabolism. With the decline in ovarian follicular function during menopause, there is a decrease in the production of estradiol and other hormones. This leads to increased osteoclast production, causing bone resorption and the loss of mineral density, resulting in osteoporosis. Bone loss accelerates along with postmenopausal years, with an increase of 1–2.3% in the first five years and 7–10% after five years, thereby increasing the risk of osteoporotic fractures [24]. In the present study, out of the total postmenopausal women included in the study, 17 women (53.1%) had osteoporosis, while 15 women (46.9%) had osteopenia.

Several nutrients, calcium and vitamin D play a crucial role in skeletal mineralization at all ages. Vitamin D is a fundamental vitamin for maintaining calcium levels in bones by reducing calcium absorption in the intestines, stimulating bone resorption by increasing the number of osteoblasts, and maintaining parathyroid hormone levels to stabilize serum calcium levels [5]. In this study, 23 women (71.9%) had insufficient serum vitamin D levels. Insufficient vitamin D levels can also lead to osteoporosis, osteoarthritis, osteopenia due to bone loss, and increased risk of fractures. Vitamin D hormone is required for bone absorption and mineralization, directly related to BMD. Decreased vitamin D results in decreased BMD, which directly leads to bone loss and increases the impact of fractures [18].

In a retrospective study of 316 postmenopausal women concluded that vitamin D deficiency could impair calcium absorption and a direct relationship has been previously found between estradiol and vitamin D levels [14]. Women with decreased vitamin D levels also concurrently experienced a decrease in estradiol levels, indicating a relationship between the two variables [14]. In postmenopausal women, estradiol levels decrease, making them vulnerable to vitamin D deficiency. Optimal intake of vitamin D and calcium is necessary to prevent bone loss. Pre-menopausal bone loss is 0.2% per year in the spinal region, which increases to 0.75% post-menopause [15]. To prevent osteoporosis complications in postmenopausal women, they should be treated with estrogen replacement therapy or hormone replacement therapy in addition to increased calcium supplement intake [17]. A study reported that vitamin D supplementation (50,000 IU weekly) for eight weeks in healthy adults aged 20–60 years showed significant changes of T-score in the intervention group than the control group (0.81 vs 0.30, $p<0.001$) [25].

This study reported a significant correlation between serum vitamin D levels and BMD in menopausal women. A study found a significant difference in vitamin D levels between women of reproductive age and postmenopausal women [18]. There is an inverse relationship between age and menopausal status with serum vitamin D levels. After reaching menopause, the body's vitamin D reserve decreases [24]. Women in their reproductive years had significantly higher BMD compared to postmenopausal women. This study also examined vitamin D and BMD in premenopausal and postmenopausal women and demonstrated that low vitamin D levels were associated with low BMD in both groups [18]. A study also showed that 80% of postmenopausal women had vitamin D deficiency, and only 5% had optimal vitamin D levels [17]. A study found that free vitamin D was significantly related to the occurrence of thoracolumbar junction fracture and lumbar BMD, which is assumed to be a positive predictor for fracture and osteoporosis prevention [26]. However, total serum vitamin D levels in this study did not have any association with BMD at different sites as well as fragile vertebral fractures [26].

A meta-analysis showed that simultaneous supplementation with calcium and vitamin D significantly reduced the risk of total bone fractures by 15% and reduced the risk of hip fractures by 30% [27]. The meta-analysis concluded that the combination of calcium and vitamin D significantly increased femoral neck BMD only when the daily vitamin D intake was less than 400 IU compared to higher doses, while calcium only did not affect femoral neck BMD [27]. Another interesting factor was found that race/ethnicity may affect bone size and BMD. A study found that black women had greater BMD in the femoral neck than white women and Japanese women tend to have lower BMD in the femoral neck than white women [16]. In this study there was no data about race or ethnicity, renal and liver disease and history of bariatric surgery which could affect the level of vitamin D. Food is essential in vitamin D levels but there was no data about how it may affect the vitamin D level of the subjects.

Conclusion

Our results suggested that there was a significant positive correlation between serum vitamin D levels and BMD in postmenopausal women. REMS could be useful as an alternative to DXA to assess bone mass density in postmenopausal women. Further research is needed by assessing other factors which could affect the vitamin D level like renal and liver disease and history of bariatric surgery of the postmenopausal women.

Ethics approval

This research was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia, No.2925/UN5.4.1.1.3/KPM/2023.

Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

Derived data supporting the findings of this study are available from the first author on request.

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