

ASSOCIATION BETWEEN SERUM 25-HYDROXYVITAMIN D CONCENTRATIONS AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA AND OSTEOPOROSIS

POVEZANOST SERUMSKIH KONCENTRACIJA 25-HIDROKSIVITAMINA D I MINERALNE GUSTINE KOSTIJU KOD ŽENA U POSTMENOPAUZI SA OSTEOPENIJOM I OSTEOPOROZOM

Milan MIRKOVIĆ^{1,2}, Ognjen MILANOVIĆ^{1,2}, Teodor GRBIĆ², Tijana IČIN^{1,2}, Dragana TOMIĆ NAGLIĆ^{1,2} and Andrijana MILANKOV^{1,2}

ORCID NUMBER

Milan Mirković – 0009-0007-0915-8938
Ognjen Milanović – 0009-0006-6566-9882
Teodor Grbić – 0009-0000-6799-9785

Tijana Ičin – 0000-0002-3886-6518
Dragana Tomić Naglić – 0000-0002-7058-9282
Andrijana Milankov – 0000-0001-5815-3892

University of Novi Sad, Faculty of Medicine, Novi Sad¹
University Clinical Center of Vojvodina, Novi Sad²

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Abstract

Introduction. Vitamin D regulates approximately 3% of the human genome, which helps explain its roles in the musculoskeletal, cardiovascular, and immune systems, as well as in the development of malignant diseases and diabetes. Its deficiency may cause rickets in children and osteomalacia and osteoporosis in adults. Every 3 seconds, an osteoporotic fracture occurs, affecting 1 in 3 women and 1 in 5 men over the age of 50 years. The study aimed to evaluate serum vitamin D concentrations in postmenopausal women with osteopenia and osteoporosis and to assess the association between vitamin D status and bone mineral density. **Material and Methods.** This retrospective study included medical records of 100 postmenopausal women diagnosed with osteopenia or osteoporosis by dual-energy X-ray absorptiometry. Participants were divided into three groups by serum 25-hydroxyvitamin D concentrations (< 50 nmol/L; 50–75 nmol/L; ≥ 75 nmol/L) and four age groups (≤ 49; 50–59; 60–69; ≥ 70 years). **Results.** The mean age of the participants was 67.14 years. The mean 25-hydroxyvitamin D concentration was 50.28 nmol/L in women with osteoporosis and 54.98 nmol/L in women with osteopenia. A statistically significant positive correlation was observed between 25-hydroxyvitamin D concentration and hip bone mineral density. **Conclusion.** Serum vitamin D concentrations in postmenopausal women with osteopenia and osteoporosis were below the desirable range. A positive and statistically significant correlation was found between serum vitamin D concentration and hip bone mineral density. Older age was associated with a higher prevalence of fractures among women with osteopenia and osteoporosis.

Key words: Bone Diseases, Metabolic; Osteoporosis; Osteoporosis, Postmenopausal; Vitamin D; Vitamin D Deficiency; Bone Density

Sažetak

Uvod. Vitamin D je potentni regulator funkcije oko 3% ljudskog genoma, čime se objašnjava njegova uloga u funkciji koštano-mišićnog sistema, imunoprocesima, kardiovaskularnom sistemu, ali i razvoju malignih bolesti i dijabetesa. Deficijencija ovog vitamina može usloviti rahitis kod dece, osteomalaciju i osteoporozu kod odraslih. Svake tri sekunde nastaje jedna osteoporotična fraktura koju pretrpi svaka treća žena i svaki peti muškarac stariji od 50 godina. Cilj rada bio je da se odrede serumske koncentracije vitamina D kod žena sa osteoporozaom i osteopenijom, te utvrdi postojanje korelacije između serumskih koncentracija vitamina D i mineralne gustine kosti. **Materijal i metode.** Sprovedena je retrospektivna analiza istorija bolesti 100 žena u postmenopauzi kod kojih je metodom dvostruke rendgenske apsorpcijometrije postavljena dijagnoza osteopenije ili osteoporoze. Ispitanice su na osnovu vrednosti 25-hidroksi vitamina D podeljene u tri grupe (< 50 nmol/L; 50–75 nmol/L; ≥ 75 nmol/L), a prema starosti u četiri grupe (≤ 49; 50–59; 60–69; ≥ 70). **Rezultati.** Prosečna starost ispitanica iznosila je 67,14 godina. Prosečna vrednost 25-hidroksi vitamina D kod ispitanica sa osteoporozaom iznosila je 50,28 nmol/L, a kod ispitanica sa osteopenijom 54,98 nmol/L. Uočena je statistički značajna pozitivna korelacija između 25-hidroksi vitamina D i mineralne gustine kosti kuka. **Zaključak.** Serumske koncentracije vitamina D kod žena u postmenopauzi sa osteopenijom i osteoporozaom su ispod opsega poželjnih vrednosti. Postoji pozitivna i statistički značajna korelacija između serumske koncentracije vitamina D i mineralne gustine kosti kuka. Starija životna dob bila je povezana sa većom učestalošću preloma kod žena sa osteopenijom i osteoporozaom.

Ključne reči: metaboličke bolesti kostiju; osteoporoza; postmenopauzalna osteoporoza; vitamin D; nedostatak vitamina d; gustina kostiju

Introduction

Vitamin D, often referred to as the “hormone of the future” with basic structure consists of four cho-

lesterol rings, has been recognised as a potent regulator of approximately 3% of the human genome. This supports its role in the musculoskeletal system, immune processes, cardiovascular function, and the

✉ Corresponding author: Milan Mirković, E-mail: milanmirkovic1@hotmail.com, andrijana.milankov@mf.uns.ac.rs

Abbreviations

D2	– ergocalciferol
D3	– cholecalciferol
25(OH)D	– 25-hydroxyvitamin D
1,25(OH) ₂ D	– 1,25-dihydroxyvitamin D (calcitriol)
DBP	– vitamin D-binding protein
VDR	– vitamin D receptor
IL	– interleukin
TNF-α	– tumour necrosis factor alpha
M-CSF	– macrophage colony-stimulating factor
PTH	– parathyroid hormone
GH	– growth hormone
IGF-1	– insulin-like growth factor 1
DEXA	– dual-energy X-ray absorptiometry
BMD	– bone mineral density
SD	– standard deviation
CMIA	– chemiluminescent microparticle immunoassay
ANOVA	– analysis of variance

development of malignant diseases and diabetes [1]. Several forms of vitamin D are known today, but only ergocalciferol (D2) and cholecalciferol (D3) exert significant physiological effects in humans. Dietary sources include foods of animal origin (D3) and plant origin (D2), while most is majority is synthesised by exposure of 7-dehydrocholesterol to ultraviolet radiation (290–315 nm), forming previtamin D3, which is subsequently converted by thermal isomerisation into cholecalciferol (D3).

Following the synthesis of vitamin D3 in the skin, it undergoes its first transformation in the liver to 25-hydroxycholecalciferol (25(OH)D) by the action of the enzyme 25-hydroxylase [2]. The resulting 25(OH)D, or calcidiol, represents the circulating metabolite whose laboratory measurement reflects vitamin D stores in the body. The second hydroxylation occurs predominantly in the kidneys under the influence of 1α-hydroxylase, resulting in the formation of 1,25-dihydroxycholecalciferol (1,25(OH)₂D), or calcitriol. In addition to renal cells, endothelial cells, pancreatic cells, pulmonary cells, parathyroid gland cells, and many others also express 1α-hydroxylase and can locally synthesise vitamin D for their own needs. After synthesis, calcitriol binds to vitamin D-binding protein (DBP) in the plasma and is transported to all cells that express the vitamin D receptor (VDR).

Vitamin D exerts its primary role through participation in osteogenesis and maintenance of bone structural integrity by regulating calcium and phosphorus homeostasis and stimulating their intestinal absorption and reabsorption in the proximal renal tubules. In addition, vitamin D represents an important component of the immune system, as recent studies have also attributed antiproliferative properties to it [3]. It is estimated that 47% of the global population has vitamin D deficiency [4]. The two most common causes of vitamin D deficiency are

inadequate dietary intake and insufficient sun exposure, which largely depend on geographical latitude. Countries of the Balkan Peninsula are located above the 35th parallel, where reduced endogenous vitamin D synthesis has been documented during the autumn and winter months [5,6]. Deficiency of this vitamin may result in numerous disorders, including rickets in children, osteomalacia and osteoporosis in adults, hyperparathyroidism, and various disturbances of the nervous, muscular, immune, and glucose-regulating systems [3]. Osteoporosis is a chronic, progressive metabolic skeletal disorder characterised by reduced bone mass and deterioration of bone microarchitecture [7,8]. The principal pathophysiological mechanism of osteoporosis is accelerated overall bone turnover with an imbalance between bone formation and bone resorption in favour of the latter. Trabecular bone is metabolically the most active, and therefore, bone loss is initially observed in the lumbar vertebrae, proximal femur, and wrist region [3].

Osteoporosis may be classified in several ways, although the most widely accepted classification is the aetiological division into primary and secondary osteoporosis. Primary osteoporosis includes idiopathic and involutional osteoporosis, the latter is further divided into postmenopausal and senile osteoporosis. Postmenopausal osteoporosis (Type I) is the most common form of the disease and occurs in women during the postmenopausal period up to the age of 70 years [9]. Oestrogen deficiency resulting from natural or artificial menopause leads to increased production of inflammatory cytokines (IL-6, IL-1, IL-11, TNF-α, M-CSF) and enhanced sensitivity of osteoblast and osteoclast precursor cells to their effects, thereby increasing osteoclast activity in the absence of the modulatory effects of hormones and growth factors (calcitonin, PTH, GH, IGF-1). During the early postmenopausal period, accelerated bone remodelling, with a predominance of bone resorption, disrupts trabecular microarchitecture. Simultaneously, reduced periosteal apposition and increased endocortical resorption impair cortical microarchitecture, leading to vertebral and distal forearm fractures. An osteoporotic fracture is defined as a fracture occurring spontaneously or after minimal trauma [10,11].

Involutional osteoporosis (Type II) occurs in older women and men after age of 70. Its pathogenesis is associated with physiological ageing processes, including reduced calcium absorption, decreased calcitriol synthesis, and increased PTH secretion. It is characterised by the loss of both trabecular and cortical bone [11,12]. Secondary osteoporosis develops as a consequence of underlying diseases (e.g., Cushing's syndrome, diabetes mellitus, cystic fibrosis) or chron-

ic use of medications (corticosteroids, antiepileptic drugs) that affect bone metabolism [9].

The gold standard for assessing bone mineral density and diagnosing of osteoporosis is dual-energy X-ray absorptiometry (DEXA) of the lumbar spine (L1–L4) and hip. Bone mineral density (BMD) is expressed in g/cm^2 and reported using T-scores and Z-scores. The T-score represents the deviation of measured bone mass from the average peak bone mass of young adults, whereas the Z-score represents the deviation from the expected average for individuals of the same age. Osteoporosis is diagnosed when the T-score is ≤ -2.5 SD, whereas osteopenia is defined as a T-score between -2.5 and -1.0 SD. Severe osteoporosis is defined as a T-score ≤ -2.5 accompanied by one or more fragility fractures. The T-score is used to assess bone density in postmenopausal women and men older than 50 years, whereas the Z-score is applied in younger individuals and premenopausal women. Osteoporosis treatment includes both non-pharmacological measures (lifestyle modification, reduction of risk factors, calcium and vitamin D supplementation) and pharmacological therapy consisting of two main groups of medications: antiresorptive agents (bisphosphonates, selective oestrogen receptor modulators, hormone replacement therapy, calcitonin, and denosumab) and anabolic agents (teriparatide, abaloparatide, and romosozumab) [8,13].

Reduced endogenous vitamin D synthesis, specifically a decrease in the concentration of its active metabolite, also plays an important role in the pathophysiology of osteoporosis, making bone more susceptible to fractures [12,14].

This study aimed to determine serum 25-hydroxyvitamin D [25(OH)D] concentrations in women with osteopenia and osteoporosis, and to assess the association between serum 25(OH)D concentrations and bone mineral density (BMD).

Material and Methods

This study was a retrospective analysis of medical records from 100 female patients treated on an outpatient basis at the Clinic for Endocrinology, Diabetes, and Metabolic Disorders. Medical records were selected from the clinic archive according to predefined inclusion and exclusion criteria, without restriction to a predefined calendar period. Approval for the study was obtained from the Clinic and the Ethics Committee of the University Clinical Center of Vojvodina.

The study included postmenopausal women diagnosed with osteopenia or osteoporosis based on DXA examination and with available serum vitamin D measurements obtained before the initiation of any

treatment. Women with secondary osteoporosis were excluded from the study. The following data were collected from medical records: demographic characteristics (age), serum 25-hydroxyvitamin D [25(OH)D] concentrations, history of fractures, and bone mineral density measurements (T-score).

Bone mineral density of the lumbar spine (L1–L4) and hip was assessed using a Lunar densitometer. T-scores and Z-scores were calculated using the device software. Osteopenia was defined as a T-score between -1.0 and -2.5 , whereas osteoporosis was defined as a T-score ≤ -2.5 . Serum vitamin D concentrations, specifically its circulating metabolite 25(OH)D, were measured using the chemiluminescent microparticle immunoassay (CMIA) method on an automated Abbott Alinity immunoassay analyser. Values equal to or above 75 nmol/L were considered sufficient, values between 50 and 75 nmol/L were classified as insufficient, and values below 50 nmol/L as vitamin D deficiency. Participants were stratified into four age groups (≤ 49 years, 50–59 years, 60–69 years, and ≥ 70 years) and into three groups according to serum 25(OH)D concentration (≥ 75 nmol/L, 50–75 nmol/L, and < 50 nmol/L).

Continuous variables were described using minimum and maximum values, means, and standard deviations. Categorical variables were expressed as percentages. The normality of continuous variables was assessed using the Shapiro–Wilk test. Differences in mean values between groups were evaluated using analysis of variance (ANOVA). Associations between continuous variables were assessed using Pearson's correlation coefficient. Statistical analyses were performed using the R statistical software package (version 4.4.0), with statistical significance set at $p \leq 0.05$.

Results

The study included 100 women diagnosed with osteopenia or osteoporosis based on DXA examination. Demographic and clinical characteristics of the study population are presented in **Table 1**. The mean age of the participants was 67.14 years, while the mean serum vitamin D concentration was 51.69 nmol/L. The mean lumbar spine (L1–L4) T-score was -2.51 . The mean hip T-score was -1.95 , which was 0.56 higher than the lumbar spine T-score. The lowest recorded T-score was -4.5 at the hip and -4.8 at the lumbar spine.

Participants were stratified into four age groups: ≤ 49 years, 50–59 years, 60–69 years, and ≥ 70 years (**Table 2**). The largest group consisted of women aged 70 years and older ($n = 45$), followed by those aged 60–69 years ($n = 40$). Eight participants were between 50 and 59 years of age, while only seven were young-

Table 1. Demographic and Clinical Data

Variable	Mean	SD	MIN	
Age (years)	67.14	9.04	41	83
25(OH)D (nmol/L)	51.69	21.08	10	98
L1-L4 T-score (SD)	-2.51	0.82	-4.8	-0.6
Hip T-score (SD)	-1.95	0.94	-4.5	0.4

Table 2. Baseline Characteristics of the Study Sample

Variable	Category	n	
Age (years)	≤ 49	7	7
	50-59	8	8
	60-69	40	40
	≥70	45	45
Fractures	Yes	47	47
	No	53	53
25(OH)D (nmol/L)	<50	45	45
	50-75	40	40
	≥75	15	15
T-score (BMD classification)	Osteopenia	30	30
	Osteoporosis	70	70

Table 3. Mean age, history of fractures, serum 25(OH)D concentrations, and bone mineral density in women with osteopenia and osteoporosis

	Age (years) (Mean ±SD)	Fractures, n	25(OH)D (nmol/L) (Mean±SD)	Hip BMD (g/cm ²) (Mean± SD)	L1-L4 BMD (g/cm ²) (Mean±SD)
Osteopenia	67.30 ± 8.61	10	54.98 ± 20.79	0.848 ± 0.07	0.967 ± 0.05
Osteoporosis	67.07 ± 9.28	37	50.28 ± 21.19	0.729 ± 0.10	0.834 ± 0.10

er than 50 years. Based on serum 25(OH)D concentrations, participants were categorised into three groups: <50 nmol/L, 50–75 nmol/L, and ≥75 nmol/L. Only 15 participants had serum 25(OH)D concentrations within the desirable range (≥75 nmol/L). The remaining participants had suboptimal vitamin D status, with 40 exhibiting vitamin D insufficiency (50–75 nmol/L) and 45 exhibiting vitamin D deficiency (<50 nmol/L). According to T-scores measured at the hip and lumbar spine, participants were classified into two groups: osteopenia (n = 30) and osteoporosis (n = 70). A history of fracture was reported in 47% of the participants.

As shown in **Table 3**, women with osteoporosis had lower mean serum vitamin D concentrations (50.28 nmol/L), lower hip BMD values (0.729 g/cm²), and lower lumbar spine (L1–L4) BMD values (0.834 g/cm²) compared with women with osteopenia, whose corresponding mean values were 54.98 nmol/L, 0.848 g/cm², and 0.967 g/cm², respectively. In addition, fractures were more common among women with osteoporosis, with 37 participants reporting a history of fracture.

By age group, the lowest mean serum vitamin D concentration was observed in women aged 70 years

and older (48.23 nmol/L), whereas the highest was found in women younger than 50 years (60.71 nmol/L). Although there was a tendency of lower mean serum vitamin D concentration with increasing age, the differences between age groups were not statistically significant (p = 0.146). Women with a history of fractures had the lowest mean serum vitamin D concentration (49.06 nmol/L), whereas those without fractures had a mean concentration approximately 5 nmol/L higher. However, this difference was not statistically significance (p = 0.242). Participants with osteopenia had slightly higher mean serum vitamin D concentrations (54.98 nmol/L) than those with osteoporosis (50.28 nmol/L); however, the difference was not statistically significant (p = 0.310) (**Table 4**).

The mean age of participants with a history of fracture was 69.51 years, compared with 65.03 years among those without a history of fracture. This difference was statistically significant (p = 0.013).

The mean age of participants with sufficient vitamin D concentrations (≥75 nmol/L) was 65.66 years, whereas the mean age was higher among those with suboptimal vitamin D status, reaching 67.47 years in the vitamin D insufficiency group (50–75 nmol/L)

Table 4. Mean serum 25(OH)D concentrations in subjects in relation to age, presence of fractures, and bone mineral density

	Category	n	Mean $\pm$ SD	
Age (years)	≤ 49	7	60.71 $\pm$ 26.08	0.146
	50-59	8	49.91 $\pm$ 17.99	
	60-69	40	54.36 $\pm$ 19.58	
	≥ 70	45	48.23 $\pm$ 21.99	
Fractures	Yes	47	49.06 $\pm$ 22.66	0.242
	No	53	54.02 $\pm$ 19.49	
BMD (g/cm ²) (classification)	Osteopenia	30	54.98 $\pm$ 20.79	0.310
	Osteoporosis	70	50.28 $\pm$ 21.19	

Table 5. Mean age in relation to serum 25(OH)D concentrations, presence of fractures, and bone mineral density

	Category	n	Mean $\pm$ SD	
Fractures	Yes	47	69.51 $\pm$ 7.34	0.013
	No	53	65.03 $\pm$ 9.93	
25(OH) (nmol/L)	<50	45	67.33 $\pm$ 9.66	0.793
	50-75	40	67.47 $\pm$ 7.30	
	≥ 75	15	65.66 $\pm$ 11.58	
BMD (g/cm ²) (classification)	Osteopenia	30	67.3 $\pm$ 8.61	0.909
	Osteoporosis	70	67.07 $\pm$ 9.28	

Table 6. Correlation between 25(OH)D concentration and bone mineral density (BMD) (N = 100)

Correlation	r	
25(OH)D vs. L1-L4 BMD	0.17	0.07
25(OH)D vs. Hip BMD	0.19	0.05

r - Pearson correlation coefficient; *p* - statistical significance of the correlation ($p \leq 0.05$)

and 67.33 years in the vitamin D deficiency group (<50 nmol/L). Although lower vitamin D concentrations were observed with increasing age, the differences were not statistically significant ($p = 0.793$). Similarly, no significant difference in age was observed between participants with osteopenia and those with osteoporosis. The mean age was 67.30 years in the osteopenia group and 67.07 years in the osteoporosis group ($p = 0.909$) (Table 5).

Pearson's correlation analysis was performed to evaluate the association between serum vitamin D concentrations and bone mineral density at the hip and lumbar spine (L1-L4) (Table 6). A positive correlation was observed between serum vitamin D concentration and lumbar spine BMD; however, the association did not reach statistical significance ($r = 0.17$, $p = 0.07$). Similarly, a weak positive correlation was observed between serum vitamin D concentration and hip BMD, which was statistically significant ($r = 0.19$, $p = 0.05$).

Discussion

Physical inactivity, a sedentary lifestyle, and numerous metabolic disorders contribute to adverse changes in the skeletal system. Today, the prevalence

of non-communicable diseases continues to increase, with osteoporosis representing not only a major health concern but also a significant socioeconomic burden [15]. Age is an important biological determinant of bone loss. Peak bone mass is estimated to be achieved by the age of 25 years, after which bone density gradually declines, with an average decrease of approximately 0.5% every four years in adulthood. Furthermore, bone mineral density loss is two to three times greater in women after menopause [16]. In a study conducted by Labronici et al., the mean age of women diagnosed with osteopenia was 69 years, whereas women with osteoporosis were older, with a mean age of 75 years. The authors reported a statistically significant difference in age between women with osteoporosis and those with osteopenia [17]. Similar findings have been reported in more recent population-based studies, which demonstrated that the prevalence of osteopenia and osteoporosis increases significantly with age, particularly among individuals older than 70 years [18]. In our study, the mean age of women with osteopenia was 67 years, while women with osteoporosis were of a similar age. Consequently, no statistically significant difference was observed between these groups. One possible

explanation is that our study did not include women with normal bone mineral density and was conducted on a relatively small sample.

The role of vitamin D as a key factor in maintaining skeletal health has received increasing attention in recent years. A decline in serum vitamin D concentrations has been observed across all age groups over recent decades. Previous studies have shown that vitamin D deficiency is more prevalent in women than in men, particularly among older women with osteopenia and osteoporosis [19].

In our study, the mean serum vitamin D concentration was 54.98 nmol/L in women with osteopenia and 50.28 nmol/L in women with osteoporosis. Although the difference was not statistically significant, both groups exhibited vitamin D concentrations below the recommended range. Similar findings were reported in a Brazilian study by Labronici et al., where mean vitamin D concentrations were 54 nmol/L in women with osteopenia and 55 nmol/L in women with osteoporosis. Likewise, no significant difference was observed between the two groups [17]. In contrast, Laktašić et al. reported somewhat lower mean serum vitamin D concentrations in women with osteopenia (48 nmol/L) and osteoporosis (45 nmol/L) [20]. These lower concentrations were observed in women with a mean age of approximately 60 years, which differs from our findings, where comparable vitamin D concentrations were recorded primarily among women older than 70 years.

Considering the geographical latitude and the greater number of sunny days, higher vitamin D concentrations might be expected among women from Brazil than among women from the Balkan region. However, substantial differences were not observed. This finding suggests that endogenous vitamin D synthesis depends not only on sunlight exposure but also on factors such as lifestyle, body mass index, dietary intake, and chronic diseases. This observation is consistent with contemporary epidemiological data demonstrating a high global prevalence of vitamin D deficiency, even in regions with abundant sunlight [4].

Numerous studies have investigated the relationship between vitamin D and bone mineral density. Malavolta et al. conducted a study among postmenopausal women in Italy. They reported a strong positive correlation between serum vitamin D concentrations and bone mineral density at both the hip and lumbar spine [21]. Laktašić et al. demonstrated a positive correlation only between vitamin D concentration and hip bone mineral density [20]. Similarly, our study identified a weak positive correlation between serum 25(OH)D concentration and hip bone mineral density that was statistically significant, whereas the cor-

relation with lumbar spine bone mineral density was also weak and positive but did not reach statistical significance. In contrast, Garnero et al. found no association between vitamin D concentrations and bone mineral density at either the hip or the spine [22]. These heterogeneous findings are likely explained by differences in ethnicity, age distribution, study design, and the fact that vitamin D deficiency represents only one of several factors contributing to reduced bone mineral density. In addition to age and female sex, decreased bone mineral density is influenced by oestrogen deficiency, physical inactivity, inadequate sun exposure, smoking, low body mass index, and numerous other factors. Previous studies have shown that women with five or more risk factors have up to a 17-fold higher incidence of hip fractures [23]. Furthermore, hip fractures are associated with mortality of up to 36% during the first year after fracture [16].

Osteoporosis represents a major global health challenge. It is estimated to cause nearly 8.9 million fractures worldwide annually. An osteoporotic fracture occurs every 3 seconds, affecting 1 in 3 women and 1 in 5 men over the age of 50 years [15]. In our study, 47% of participants had a history of fracture. The mean age of women with fractures was 69 years, whereas women without fractures were approximately four years younger. This difference was statistically significant. The importance of age as a risk factor for fractures was also demonstrated by Labronici et al., who reported a mean age of 75 years among women with fractures, six years older than the women in our cohort. However, the prevalence of fractures in their study was lower (25%) [17]. Similar findings have been reported in more recent population-based and cohort studies, indicating that the risk of osteoporotic fractures increases exponentially after the age of 65 years, with a further increase after the age of 70 years, regardless of geographic region or ethnicity [24]. Although our study did not demonstrate a statistically significant difference, mean vitamin D concentrations were lower among women with fractures (49 nmol/L) than among those without fractures (54 nmol/L). Fisher et al. similarly reported a high prevalence of vitamin D deficiency among women with fractures, with vitamin D insufficiency present in nearly 80% of hip fracture cases [25]. Comparable findings were reported in a recent meta-analysis by Lv et al., which demonstrated a dose-dependent association between lower serum 25(OH)D concentrations and an increased risk of hip and non-vertebral fractures, particularly among older women [26].

Numerous studies emphasise the importance of early vitamin D and calcium supplementation for fracture prevention. Larsen et al. reported that individuals

older than 65 years receiving vitamin D supplementation at doses greater than 400 IU/day had a 16% lower fracture risk [27]. However, vitamin D supplementation should be used with caution. Sanders et al. demonstrated that very high annual doses of vitamin D (500,000 IU once yearly for five years) administered to women aged 70 years and older paradoxically increased fracture risk [28]. More recent meta-analyses and randomised controlled trials have shown that vitamin D supplementation alone does not significantly reduce fracture risk in the general population. Any potential benefit on bone mineral density appears to be modest and is most consistently observed when vitamin D is administered in combination with calcium [29]. These findings further emphasise the importance of comprehensive osteoporosis assessment and the timely identification of modifiable risk factors in routine clinical practice [30].

Limitations

Several limitations of this study should be acknowledged. First, its retrospective design, relatively small sample size, and single-centre setting may limit

the generalisability of the findings. In addition, several factors that may influence vitamin D status and bone mineral density, including body mass index, physical activity, and dietary habits (particularly calcium and vitamin D intake), were not evaluated. Future large-scale prospective studies are needed to clarify further the relationship between vitamin D status and bone mineral density in postmenopausal women.

Conclusion

Our study confirmed that postmenopausal women with osteopenia or osteoporosis have serum vitamin D concentrations below the recommended range. A weak positive correlation between serum 25-hydroxyvitamin D concentration and hip bone mineral density was statistically significant, whereas the weak positive correlation with lumbar spine bone mineral density did not reach statistical significance. Increasing age was associated with a higher prevalence of fractures among women with osteopenia and osteoporosis.

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