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Original Article

Vitamin D and its Relation to Bone Mineral Density in Postmenopause Women

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ABSTRACT

Objective: Compare the level of vitamin D with the bone mineral density (BMD) in postmenopausal women, with or without fractures. *Methods:* 250 women with mean age of 71.1 were evaluated. The serum levels of vitamin D considered sufficient were $\geq$ 30 ng/mL, insufficient between 20 and 30 ng/mL and deficient < 20 ng/mL. The bone mineral density was measured and considered osteopenia when T value total of lumbar spine or hip was between -1 and -2.5 and osteoporosis < 2.5. The patients with fractures accounted for 25.2%. *Results:* There was no significant difference in the vitamin D (ng/mL) levels among the age groups (p = 0.25), the levels of fractures (p = 0.79) and the levels of BMD (p = 0.76). *Conclusion:* 82% of the patients presented deficient and insufficient blood levels of vitamin D. Ours results showed any significant correlation between vitamin D levels and bone mineral density after adjusting for age.

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Introduction

The loss of bone density in postmenopausal women has been linked to a subclinical deficiency in vitamin D, which is considered to be a risk factor for fractures due to the susceptibility of this population to falls and inappropriate neuromuscular responses.[1-4] Vitamin D insufficiency can result from nutritional deficiency and/or low sun exposure in confined elderly patients and inpatients with chronic diseases.[5-8]

Studies have shown that female patients who ingest high levels of calcium exhibit high bone mineral density when compared to female patients with low calcium ingestion. Vitamin D and calcium supplements aid in the prevention of bone loss by reducing bone renewal and the number of non-vertebral fractures.[9]

Supplemental vitamin D and calcium (500-1,200 mg/d) seems to reduce the risk of secondary hyperparathyroidism due to vitamin D insufficiency.[10] Vitamin D is absorbed through two mechanisms: the activation of the 7-dehydrocholesterol pathway in the skin by sunlight and the intestinal absorption of the vitamin D in food. The appropriate serum level of vitamin D is approximately 30 to 55 ng/mL. Values below 20 ng/mL are considered to be deficient and levels in the 20 to 30 ng/mL range are considered inappropriate.[11,12]

The objective of this paper was to compare the vitamin D levels and BMD of postmenopausal women with or without fractures.

Materials and Methods

Two hundred fifty women with a mean age of 71.1 years old (45 to 98) were evaluated between January 2010 and December 2011. The included patients were postmenopausal women who had reached menopause two years before and had received a bone densitometry scan at least six months prior to the initial visit. The women underwent analysis to determine their vitamin D level and were not using a corticosteroid. The serum vitamin D levels were measured by electrochemiluminescence; values ≥ 30 ng/mL were considered normal, values between 20 and 30 ng/mL were considered insufficient and values < 20 ng/mL were considered deficient. The patients' BMD in the region of the hips and the lumbar spine was measured with GER's Lunar Prodigy Advance Densitometer with fan bean technology. The hip densitometry measurement included the trochanter, the femur neck and the intertrochanteric region. The lumbar spine densitometry measurement included the lumbar vertebrae L1- L4. The included software calculated the T and Z values relative to North-American reference values. Osteopenia was defined as a T-score between -1 and -2.5 at the lumbar spine or hips and osteoporosis was defined as a T-score < -2.5.

The sample characterization was aimed at developing a general profile of the 250 female patients studied. Table 1 shows the mean, the standard deviation (SD), the median,

Table 1 - General Description of Numeric Variables.

Variable	Mean	SD	Median	Minimum	Maximum
Age (years)	71.1	10.3	71	45	98
Vitamin D	2.8	10.5	21.8	5.7	80.9
Spine BMD	-1.4	1.4	-1.5	-4.6	3.7
Femur BMD *	-1.3	1.2	-1.3	-5.4	2

SD: Standard Deviation. * corresponds to the lower BMD value in the bilateral cases. Source: Hospital Santa Teresa, Petrópolis, RJ.

and the minimum and maximum numeric variables. Table 2 provides the frequency (n) and the percentage (%) of the categorical variables.

Statistical Methodology

The tables summarize the data observed, which were expressed as the frequency (n) and percentage (%) for categorical (qualitative) data and as the mean, standard deviation, median and the minimum and maximum for numeric data.

The statistical analysis consisted of the following methods:

- the numeric variables for two subgroups were compared using the Student's t test for independent samples or the Mann-Whitney test; comparisons among three subgroups were analyzed using a one-way ANOVA or the Kruskal-Wallis Anova test (non-parametric). Tukey's or Dunn's multiple comparison tests (non-parametric) were applied to identify which groups were significantly different from each other at the level of 5%, and
- the categorical variables for the subgroups were compared using the χ^2 test.

Table 2 - General Description of Categorical Variables.

Variable	Category	n	%
Age (years)	45 to 49	4	1.6
	50 to 59	28	11.2
	60 to 69	76	30.4
	70 to 79	89	35.6
	80 to 89	45	18.0
	90 to 99	8	3.2
Fracture	yes	63	25.2
	no	187	74.8
Vitamin D (classification)	≤ 20	94	37.6
	21 to 29	111	44.4
	≥ 30	45	18.0
BMD (classification)	normal	58	23.2
	osteopenia	114	45.6
		78	31.2

Source: Hospital Santa Teresa, Petrópolis, RJ.

Non-parametric tests were applied because some variables did not present a normal distribution (Gaussian); due to data dispersion, the null hypothesis was rejected according to the Kolmogorov-Smirnov test. Significance was defined at the level of 5%. SAS 6.11 (SAS Institute, Inc., Cary, North Carolina, USA) software was used to complete the statistical analysis.

Results

The first objective was to verify if there were significant differences between fracture status (present or not), vitamin D level (deficient, insufficient and sufficient) and BMD (normal, osteopenia and osteoporosis) with relation to the mean age of the patients (in years).

Table 3 summarizes the mean ± standard deviation (SD) of the patients' age based on the fracture status, vitamin D level and BMD and the corresponding *p values* calculated by the appropriate statistical test.

The statistical analysis utilized the Student's *t* test for independent samples to compare two categories (levels) or the one-way Anova to compare three categories. Tukey's multiple comparison test was used to identify which categories were significantly different from each other at a level of 5%.

The mean age of the subgroup of patients with fractures was significantly higher than the mean age of the subgroup without fractures ($p = 0.0002$). The mean ages of the patients with differing BMD levels were also significantly different ($p = 0.0001$). The mean age of the subgroup of patients with osteoporosis was significantly higher than the mean ages of the subgroups with normal BMD and osteopenia.

There was no significant difference in the mean age of patients with different vitamin D levels ($p = 0.13$).

The second objective was to verify if there was significant difference in the vitamin D levels (in ng/mL) of the patients with different ages, fracture statuses and BMD levels. Table 4 summarizes the median, the minimum and maximum vitamin D levels (ng/mL) for each age group (45 to 59, 60 to 69, 70 to 79 and 80 to 99 years old), fracture status (present or not) and BMD level (normal, osteopenia and osteoporosis) and the corresponding *p value* of the statistical test used for the comparison.

The statistical analysis utilized the Mann-Whitney test to compare two categories (levels) or the Kruskal-Wallis Anova to compare three categories. Dunn's multiple comparison test was used to identify which categories were significantly different from each other at a level of 5%.

There were no significant differences in the vitamin D levels (ng/mL) among the age groups ($p = 0.25$), the fracture status ($p = 0.79$) or the BMD levels ($p = 0.76$) (Fig. 1).

The third objective sought to identify whether there was significant association among the following variables: age group, fracture status, vitamin D level and BMD. Tables 5, 6, 7 and 8 provide the frequency (n) and the percentage (%) of the contingency tables for the four variables studied and the corresponding *p value* of the χ^2 test. The analyses were repeated and are only presented if the results differed.

Age group was significantly associated with the presence of fracture ($p < 0.0001$) and osteoporosis ($p = 0.006$).

The presence of fracture was significantly associated with age group ($p < 0.0001$) and osteoporosis ($p = 0.011$).

Vitamin D levels were not significantly associated with age group ($p = 0.22$), fracture ($p = 0.82$) or BMD ($p = 0.77$) (Fig. 2).

Table 3 - Mean patient age (years) for each of the fracture, vitamin D3 and BMD categories.

Subgroup	Category	n	Mean ± SD	p value[a]
Fracture	yes	63	75.3 ± 11.5	0.0002
	no	187	69.7 ± 9.5	
BMD (classification)	normal	58	68.4 ± 10.4	0.0001
	osteopenia	114	69.6 ± 9.7	
	osteoporosis	78	75.3 ± 10.0	
Vitamin D (classification)	deficiency	94	72.6 ± 10.5	0.13
	insufficient	111	69.7 ± 9.6	
	sufficient	45	71.5 ± 11.3	

[a]Student's *t* test for independent samples or one-way Anova.

Table 4 - Vitamin D level (ng/mL) for each age group, fracture status and BMD category.

Variable	Category	n	Median	Minimum	Maximum	p value[a]
Age (years)	45 to 59	32	21.7	14.1	56.9	0.25
	60 to 69	76	22.2	9.7	64.7	
	70 to 79	89	20.8	9.0	80.9	
	80 to 99	53	22.6	5.7	72.0	
Fracture	yes	63	22.1	5.7	72.0	0.79
	no	187	21.6	6.2	80.9	
BMD (classification)	normal	58	21.2	9.3	64.7	0.76
	osteopenia	114	21.9	9.0	52.4	
	osteoporosis	78	22.2	5.7	80.9	

[a]Mann-Whitney test or Kruskal-Wallis Anova. Source: Hospital Santa Teresa. Petrópolis. RJ.
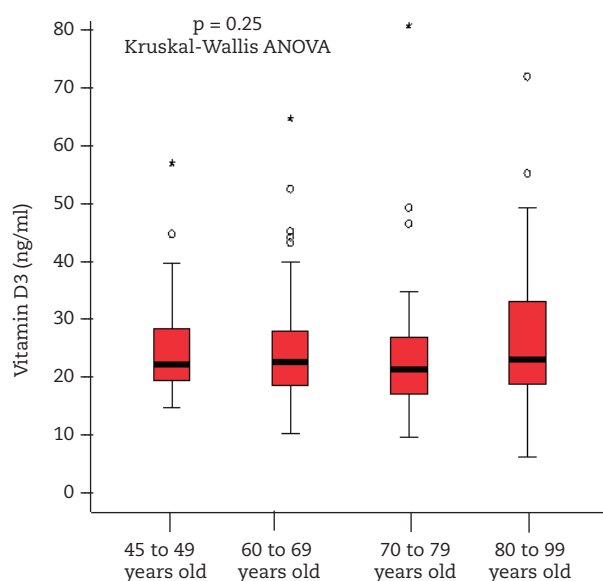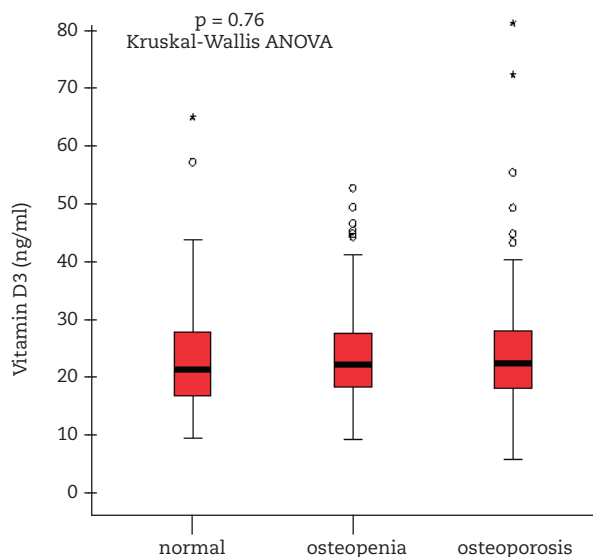
Fig. 1- Relationship between vitamin D level and age.

Fig. 2 - Vitamin D levels for each BMD category.

Table 5 – Association between each of the variables and age.									
Variable	**Category**	**45 to 59 years old**		**60 to 69 years old**		**70 to 79 years old**		**80 to 99 years old**	*p value*[a]
		n	%	n	%	n	%	n	%	
Fracture	yes	7	**21.9**	12	**15.8**	19	**21.4**	25	**47.2**	**< 0.0001**
	no	25	78.1	64	84.2	70	78.7	28	52.8	
Vitamin D (classification)	deficiency	10	31.3	26	34.2	39	43.8	19	35.9	
	insufficient	16	50.0	36	47.4	40	44.9	19	35.9	0.22
	sufficient	6	18.8	14	18.4	10	11.2	15	28.3	
DMO (classification)	normal	12	37.5	19	25.0	19	21.4	8	15.1	
	osteopenia	15	46.9	40	52.6	41	46.1	18	34.0	**0.006**
	osteoporosis	5	**15.6**	17	**22.4**	29	**32.6**	27	**50.9**	

[a] χ^2 test. Source: Hospital Santa Teresa, Petrópolis, RJ.

Table 6 - Association between each of the variables and fracture status.						
Variable	**Category**	**With Fracture**		**Without Fracture**		*p value*[a]
		n	%	n	%	
Age (years)	45 to 59	7	11.1	25	13.4	
	60 to 69	12	19.1	64	34.2	
	70 to 79	19	30.2	70	37.4	< 0.0001
	80 to 99	25	**39.7**	28	**15.0**	
Vitamin D (classification)	deficiency	23	36.5	71	38.0	
	insufficient	27	42.9	84	44.9	0.82
	sufficient	13	20.6	32	17.1	
BMD (classification)	normal	7	11.1	51	27.3	
	osteopenia	29	46.0	85	45.5	**0.011**
	osteoporosis	27	**42.9**	51	**27.3**	

[a] χ^2 test. Source: Hospital Santa Teresa, Petrópolis, RJ.

Table 7 - Association between each of the variables and vitamin D level.

Variable	Category	Deficient		Insufficient		Sufficient		p value[a]
		n	%	n	%	n	%	
Age (years)	45 to 59	10	10.6	16	14.4	6	13.3	
	60 to 69	26	27.7	36	32.4	14	31.1	0.22
	70 to 79	39	41.5	40	36.0	10	22.2	
	80 to 99	19	20.2	19	17.1	15	33.3	
Fracture	yes	23	24.5	27	24.3	13	28.9	0.82
	no	71	75.5	84	75.7	32	71.1	
BMD (classification)	normal	25	26.6	22	19.8	11	24.4	
	osteopenia	39	41.5	55	49.6	20	44.4	0.77
	osteoporosis	30	31.9	34	30.6	14	31.1	

[a] χ^2 test. Source: Hospital Santa Teresa, Petrópolis, RJ.

Table 8 - Association between each of the variables and BMD.

Variable	Category	Normal		Osteopenia		Osteoporosis		p value[a]
		n	%	n	%	n	%	
Age (years)	45 to 59	12	20.7	15	13.2	5	6.4	
	60 to 69	19	32.8	40	35.1	17	21.8	0.006
	70 to 79	19	32.8	41	36.0	29	37.2	
	80 to 99	8	**13.8**	18	**15.8**	27	**34.6**	
Fracture	yes	7	**12.1**	29	**25.4**	27	**34.6**	0.011
	no	51	87.9	85	74.6	51	65.4	
BMD (classification)	deficiency	25	43.1	39	34.2	30	38.5	
	insufficient	22	37.9	55	48.3	34	43.6	0.77
	sufficient	11	19.0	20	17.5	14	18.0	

[a] χ^2 test. Source: Hospital Santa Teresa, Petrópolis, RJ.

Osteoporosis was significantly associated with age group (p = 0.006) and the presence of fracture (p = 0.011).

Discussion

Vitamin D is extremely important for calcium absorption. When serum vitamin D levels decrease, the parathyroid hormone level increases and calcium absorption decreases. Vitamin D is absorbed through two mechanisms: the activation of the 7-dehydrocholesterol pathway in the skin by sunlight and intestinal absorption from the diet. Although vitamin D deficiency is relatively rare in the healthy young population, this deficiency is common in the elderly population, especially among inpatients or individuals who live in countries where sunlight is limited.[12] It is worth mentioning that vitamin D deficiency is not only limited to the bones or muscles. Recent epidemiological data on vitamin D deficiency have shown an association with arthritis, as well as with non-skeletal diseases such as prostate, colon and breast cancer; diabetes mellitus types 1 and 2; multiple sclerosis; hypertension; cardiovascular disease and schizophrenia.[11] This study analyzed the relationship between vitamin D levels and age but did not find any significant difference in the vitamin D levels of different age groups. However, more than 70% of the patients in each of the age groups exhibited deficient or insufficient levels of vitamin D. Therefore, it is advisable to

measure serum vitamin D levels at all ages, as deficient and insufficient levels may accelerate bone deterioration and cause osteoporosis.

The link between vitamin D and bone mineral density is still being discussed. An evaluation of the vitamin D level in patients with osteoporosis is essential for two reasons. First, vitamin D deficiency in patients with osteoporosis causes demineralization that may reduce bone mass.[13,14] Second, it is important to achieve suitable levels of vitamin D in patients with osteoporosis to maximize the response to antiresorptive therapy, facilitate changes in bone mineral density and efficiently manage fractures.[15] Several studies have suggested that low serum vitamin D levels are associated with low bone mineral density.[16-18] Bischoff-Ferrari et al.[19] found a positive relationship between vitamin D levels and bone mineral density in young Caucasians and elderly men. However, other studies have not supported this association.[20-22] The heterogeneity of the results can be partially explained by ethnic differences in the patient populations and differing age groups, as well as by the fact that the studies focused on different regions of the human body. Garnero et al.[23] and Allali et al.[24] were unable to show a significant correlation between vitamin D levels and bone mineral density. Rassouli et al.[25] found a correlation with the bone mineral density of the spine, but not the hips. Sadat-Ali et al.[26] found that most patients with vitamin D insufficiency exhibit low bone mass and that all patients with vitamin D deficiency have bone mineral densities varying between osteopenia and osteoporosis. This group also found a correlation between vitamin D levels and bone mineral density in most patients, particularly those groups exhibiting insufficiency and deficiency. The authors emphasized the importance of measuring vitamin D levels in patients with low bone mass instead of relying only on bone densitometry. Bandeira et al.[27] found vitamin D deficiencies in healthy postmenopausal women of all ages during routine doctor's appointments. The authors concluded that those individuals exhibiting vitamin D levels lower than 25 ng/mL were elderly patients who had reached menopause a long time ago. These patients also exhibited low bone mineral density on the femur neck and high levels of parathyroid hormone. This study indicated that 91.1% of the patients with osteopenia exhibited deficient and insufficient serum vitamin D levels (41.5% and 49.6%, respectively) and that 62.5% of the patients with osteoporosis exhibited deficient and insufficient serum vitamin D levels (31.9% and 30.6%, respectively). However, 46.4% of the normal patients exhibited deficient and insufficient serum vitamin D levels (26.6% and 19.8%, respectively). It is worth mentioning that all of the women in this study were Caucasians from the same region (latitude and altitude).

Recent evidence has indicated that sun exposure does not guarantee a healthy vitamin D level. Brinkley et al.[28] evaluated 93 young adults from Hawaii who experienced sun exposure without protection for more than 20 hours per week, finding that 51% of the individuals studied exhibited inappropriate levels of vitamin D (< 30 ng/mL). Because Brazil is a tropical country, the population is expected to have adequate vitamin D levels. However, two studies conducted in elderly patients in the southeastern region of the country (latitude 20-30°S) found a high prevalence of vitamin D deficiency.[29-32]

Vitamin D deficiency is present in all regions, but is higher in southern Asia and the Middle East.[33] In our study, we analyzed well nourished Caucasian women who had reached menopause two years before commencement of the study who lived in the same region (22° 30' 16.70"S latitude, 43° 10' 56.38"W longitude in a region with a highland tropical climate) in a city lying 838 meters above the sea level. The study results indicated that 37.6% of the patients exhibited deficient serum vitamin D levels. Eighty-two percent of the patients had insufficient and deficient serum vitamin D levels. In the United States of America, the results of the *National Health and Nutrition Examination Survey* registered deficient vitamin D values in 30% of the patients studied, with 70% of those studied falling into the insufficient and deficient categories.[34] Patton et al.[35] reported that, regardless of the cut-off value, vitamin D levels were relatively low in women when compared with men and low in the Hispanic and Afro-descendant population when compared with the Caucasian population.

Hypovitaminosis D has been identified in patients with orthopedic pathologies, especially fractures. Several authors have reported vitamin D insufficiency after orthopedic surgeries, with prevalence varying from 15 to 24%.[36,37] Approximately 80% of patients in an Australian hip fracture study presented with insufficient vitamin D levels, with more than 30% of these patients also exhibiting secondary hyperparathyroidism.[38] Despite the fact that the results of this study were not statistically significant, 42.9% of the patients with fractures exhibited vitamin D insufficiency.

It is worth mentioning that this research did not investigate parathyroid hormone levels, which could confound the bone density evaluation (secondary hyperparathyroidism) and lead to osteoporosis in the presence of vitamin D deficiency.

Conclusion

Although this study was carried out in a region with a highland tropical climate, 82% of the patients exhibited deficient or insufficient serum vitamin D levels. Our results did not show a significant correlation between vitamin D levels and bone mineral density according to age.

Conflict of Interest

The authors have no conflict of interests associated with this paper.

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