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Influence of vitamin D levels on bone mineral density and osteoporosis

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BACKGROUND AND OBJECTIVES: The effects of vitamin D on bone mass remain to be understood. This study was conducted with the objective of evaluating the influence of 25-hydroxyvitamin D (25OHD) levels on bone mineral density (BMD) among Saudi nationals.

DESIGN AND SETTING: Cross-sectional study carried out at university hospital from 1 February 2008 to 31 May 2008.

SUBJECTS AND METHODS: Healthy Saudi men and women in the peak bone mass (PBM) age group and those aged ≥50 years were recruited from the outpatient department of King Fahd University Hospital, Al Khobar, Saudi Arabia, between February 1, 2008, and May 31, 2008. Patient age and sex were documented, and body mass index was calculated. Hematological, biochemical, and serum 25OHD tests were performed. BMD was determined by dual-energy x-ray absorptiometry of the upper femur and lumbar spine. Patients were divided into three groups, based on their 25OHD level.

RESULTS: Data from 400 patients were analyzed. Among individuals with a normal 25OHD level, 50% of women and 7% of men in the PBM age group and 26.4% of women and 49.2% of men aged ≥50 years had low bone mass. In patients with 25OHD insufficiency, 84.2% of women and 88.9% of men in the PBM age group and 83.3% of women and 80% of men aged ≥50 years had low bone mass. Results for patients with 25OHD deficiency revealed that none of the men and women in the PBM age group or ≥50 years old had normal BMD. Significant positive correlations between 25OHD level and BMD and significant negative correlations with parathyroid hormone were shown in most of the groups.

CONCLUSIONS: This study showed that the vitamin D level significantly influences BMD reading among Saudi individuals. Evaluation and treatment of hypovitaminosis D should be considered during management of low bone mass.

Adequate levels of vitamin D have an important effect on bone mass in the young and old. Hypovitaminosis D adversely affects calcium metabolism, osteoblastic activity, matrix ossification, bone remodeling, and hence bone density.[1,2] Low 25-hydroxyvitamin D (25OHD) was also reported to be associated with secondary hyperparathyroidism and increased bone turnover.[3] Vitamin D deficiency can be an important risk factor for osteoporosis.[4,5] On the other hand, an adequate vitamin D level has been shown to prevent osteoporotic fractures.[6,7]

Bone mineral density (BMD), which measures the quantity of the calcified bone, at present is the gold standard technique for the diagnosis of osteopenia and osteoporosis. Unfortunately, BMD does not differentiate between osteomalacia and osteoporosis, which means patients with osteomalacia or osteoporosis may be misdiagnosed, one for the other, and thus mismanaged, if the vitamin D level is not measured. In general, serum 25OHD is a robust and reliable marker of vitamin D status,[8] and although there is no consensus on the definition of an optimal serum 25OHD level, vitamin D deficiency is defined by most experts as a serum 25OHD level <50 nmol/L (<20 ng/mL), whereas a serum 25OHD level of >75 nmol/L (>30 ng/mL) is considered to be normal, and a level of 50-75 nmol/L (20-30 ng/mL) defines vitamin D insufficiency.[9]

Ethnically, Saudi Arabians are known to have low vi-

tamin D levels,10-13 and the incidence of osteoporosis among healthy Saudi individuals has been reported to be between 23% and 31%.[14,15] In light of the high prevalence of both a vitamin D deficiency and low bone mass among Saudi nationals, we hypothesized that vitamin D deficiency contributes to low bone mass among Saudi Arabs. This study was carried out with the objective of evaluating the relationship between vitamin D levels and bone mass among Saudi individuals. To our knowledge, the relationship between vitamin D and bone mass among both the male and female Saudi population has not been evaluated. Also, there are a scarcity of reports from the Middle East on this topic.

SUBJECTS AND METHODS

This cross-sectional observational study was carried out at the King Fahd University Hospital, Al Khobar, located in the eastern province of Saudi Arabia. This study was performed from February 1 to May 31, 2008. We recruited 400 healthy Saudi Arabian men and women: 200 subjects (100 men and 100 women) were at the age of peak bone mass (PBM) (between 25 and 35 years) and 200 subjects (100 men and 100 women) were ≥50 years of age. The study was approved by the Ethical and Research Committees of King Fahd University Hospital and King Faisal University, Dammam. Informed verbal consent was obtained. None of the participants received any form of remuneration for participation.

Physical examination was performed and history was compiled for all subjects. Data collected included age, sex, and lifestyle. Weight and height measurements were taken while patients wore light clothes, using a Detecto scale to the nearest 0.1 kg and 0.5 cm. Body mass index was calculated using the formula "weight in kilograms divided by the square of the height in meters." Exclusion criteria included the presence of organ dysfunction and chronic medical illnesses or being on medications that can alter the level of vitamin D or affect bone mass. Pregnant, lactating, and postpartum females were also excluded. Blood was drawn in the morning between 7 am and 10 am in a fasting state for serum calcium, serum phosphorous, serum albumin, alkaline phosphatase, serum parathyroid hormone (PTH), and serum 25OHD. Serum 25OHD levels were measured by radioimmunoassay using Wallac1470 Gamma Counter (Wallac Inc., Gaithersburg, MD, USA). In this study, the 25OHD level was considered to be normal if it was ≥30 ng/mL (≥75 nmol/L), insufficient if it was between 20 and 30 ng/mL (50 and 75 nmol/L), and deficient if it was <20 ng/mL (<50 nmol/L). Based on 25OHD levels, subjects were divided into three groups (group 1, with vitamin D sufficiency; group 2, with vitamin D insufficiency; and group 3, with vitamin D deficiency). Intact PTH was determined by an immunoradiometric assay. The normal range for PTH at our laboratory is 1.3-7.6 pmol/L. Serum calcium, serum phosphorous, serum albumin, and alkaline phosphatase were determined according to standard laboratory procedures. BMD was measured using dual-energy x-ray absorptiometry (DXA) scan (Hologic, Waltham, MA, USA) at the hip region and the lumbar spine. Hip BMD included trochanter, femoral neck, and intertrochanteric regions; lumbar spine BMD included lumbar vertebrae L1-L4. Both T and Z scores were obtained. The reference value of T and Z scores was entered in the DXA machine with software for the Asian reference value. We considered osteopenia when the T score of total lumbar spine or total hip was between -1 and -2.5, and osteoporosis was considered when the T score was <-2.5.[16]

Data were analyzed using the Statistical Package for Social Sciences (SPSS), version 14.0 (Chicago, IL, USA). Data are expressed as mean and standard deviation (SD). Statistically significant differences between groups were determined with a Student t test. *P* values less than .05 and a CI of 95% were used to indicate statistical significance.

RESULTS

The data of 400 subjects were analyzed. Men and women with vitamin D deficiencies were significantly older than those with normal vitamin D levels (P=.01 and P=.03, respectively). Among subjects with normal 25OHD levels, only 7.2% of women and 2.8% of men in the PBM age group had BMD readings consistent with osteoporosis, whereas more than 42.9% of women had BMD readings in the range of osteopenia compared to approximately 4.2% of men (P≤.001). The results of individuals aged ≥50 years with a normal 25OHD level revealed that 17.6% of women and 11.1% of men had BMD readings consistent with osteoporosis, whereas 38.1% of men and 8.8% of women had BMD readings in the range of osteopenia (P≤.001) (**Table 1**). The majority of individuals with 25OHD insufficiency had low BMD. Only 15.8% of women and 11.1% of men in the PBM age group and 16.7% of women and 20% of men aged ≥50 years had normal BMD, with more men in the PBM age group and more women at older age having BMD readings in the range of osteopenia (**Table 2**). As shown in **Table 3**, none of the subjects in both age groups had normal BMD, and the majority had BMD readings consistent with osteoporosis. Female and male subjects aged ≥50

Table 1. Results of men and women with normal 25OHD (>30 pg/mL) (group 1).

Number of healthy individuals screened	Age (years)	Sex	Bone mineral density, g/cm²	Normal (%)	Osteopenia (%)	Osteoporosis (%)
70 (25-35 y)	29.81 (3.8)	Female	0.844 (0.14)	35 (50)	30 (42.85)	5 (7.15)
45 (≥50 y)	56.13 (4.1)	Female	0.861 (0.12)	33 (73.6)	4 (8.8)	8 (17.6)
72 (25-35 y)	27.96 (3.5)	Male	1.10 (0.09)	67 (93)	3 (4.2)	2 (2.8)
63 (≥50 y)	59.57 (8.2)	Male	0.961 (0.10)	32 (50.8)	24 (38.1)	7 (11.1)

Data are presented as means (SD). 25OHD: 25 hydroxyvitamin D.

Table 2. Results of men and women with insufficiency of 25OHD (21-29 pg/mL) (group 2).

Number of healthy individuals screened	Age (years)	Sex	Bone mineral density, g/cm²	Normal (%)	Osteopenia (%)	Osteoporosis (%)
19 (25-35 y)	28.05 (3.13)	Female	0.747 (0.09)	3 (15.8)	9 (47.4)	7 (36.8)
36 (≥50 y)	55.76 (6.9)	Female	0.783 (0.46)	6 (16.7)	14 (38.9)	16 (44.4)
18 (25-35 y)	28.89 (4.28)	Male	0.903 (0.13)	2 (11.1)	11 (61.1)	5 (27.8)
25 (≥50 y)	57 (8.7)	Male	0.840 (0.27)	5 (20)	15 (60)	5 (20)

Data are presented as means (SD). 25OHD: 25 hydroxyvitamin D.

Table 3. Results of men and women with deficiency of 25OHD (<20 pg/mL) (group 3).

Number of healthy individuals screened	Age (years)	Sex	Bone mineral density, g/cm²	Normal (%)	Osteopenia (%)	Osteoporosis (%)
11 (25-35 y)	23.9 (1.87)	Female	0.618 (0.13)	0	6 (54.5)	5 (45.5)
19 (≥50 y)	56.29 (6.43)	Female	0.702 (0.29)	0	4 (21)	15 (79)
10 (25-35 y)	28.5 (4.5)	Male	0.612 (0.25)	0	4 (40)	6 (60)
12 (≥50 y)	62.53 (14.7)	Male	0.803 (0.06)	0	3 (25)	9 (75)

Data are presented as means (SD). 25OHD: 25 hydroxyvitamin D.

years were found to be at greater risk of having BMD readings consistent with osteoporosis than subjects in the PBM age group. **Tables 4-7** show the correlations between vitamin D level, BMD, and PTH among male and female subjects in the PBM and ≥50 years of age groups. With few exceptions, there was a significant positive correlation between vitamin D level and BMD and a significant negative correlation between vitamin D status and PTH level.

DISCUSSION

An evaluation of vitamin D status in patients with osteoporosis is essential for two main reasons. First, vitamin D deficiency causes defective bone mineralization and leads to low bone mass.[1,2] Second, optimal vitamin D repletion in patients with osteoporosis is important to maximize the response to anti-resorptive therapy in terms of both BMD changes and anti-fracture efficacy.[17] Our study revealed that the majority of subjects with an insufficiency of 25OHD had low bone mass, whereas 100% of subjects with 25OHD deficiency had BMD readings in the range of osteopenia or consistent with osteoporosis. This study also showed a positive correlation between BMD and 25OHD in most subjects, particularly in the insufficiency and deficiency groups. On the basis of our findings, we emphasize that it is important to measure 25OHD levels in Saudi patients with low bone mass, rather than relying on BMD alone.

The association between 25OHD and BMD is still debatable. Some studies suggest that a low serum 25OHD level is associated with low BMD.[18-21] In fact,

Table 4. Correlation of 25OHD to other assessed parameters in postmenopausal women aged ≥50 years.

	Normal 25OHD (45)				Insufficiency of 25OHD (36)				Deficiency of 25OHD (19)			
	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD
VitD												
PC	1	0.001	.288	.042	1	.166	.443	.758	1	-.347	.477	.478
Sig		.996	.052	.781		.345	.006	.000		.170	.053	.052
PTH												
PC	.001	1	.169	.131	-.16	1	-.116	-.206	-.349	1	-.434	-.527
Sig	.996		.261	.386	.345		.495	.221	.170		.082	.030
BMC												
PC	.288	.169	1	.230	.443	-.116	1	.763	.477	-.434	1	.980
Sig	.052	.261		.123	.006	.495		.000	.053	.082		.000
BMD												
PC	.042	.131	.230	1	.758	-.206	.763	1	.478	-.527	.980	1
Sig	.781	.386	.123		.000	.221	.000		.052	.030	.000	

VitD: 25 hydroxyvitamin D3, PTH: parathyroid hormone, BMC: bone mineral content, BMD: bone mineral density, PC: Pearson coefficient, Sig: significant 2-tailed, 25OHD: 25 hydroxyvitamin D. Normal 25OHD levels: Positively correlated with all variables without significance. Insufficiency of 25OHD: Correlated negatively with PTH but correlated positively with BMC (r=0.443, *P*<.006) and BMD (r=0.758, *P*<.0001). Deficiency of 25OHD: Correlated negatively with PTH and positively (borderline significance) with BMC and BMD.

Table 5. Correlation of 25OHD to other assessed parameters in women aged ≤35 years.

	Normal 25OHD (70)				Insufficiency of 25OHD (19)				Deficiency of 25OHD (11)			
	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD
VitD												
PC	1	-.062	.076	.256	1	.890	.156	.619	1	.539	.405	.636
Sig		.608	.528	.031		.000	.524	.005		.087	.216	.035
PTH												
PC	-.062	1	-.203	.198	-.89	1	.065	-.832	-.539	1	-.562	-.896
Sig	.608		.090	.098	.000		.792	.000	.087		.072	.000
BMC												
PC	.076	-.203	1	.569	.156	.156	1	.077	.405	-.562	1	.741
Sig	.528	.090		.000	.524	.524		.754	.216	.072		.009
BMD												
PC	.256	.198	.569	1	.619	.619	.077	1	.636	-.527	.980	1
Sig	.031	.098	.000		.005	.005	.754		.035	.000	.009	

VitD: 25 hydroxyvitamin D3, PTH parathyroid hormone, BMC: bone mineral content, BMD: bone mineral density, PC: Pearson coefficient, Sig: significant 2-tailed. Normal 25OHD levels: Positively correlated with BMD (r = 0.25, *P*=.031), positively with BMC, and negatively with PTH (not significant). Insufficiency of 25OHD: Correlated negatively with PTH (r=0.89, *P*<.0001) and BMD (r=0.619, *P*<.005).Deficiency of 25OHD: Correlated negatively with PTH, positively with BMC, and positively significantly with BMD (r=0.634, *P*=.03).

Table 6. Correlation of 25OHD to other assessed parameters in men aged ≥50 years.

	Normal 25OHD (63)				Insufficiency of 25OHD (25)				Deficiency of 25OHD (12)			
	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD
VitD												
PC	1	.163	.233	.310	1	.502	.656	.642	1	.582	.362	.312
Sig		.199	.064	.013		.012	.000	.001		.009	.127	.193
PTH												
PC	.163	1	.456	.198	.502	1	.222	.205	.582	1	.565	.603
Sig	.199		.000	.117	.000		.297	.337	.009		.012	.006
BMC												
PC	.233	.456	1	.716	.656	.222	1	.861	.362	.565	1	.667
Sig	.064	.000		.000	.000	.297		.000	.127	.012		.002
BMD												
PC	.310	.198	.716	1	.642	.205	.861	1	.312	.603	.667	1
Sig	.013	.117	.117		.001	.337	.000		.193	.006	.002	

VitD: 25 hydroxyvitamin D3, PTH: parathyroid hormone, BMC: bone mineral content, BMD: bone mineral density, PC: Pearson coefficient, Sig: significant 2-tailed, 25OHD: 25 hydroxyvitamin D. Normal levels of VitD correlated positively with all variables but only significantly with BMD (r=0.31, *P*=.013). Insufficiency of vitamin D correlated positively significantly with all variables: PTH (r=0.502, *P*=.012), BMC (r=0.656, *P*<.0001), and BMD (r=0.642, *P*=.001). With vitamin D deficiency, it correlated positively with all 3 variables but correlated significantly only with PTH (r=0.582, *P*=.009). Normal 25OHD levels correlated negatively with all variables with no significance. Insufficiency of 25OHD: Correlated with all variables but significantly only with PTH (r = 0.582, P<.009). Deficiency of 25OHD: Correlated negatively with PTH, positively and significantly with BMC (r= 0.986, *P*=.0001) and BMD (r=0.92, *P*=.001).

Table 7. Correlation of 25OHD to other assessed parameters in men aged ≤35 years.

	Normal 25HVitD (72)				Insufficiency of 25HVitD (18)				Deficiency of 25HVitD (10)			
Variable	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD	VitD	PTH	BMC	BMD
VitD												
PC	1	-.197	-.208	-.015	1	.582	.362	.312	1	.221	.986	.917
Sig		.095	.077	.901		.009	.127	.193		.559	.000	.001
PTH												
PC	-197	1	.150	-.275	.582	1	.565	.603	-.221	1	-.238	-.355
Sig	.095		.206	.019	.009		.012	.006	.599		.571	.389
BMC												
PC	-.208	-.150	1	.464	.362	.565	1	.667	.986	-.238	1	.963
Sig	.077	.206		.000	.127	.012		.002	.000	.571		.000
BMD												
PC	-.015	-.275	.464	1	.312	-.603	.67	1	.917	-.355	.963	1
Sig	.901	.019	.000		.193	.006	.002		.001	.389	.000	

VitD: 25 hydroxyvitamin D3, PTH: parathyroid hormone, BMC: bone mineral content, BMD: bone mineral density, PC: Pearson coefficient, Sig: significant 2-tailed, 25OHD: 25 hydroxyvitamin D. Normal 25OHD levels correlated negatively with all variables with no significance. Insufficiency of 25OHD: Correlated with all variables but significantly only with PTH (r=0.582, *P*<.009). Deficiency of 25OHD: Correlated negatively with PTH and positively and significantly with BMC (r=0.986, *P*=.0001) and BMD (r=0.92, *P*=.001).

the initial results of the study by Bischoff-Ferrari et al[18] showed a strong positive relationship between 25OHD and BMD among white young and older males. However, no such association has been found in other studies.[22-24] The above heterogeneity in the results of the relationship between vitamin D status and BMD can be partially explained by differences in populations, differences in age groups, and differences in the sites of the body studied. For example, Garnero et al in the Os des Femmes de Lyon (OFELY) study[25] and Allali et al[26] failed to show any significant correlation between 25OHD levels and BMD after adjusting for age. However, Rassouli et al[27] found a positive correlation with spine BMD, but not with hip BMD.More important is the fact that different vitamin D levels were used to define vitamin D deficiency and insufficiency during such studies.[23-25]

On the other hand, we found a significant negative correlation between 25OHD and PTH levels. The elevated PTH level in subjects with low 25OHD levels possibly contributed to low bone mass.[3,28] Age could also be another contributing factor, since men and women with vitamin D deficiencies are significantly older than individuals with normal vitamin D levels.

This study has some limitations, including the fact that only a single measurement of vitamin D was done. In addition, apart from alkaline phosphatase, no other bone markers were studied. Also, no multivariate analysis was carried out to evaluate the effects of other confounding factors on bone mass, such as age, sex, and lifestyle. Despite the above limitations, this study supported our initial hypothesis that vitamin D deficiency can be an important contributing factor to low bone mass among the Saudi population.

In conclusion, our study showed a positive association between vitamin D levels and low bone mass in Saudi men and women in both the PBM and older age groups. Because prevention of low bone mass can be achieved by nonpharmacological means, adequate intake of vitamin D and calcium becomes imperative and should be encouraged. There is still a paucity of data on hypovitaminosis D and its effects on bone mass and PTH among Saudi citizens, but we strongly emphasize that proper evaluation and treatment of hypovitaminosis D should be considered during the management of low bone mass.

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