Original Article

PREVALENCE OF OSTEOPOROSIS IN AMBULATORY POSTMENOPAUSAL WOMEN FROM A SEMIURBAN REGION IN SOUTHERN INDIA: RELATIONSHIP TO CALCIUM NUTRITION AND VITAMIN D STATUS

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ABSTRACT

Objective: To assess the prevalence of osteoporosis in healthy ambulatory postmenopausal Indian women as measured by dual-energy x-ray absorptiometry and to study the dietary calcium intake and vitamin D status and their influence on bone mineral density (BMD).

Methods: We conducted a community-based cross-sectional study in a semiurban region. A randomized cluster sampling technique was used. The study cohort consisted of 150 ambulatory postmenopausal women (≥50 years old). Dual-energy x-ray absorptiometry for BMD was performed at the lumbar spine and femoral neck. Dietary calcium intake and biochemical variables were assessed.

Results: The prevalence of osteoporosis was 48% at the lumbar spine, 16.7% at the femoral neck, and 50% at any site. The mean dietary calcium intake was much lower than the recommended intake for this age-group. There was a significant positive correlation between body mass index and BMD at the lumbar spine and the femoral neck ($r = 0.4$; $P = .0001$). BMD at the femoral neck was significantly less (mean, 0.657 versus 0.694 g/cm^2) in the vitamin D-insufficient study subjects in comparison with the vitamin D-sufficient women ($P = .03$).

Conclusion: The high prevalence of osteoporosis and vitamin D insufficiency in this semiurban group of postmenopausal women in India is a major health concern. Measures such as adequate calcium intake and vitamin D supplementation in women of this age-group may be beneficial. **(Endocr Pract. 2008;14:665-671)**

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Abbreviations:
BMD = bone mineral density; **BMI** = body mass index; **25-OHD** = 25-hydroxyvitamin D

INTRODUCTION

Osteoporosis is the most common metabolic bone disorder (1). It is a disorder characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk (2,3). It is an important public health issue in postmenopausal women, and when the condition is left untreated, 60% of these women will experience fragility fractures during their lifetime. Fractures, especially of the spine, hip, and wrist, are a frequent clinical complication of osteoporosis. Initially, spinal fractures can be asymptomatic, but they are associated with substantial morbidity and mortality (4). Femoral neck fractures cause considerable morbidity and mortality; moreover, treatment of hip fractures in elderly patients is expensive. Therefore, prevention of fractures is of paramount importance.

Vitamin D has a major role in bone metabolism (5). Exposure to sunlight and dietary intake of vitamin D are major determinants of serum 25-hydroxyvitamin D (25-OHD) levels. Although few patients with osteoporosis exhibit obvious biochemical signs of hypovitaminosis D, vitamin D insufficiency has been shown to have adverse effects on calcium metabolism, osteoblastic activity, matrix ossification, bone mineral density (BMD), and bone remodeling. Low serum 25-OHD concentrations are also associated with secondary hyperparathyroidism, increased bone turnover, reduced BMD, and increased risk of osteoporotic fractures (6,7). Although India is a tropical country, women—particularly those in the older age-group—confine themselves indoors most of the time; minimal exposure to sunlight makes them susceptible to vitamin D insufficiency.

Dietary intake of calcium is also important for bone mineralization and for bone strength (8). The process of aging is associated with decreased calcium absorption from the gut, especially in postmenopausal women; thus,

there is an increased requirement of calcium intake in these women. Insufficient dietary calcium intake attributable to socioeconomic constraints and lack of awareness increases the risk of osteoporosis. The current study was undertaken to assess the relationships between vitamin D insufficiency, dietary calcium intake, and BMD and the prevalence of osteoporosis in healthy, community-dwelling, ambulatory postmenopausal women in a semiurban setting.

SUBJECTS AND METHODS

Inclusion and Exclusion Criteria

Women who were 50 years old or older and had been postmenopausal for at least 1 year were eligible for inclusion in this study. They also had to be ambulatory and able to perform day-to-day activities. Postmenopausal women younger than 50 years and those who were confined to bed or were nonambulatory were excluded from this analysis.

Evaluation

Patients who fulfilled the eligibility criteria were selected for the study. The following variables were assessed.

Nutritional History

The dietary calcium intake was assessed by an experienced dietitian. Qualitative and quantitative aspects of food intake were assessed with use of an oral semiquantitative food frequency questionnaire (9).

Sunlight Exposure

A history of exposure to sunlight (number of hours per day) was solicited. In addition, the usual type of clothing was assessed to determine the extent of body area exposed to sunlight (10).

Assessment of Biochemical Variables

Fasting blood samples were collected for the assessment of serum calcium, phosphorus, alkaline phosphatase, albumin, creatinine, and 25-OHD. All biochemical variables except 25-OHD were measured in a fully automated and computerized microanalyzer (Hitachi model 911; Boehringer Mannheim, Mannheim, Germany). The intra-assay and interassay coefficients of variation for these analyses were 1% to 5%.

A radioimmunoassay (DiaSorin, Stillwater, Minnesota) was used for determination of 25-OHD. The analytical sensitivity of this assay, when defined as the lowest quantity differentiated from zero at 2 SD above the mean counts per minute of the zero calibrator (N = 20), has been shown to be 1.5 ng/mL. With this test, the normal range is 9.0 to 37.6 ng/mL, and the intra-assay coefficient of variation is 5.5% at a vitamin D level of 15.6 ng/mL and 9.3% at a vitamin D level of 52.5 ng/mL. Although debatable, we chose to define vitamin D sufficiency as serum 25-OHD levels of more than 20 ng/mL, vitamin D insufficiency as levels from 10 to 20 ng/mL, and vitamin D deficiency as levels <10 ng/mL.

Dual-Energy X-Ray Absorptiometry

Bone mineral density was assessed by using the Hologic machine (QDR 4500; Hologic, Inc., Waltham, Massachusetts) at the lumbar spine (L1 to L4) and the femoral neck. The reference population consisted of normal Caucasian subjects (manufacturer's database). The precision was 2% at both measured sites (spine and neck of femur). The World Health Organization has defined osteoporosis as a bone density with a *T* score of −2.5 or less and osteopenia as a bone density with a *T* score between −1.0 and −2.5. There are no reference data on large numbers of Indian women for peak adult bone mass. One investigation, however, studied BMD in 22 female recruits in the Indian army (11). With use of these values, *T* scores were derived, and the data in our patients were interpreted as reflecting normal BMD, osteopenia, or osteoporosis on the basis of the World Health Organization criteria.

Sample Size Calculation

The average published figure for the prevalence of osteoporosis is 25% to 30% in women older than 50 years. The total number of women in this semiurban area was 7,082. The number of women who had attained menopause (based on a house-to-house survey) was 1,040. The sample size was calculated to detect a prevalence of osteoporosis of 23% to 37% with 95% confidence. The number of women needed to be studied was 145. Study subjects (30 clusters of 5 each) were randomly selected after a house-to-house survey by using the cluster sampling technique.

Statistical Analysis

An independent *t* test was used to compare the means of 2 continuous variables if they were normally distributed, and nonparametric tests were used if their distribution was not normal. The correlation between 2 continuous variables was assessed with use of the Pearson correlation. Logistic regression was done to assess the effect of multiple variables on BMD and osteoporosis. The difference in proportion of obese and nonobese subjects with osteoporosis was analyzed, and odds ratios were calculated to determine the effect of obesity. The statistical analyses were performed with use of the SPSS version 11 software package (SPSS Inc., Chicago, Illinois).

RESULTS

Anthropometric data, various factors affecting BMD, and biochemical results are summarized in Table 1. Of the 150 study subjects, 84 (56%) were 60 years old or older. Overall, 19 of the study subjects (13%) were obese (body mass index >30 kg/m^2). Only 0.7% (1) of subjects had a dietary calcium intake that exceeded the recommended

daily allowance of >1,000 mg daily. Two patients, one with a serum creatinine concentration of 2.9 mg/dL and a serum calcium level of 7.3 mg/dL and another with a serum phosphorus value of 1.9 mg/dL, were excluded from the analysis of correlations. The BMD at the lumbar spine was 0.798 ± 0.142 g/cm^2 (mean ± SD). The BMD at the femoral neck was 0.675 ± 0.108 g/cm^2 (mean ± SD).

The prevalences of osteoporosis and osteopenia at the lumbar spine and femoral neck, computed by using Caucasian and Indian normative data, are shown in Table 2. In another study, the mean (±SD) values for peak adult bone mass at the lumbar spine and at the femoral neck were 0.981 (±0.092) g/cm^2 and 0.850 (±0.101) g/cm^2, respectively, in 22 female recruits in the Indian army (11). The BMD values in our study subjects were reanalyzed by using *T* scores derived from the Indian data. With use of the Indian normative data, the percentage of women with osteoporosis at the lumbar spine decreased, but the percentage of women with osteoporosis at the femoral neck increased.

The vitamin D status and BMD of the study subjects are shown in Table 3. Of the subjects in this analysis, 74 (50%) had vitamin D sufficiency (>20 ng/mL), 59 (40%) were found to have vitamin D insufficiency (10 to 20 ng/mL), 14 (9.5%) had vitamin D deficiency (5 to 10 ng/mL), and 1 (0.7%) had severe vitamin D deficiency (<5 ng/mL). The subject with severe vitamin D deficiency had normal renal and liver function. The BMD at the femoral neck was significantly lower in the vitamin D-insufficient subjects in comparison with the vitamin D-sufficient study subjects (mean, 0.657 versus 0.694 g/cm^2; P = .03). Although BMD at the lumbar spine was also found to be lower in the vitamin D-insufficient group than in the group with vitamin D sufficiency (mean, 0.780 versus 0.816 g/cm^2), the difference did not reach statistical significance (P = .13). A weak positive correlation was noted at the femoral neck between BMD and vitamin D levels (r = 0.160; P = .052), but there was no correlation between 25-OHD levels and BMD at the lumbar spine. There was no significant difference (P = .25) in mean vitamin D levels (mean, 19.65 versus 21.98 ng/mL) or in dietary calcium intake (mean, 386 versus 410 mg/24 h) between subjects with and those without osteoporosis, respectively (P = .39).

The correlation of various factors with BMD at the lumbar spine and femoral neck is outlined in Table 4. There was a significant positive correlation between body mass index (BMI) and BMD (r = 0.4; P = .0001) at the femoral neck and the lumbar spine. In logistic regression analysis, a BMI of more than 30 kg/m^2 had a protective effect against osteoporosis [odds ratio = 0.89 (95% confidence interval, 0.81 to 0.97) (P = .008) at the lumbar spine and 0.86 (95% confidence interval, 0.76 to 0.96) (P = .01) at the femoral neck]. There was a significant negative correlation (r = –0.392; P = .001) between the number of years since menopause and the BMD at the lumbar spine and the femoral neck. Similarly, there was a significant negative correlation between parity and BMD (r = –0.249 and P = .03 at the lumbar spine; r = –0.227 and P = .009 at the femoral neck). No significant correlation was found between exposure to sunlight and 25-OHD levels (r = 0.074; P = .52).

Table 1
Anthropometric Data, Factors Affecting Bone Mineral Density, and Results of Biochemical Tests in the Study Cohort

Characteristic	Mean (SD)	Range
Age (y)	60.1 (5.0)	50-80
Height (m)	1.52 (0.054)	1.38-1.68
Weight (kg)	57.28 (10.79)	30-94
Body mass index (kg/m^2)	24.74 (4.35)	13.92-38.04
Calcium intake[a] (mg/24 h)	398.76 (190.13)	61-1,044
Sunlight exposure (hours/d)	0.67 (0.36)	0-2
Years since menopause	11.7 (7.3)	2-46
Number of children	3.5 (1.5)	0-9
Corrected calcium (mg/dL)	9.41(0.47)	7.3-10.4
Phosphorus (mg/dL)	3.94 (0.670)	1.9-7.6
Alkaline phosphatase (U/L)	103.04 (28.3)	38-200
Creatinine (mg/dL)	0.8 (0.21)	0.5-2.9
25-Hydroxyvitamin D (ng/mL)	20.85 (8.63)	5.0-49.8

[a] All except 4 study subjects had a dietary calcium intake of less than 600 mg daily.

Table 2
Percentage of Study Subjects With Osteoporosis and Osteopenia at Various Anatomic Sites

Characteristic	Lumbar spine		Femoral neck		Osteoporosis at any site
	Osteoporosis	Osteopenia	Osteoporosis	Osteopenia	
Normative data used					
Caucasian	48	35.3	16.7	56.7	50
Indian	37	38	22	55	43

DISCUSSION

Osteoporosis is an important public health issue in postmenopausal women, and when it is left untreated, it can lead to fractures. The exact prevalence of postmenopausal osteoporosis in women in India is unknown, even though Indian census figures show that at least 100 million postmenopausal women are at risk. This study, undertaken in a random sample of semiurban healthy ambulatory southern Indian postmenopausal women, demonstrated that the prevalence of osteoporosis was 48% at the lumbar spine and 17% at the femoral neck with use of Caucasian normative data. The prevalence of osteoporosis at any site was 50%. Using limited normative data from Indian female army recruits reduced the prevalence of osteoporosis at the lumbar spine by 11% (to 37%) but marginally increased the prevalence of osteoporosis at the femoral neck by 5% (to 22%) and decreased the overall prevalence of osteoporosis at any site from 50% to 43%. Studies from Sri Lanka and Saudi Arabia have reported a similar prevalence of osteoporosis (39.5% to 46.7%) with use of Caucasian normative data in women older than 50 years (12-14).

One of the reasons for the seemingly high prevalence of osteoporosis in the current study may be the use of Caucasian normative data. Studies done in Lebanon, Taiwan, and India have shown that the spine and hip BMD values in women are 2% to 8% lower than those in Caucasian subjects between the ages of 20 and 59 years (11,15,16). This racial difference in BMD may be related more to a difference in body size and bone size than to genetic heterogeneity (17). When we used the limited normative data available for Indian women, we found that the overall prevalence of osteoporosis was not substantially altered.

Dietary Calcium

The decreased intestinal calcium absorption and renal calcium reabsorption in menopausal women necessitate an augmented daily calcium intake of 1,000 to 1,500 mg to

Table 3
Bone Mineral Density, Stratified by Vitamin D Status of Study Subjects[a]

Characteristic	Vitamin D-sufficient group (>20 ng/mL)	Vitamin D-insufficient group (10-20 ng/mL)	*P* value
Number (%)	74 (50)	59 (40)	…
Bone mineral density			
Lumbar spine (g/cm^2)	0.816	0.780	.13
Femoral neck (g/cm^2)	0.694	0.657	.03

[a] There were 15 patients with vitamin D deficiency. The bone mineral density at the lumbar spine (mean ± SD) was 0.733 ± 0.151 and at the femoral neck (mean ± SD) was 0.649 ± 0.102. Because the number of patients in this group was very small, we did not include them in this statistical analysis.

Table 4
Correlation of Various Factors With Bone Mineral Density

Site	Body mass index		No. of years since menopause		Parity	
	r	*P* value	*r*	*P* value	*r*	*P* value
Bone mineral density						
Lumbar spine	0.4	.0001	–0.392	.001	–0.249	.03
Femoral neck	0.4	.0001	–0.392	.001	–0.227	.009

prevent deleterious skeletal effects (18). The mean dietary calcium intake in our population of healthy postmenopausal women (399 mg/24 h; range, 61 to 1,044) was much lower than current dietary recommendations (1,000 to 1,500 mg/d) advised for this age-group. Nevertheless, it was very similar to the dietary calcium intake in postmenopausal women studied in a neighboring Indian state (323 ± 66 mg/d) (19). A still lower mean intake of dietary calcium (270 ± 57 mg/d) has also been reported in another study among Indian women (20). The dietary calcium intake in all these studies, assessed by an oral semiquantitative food frequency questionnaire, may be greater than the bioavailable calcium from the diet, inasmuch as the traditional southern Indian diet is rich in phytates (21,22). The lack of correlation between dietary calcium intake and BMD in our study may be attributable to the overall poor calcium intake (less than 600 mg of calcium per day) in all except 4 study subjects.

BMI, Years Since Menopause, and Parity

The significant correlation between BMI and BMD at both the lumbar spine and the femoral neck noted in the current study has been previously well documented (1,23). It has been attributed to the higher levels of circulating endogenous estrogen from adipose tissue and muscle and the higher gravitational load on the femoral neck and lumbar spine (24). The number of years since menopause had a significant effect on BMD in the current study, consistent with findings in previous reports (25).

Parity correlated negatively with BMD in the current study. It is possible that low dietary calcium intake during pregnancy and lactation may be responsible for our findings. Other studies have found a similar negative influence of parity on BMD (26,27). In a study of Old Order Amish multiparous women, however, a limited protective effect of parity on BMD was found in the age-group 50 to 59 years—probably attributable to a delay in the age at menopause (28). In this context, the mean age at menopause in Indian women is 47 years.

Vitamin D Status

Measurement of serum 25-OHD is the most reliable method of assessing vitamin D status. It reflects the sum total of vitamin D absorbed from the intestine and the vitamin D synthesized by the skin. It has been clearly demonstrated that cutaneous vitamin D synthesis decreases with advancing age. MacLaughlin and Holick (29) showed a decline of about 50% in skin concentration of 7-dehydrocholesterol from age 20 to age 80 years. The definition of vitamin D status as deficient or sufficient varies in different studies. Even though Vellore (latitude 12° 56′ N, longitude 79° 8′ E) has abundant sunshine throughout the year, the tendency of elderly women to stay indoors probably explains such a high prevalence of vitamin D insufficiency and deficiency. In our study group, only 50% of the subjects had vitamin D sufficiency, whereas the other 50% had vitamin D insufficiency or deficiency based on the criteria used by Lips (30). Overall, studies performed in various populations in India have shown a poor vitamin D status, similar to the trends reported from Japan (10,19,31,32).

The lack of correlation between exposure to sunlight and vitamin D levels in our current study may be related to increased skin pigmentation in our study subjects, the older age-group studied, patient-related bias in reporting the duration of exposure to sunlight, and seasonal variations in sunlight exposure (33). Whether vitamin D or parathyroid hormone gene polymorphisms (34) alter the relationship between serum 25-OHD levels and BMD at different sites in our population remains to be explored.

The positive correlation between 25-OHD levels and femoral neck BMD and the lower femoral neck BMD in vitamin D-insufficient subjects in our study suggest that the 50% prevalence of vitamin D insufficiency in our population is clinically relevant. Other studies have shown the positive correlations between 25-OHD levels and BMD at the lumbar spine and femoral neck (1). In a meta-analysis of studies on vitamin D status from Japan, Nakamura (32) suggested that higher serum 25-OHD concentrations (>20

ng/mL) should be maintained to prevent vitamin D insufficiency-induced secondary hyperparathyroidism and consequent bone loss. Despite the lack of correlation among dietary calcium intake, serum 25-OHD concentration, and BMD at different sites, previous interventional studies have demonstrated benefit in terms of reduction in fracture rates (8,35,36).

Limitations of This Study

The use of Caucasian normative data for peak adult bone mass may have led to overestimation of the prevalence of osteoporosis; nevertheless, with use of the limited Indian normative data derived from female army recruits, osteoporosis at any site still showed a high prevalence. There is a need to derive Indian population-based values for peak adult bone mass. Army recruits, who are more active than the average population during their youth, may have higher peak adult bone mass, and this factor may skew the mean peak adult bone mass in the positive direction. The available values, however, may represent the maximal possible peak adult bone mass in Indian subjects.

In our study, vitamin D status was based on levels suggested by Lips (30) because no Indian studies have defined vitamin D sufficiency in our population. We did not determine intact parathyroid hormone levels or bone markers in this study. It is widely accepted, however, that measurement of the 25-OHD level is probably the best available test for assessing vitamin D status (5,32).

CONCLUSION

This community-based randomized study shows the prevalence of osteoporosis at any anatomic site in postmenopausal women to be about 40% to 50% and the prevalence of vitamin D insufficiency or deficiency to be 50%. When we consider the number of women in this age-group in India (approximately 100 million), the magnitude of the problem is substantial. Simple interventions such as adequate calcium intake and vitamin D supplementation combined with mass education may significantly reduce morbidity and mortality associated with osteoporotic fractures in this population. In particular, we need to ensure that the calcium intake and vitamin D status are optimized before initiation of other therapeutic measures, such as bisphosphonates, for osteoporosis. Although sensible exposure to sunlight is a good means of generating vitamin D, skin darkening because of exposure to sunlight and high ambient temperatures in Vellore (>40°C in summer) discourage this practice in India. Buttermilk and lassi, which are good natural sources of calcium, are readily available, relatively inexpensive, and acceptable to large sections of the Indian society. They have the additional advantage of low fat content, which makes them more suitable for the elderly population in whom cardiovascular disease is a concern. They are better tolerated than milk, and it may be possible to fortify these products with vitamin D. Because these products are consumed as such, cooking-related losses would be minimal. Ideally, they should be promoted in the electronic media instead of unhealthful carbonated drinks, which are widely promoted currently.

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DISCLOSURE

The authors have no conflicts of interest to disclose.

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