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Original Article

Bone densitometry status and its associated factors in peri and post menopausal females: A cross sectional study from a tertiary care centre in India☆

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ABSTRACT

Objective: Osteoporosis is a skeletal disorder characterized by diminished bone strength that increases the risk of fracture at instances of trivial trauma. Asians have a lower bone mass than the west. The present study was designed to add data from India on women above the age of 40 years with respect to low bone mineral density (BMD) and its associated high risk factors.

Materials and Methods: After a written informed consent, a detailed history was taken. Basal metabolic index was recorded, and biochemical and endocrine tests were done, followed by dual X ray absorptiometry scan.

Results: Average age of the study population was 46.54 years and BMI 26.58. The prevalence of osteopenia in the study was 36%, and that of osteoporosis, 4%; the overall prevalence of low BMD being 40%. Proportion of women with low BMD increased with advancing age and menopausal status. On endocrine evaluation, 53.44% cases with insufficient vitamin D, 62.5% with hyperparathyroidism, 100% with hypothyroidism, 75% with hyperthyroidism suffered from low BMD. Among chronic diseases, 75% women with diabetes, 33.3% with hypertension, 25% with deranged liver function and 50% with rheumatoid arthritis were found to have low BMD. 46.75% women with sun exposure less than one hour daily had poor bone mineralization. The proportion of women with normal BMD decreased from 84.09% to 43.33% with decrease in daily physical work. On logistic regression analysis, insufficient serum vitamin D concentrations, less physical work and inadequate sun exposure were found to be significantly associated with low BMD.

Conclusion: Low BMD is not a disorder confined to postmenopausal women alone. It is widely prevalent in women above 40 years of age. Screening women above 40 in the absence of any high risk factors has the potential of nipping this silent killer in the bud.

Introduction/background

Osteoporosis is a skeletal disorder characterized by diminished bone strength that increases the risk of fracture at instances of trivial trauma [1]. As per ICD 10 classification (2017) it is classified as M 81.0. With increased life expectancy, the world is going to witness an unprecedented surge in the geriatric population with its concomitant increase in osteoporosis related morbidity. India currently has 10% of its population over 50 years. Emerging population trends based on 2011 census show, 22% of our people falling in the geriatric age group by 2025, and 33% by 2050. Forty-six million of Indian women above the age of 50 years (20%) are believed to be osteoporotic [2].

Asians have a lower bone mass than Caucasians and Afro-Caribbeans and the peak incidence of osteoporosis is believed to occur 10–20 years earlier in Indians than in the Western population [3–7]. It is possible that a dietary deficiency of calcium, beginning

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early in life, leads to a lower peak bone mass, and consequently osteoporosis at an earlier age. Malabsorption of calcium due to a subclinical deficiency of vitamin D may lead to osteoporosis, without causing osteomalacia. Dark skin, reduced outdoor activity and conservative dressing have increased Vitamin D deficiency [8]. Women are more prone to have lower bone mass due to pregnancy, childbirth, and later menopause resulting in depletion of bone [5].

Osteoporosis is a condition that can be prevented and treated if diagnosed early. Unfortunately, it is often undiagnosed until a fracture occurs. Therefore, it appears logical to increase the ambit of screening for this ailment.

Dual-energy x-ray absorptiometry (DEXA) is currently the gold standard in the measurement of bone mineral density (BMD). This technique offers several advantages as compared to others. It correlates with risk of fractures at the site evaluated, assess anti fracture treatments and helps in monitoring response to therapy. It reports the subject's bone mineral density as a T-score which is a measure of the subject's BMD compared to healthy controls who are at the peak of their bone mass. Any score upward of −1 is considered normal. Scores between −1 and −2.5 denote osteopenia. Results less than −2.5 suggest osteoporosis [9].

Much attention has been focused on screening postmenopausal females for this disorder. Currently, there are no recommendations for screening perimenopausal women with low risk for fractures, with bone mineral densitometry [10]. The present study was designed to add data from India on perimenopausal and postmenopausal women above the age of 40 years with respect to low bone mineral density and its associated high risk factors.

Aims and objectives

1. To assess the prevalence of osteoporosis and osteopenia in women over 40 years attending the gynae out patient department (OPD).
2. To study the biochemical parameters related to bone mineral density in peri and postmenopausal females attending the gynecology outpatient department.
3. To study the correlation of endocrine profile of peri and postmenopausal females attending the gynae OPD vis-a-vis their bone densitometry status.
4. To study life style patterns of peri and post menopausal females in relation to bone densitometry status.

Material and methods

Type of study: It is a cross sectional observational study.

Inclusion criteria: All patients above 40 years of age who visited the main Gynae Outpatient Department, Department of Obstetrics and Gynecology, of a tertiary care hospital, during the study period (i.e. June to July 2015) for gynecological complaints, were enrolled in the study.

Exclusion criteria: Pregnancy, documented osteoporosis or osteopenia, patients not willing for continued follow up and non ambulatory women.

Time period: It was a time bound study where participants were recruited from June 1, 2016 to July 31, 2016. Data including history and anthropometry were collected at the time of recruitment. Results of biochemical, endocrine and DEXA scan tests were collected in the following fortnight followed by analysis.

Procedure

After a written informed consent, a detailed history which included age, obstetric history, history of fractures in the past, any history of fracture in the parents, history of chronic diseases such as diabetes, hypertension, thyroid disorders etc, drug history specifically with respect to glucocorticoids, daily sun exposure, dietary history and exercise history were elicited. History related to smoking and alcohol intake was also included. History related specifically to common symptoms of menopause and perimenopause such as hot flashes, night sweats, sleep disturbances, vaginal dryness, lack of concentration, mood swings, menstrual disturbances etc. was elicited with leading questions.

The height and weight of all subjects was recorded in the out patient department by a digital apparatus. The weight in kilograms was divided by the square of the height measured in meters to calculate the Body Mass Index (BMI) for each subject.

The participants were then asked to undergo biochemical testing including liver and kidney function tests, serum calcium and fasting and post prandial blood sugar values; and endocrine evaluation including, thyroid stimulating hormone, follicle stimulating hormone, parathyroid hormone, 25 hydroxyvitamin D3, and glycosylated hemoglobin (in case of deranged blood sugars).

Hemoglobin was measured in the hospital laboratory by automated blood cell counter, Sysmex KX 21. Estimates of liver function test, renal function test, blood sugar, HbA1C and serum calcium were done by fully automated biochemistry analyzer, model EM-360. Serum follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), parathyroid hormone (PTH) and 25 hydroxyvitamin D3 were done on a fully automated single dose entry immuno analyser, Biomerieux Vidas.

The reference range for TSH was taken between 0.5 and 5.0 IU/ml; Vitamin D was considered insufficient if less than 30 mIU/ml. The cut off for serum parathyroid hormone was taken as, 10–65 ng/ml.

The subjects were then asked to undergo bone mineral densitometry using DEXA scan. The aforesaid scan was performed on, Hologic DXA scan machine. NHANES III data were used as the reference standard to calculate T-scores at the neck of femur [9].

For the purpose of descriptive analysis, the BMI was classified according to the criteria proposed by WHO [11]. The quantum of daily physical activity was assessed to be moderate for subjects performing only domestic chores, heavy for those involved in some form of exercise such as walking, jogging or yoga for at least 30 min a day for at least five days a week, in addition to domestic work. Those responders who were ambulatory but claimed to undertake no significant routine physical activity, were classified as sedentary.

Daily sun exposure was divided into less than one hour, one to five hours and more than five hours of exposure during day time.

A note was made of the usual attire worn by the subjects. This was not included in analysis since all our responders were used to wearing half to full sleeved clothes that exposed only face, neck and a variable area of arms and feet.

Ethical consideration

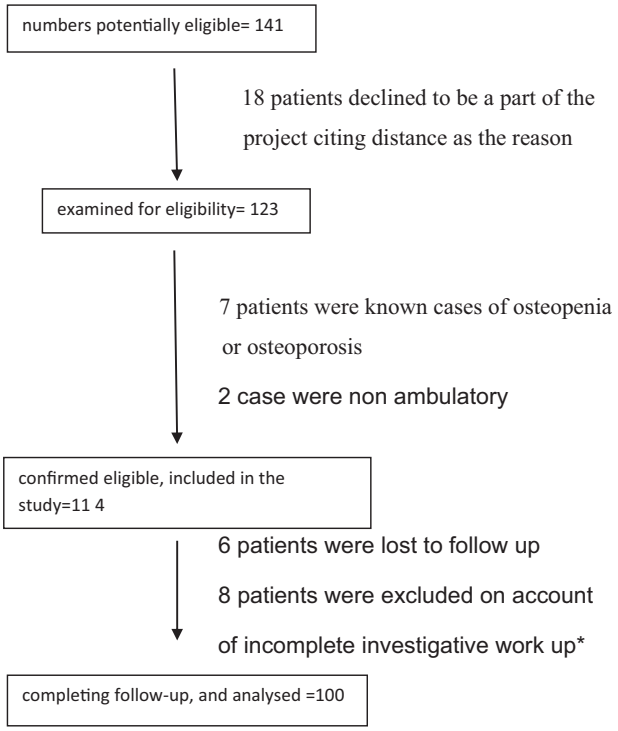
Due clearance was obtained from the institutional ethical clearance committee prior to initiation of the study.

Statistical analysis

Data was expressed as means (SD) and frequencies (%). Chi square test was applied to categorical variables and Student's t-test to continuous variables. SPSS version 20 was used for performing all statistical analysis. A p value <0.05 was considered statistically significant.

Results

osteoporosis, 4%; the overall prevalence of low bone mineral density being 40%. As is evident, the proportion of population with low bone mineral density, both osteopenia as well as osteoporosis



*2 patients out of 100 (2%) did not undergo DEXA scan , three did not have serum vitamin D concentrations, one each did not have information on PTH values, liver function tests and blood sugar levels

Strobes flow chart for patient influx

Table 1 summarizes the overall profile of the participants in the study.

Table 2 traces the association of age, endocrine parameters, chronic diseases and medications with bone mineral density. The prevalence of osteopenia in the study was 36%, and that of

Table 1
Characteristics of study participants.

Variable	Mean (±SD)
Age (in years)	46.54 (6.144)
Weight (in kilograms)	64.489 (9.834)
Height (in centimeters)	155.52 (6.292)
Femoral neck BMD	0.845 (0.189) t score −0.529
BMI[a] (in kg/m2)	26.58 (3.29)
Hemoglobin (in gm/dl)	12.02 (2.247)
Serum calcium (in mg/dl)	8.837 (0.6655)
TSH[b] (in mIU/l)	3.146 (1.483)
PTH[c] (in ng/ml)	43.938 (36.710)
FSH[d] (in mIU/ml)	42.108 (24.801)
Vitamin D (in ng/ml)	27.00 (13.660)

[a] Body mass index.
[b] Thyroid stimulating hormone.
[c] Parathyroid hormone.
[d] Follicle stimulating hormone.

Table 2
Profile of age, endocrine factors and chronic diseases and mediations with respect to bone mineral density.

	Overall	Osteopenia	Osteoporosis	Normal
Age (yrs)				
<50	76	26 (34.21%)	3 (3.94%)	47 (61.84%)
>50	24	10 (41.66%)	1 (4.16%)	13 (54.16%)
Endocrine parameter				
FSH				
<30	49	20 (40.81%)	0	29 (59.18%)
>30	51	19 (37.25%)	4 (7.84%)	28 (54.9%)
Hypovitaminosis D	58	28 (48.27%)	3 (5.17%)	27 (46.55%)
Hyperparathyroidism	8	4 (50%)	1 (12.5%)	3 (37.5%)
Hypothyroidism	4	1 (25%)	3 (75%)	0
Hyperthyroidism	4	2 (50%)	1 (25%)	1 (25%)
Chronic diseases				
Diabetes mellitus	4	2 (50%)	1 (25%)	1 (25%)
Hypertension	3	1 (33.33%)	0	2 (66.66%)
Gout	1	0	0	1 (100%)
Deranged liver function	4	1 (25%)	0	3 (75%)
Deranged kidney function	0	0	0	0
Rheumatoid arthritis	4	2 (50%)	0	2 (50%)
Medications/Chemicals				
Prolonged steroid therapy	1	0	0	1 (100%)
Smoking	1	1 (100%)	0	0
Alcohol	0	0	0	0

continues to rise with age with a corresponding decline in the number of people with normal BMD values.

51% of our subjects were postmenopausal on the basis of symptomatology as well as serum FSH measurements (Remaining were perimenopausal). 40.81% women in the perimenopausal group were osteopenic, and 37.25% in the menopausal group were so. While 7.84% of women in the postmenopausal group were osteoporotic, none from the perimenopausal group was found to have BMD less than −2.5.

58% of women in our study had insufficient levels of serum 25 hydroxyvitamin D3. Of these nearly half were suffering from osteopenia and 5.17% had osteoporosis. 16% women in the study population had abnormal thyroid or parathyroid hormone values. Their BMD distribution is as shown in Table 2.

13% women in the study had chronic diseases such as diabetes mellitus [4], hypertension [2], deranged hepatic function, rheumatoid arthritis and gout. Of these 75% subjects with diabetes, 33.33% with hypertension, 25% with deranged liver function and 50% with rheumatoid arthritis had low bone mineral density. Two women had diabetes as well as hypertension (Table 2). We had only one participant with a history of smoking. She was osteopenic.

Life style factors that were studied in relation to BMD included daily physical work and sun exposure and diet. While 15.9% women performing heavy physical work had low BMD, this number rose to 56.57% for moderate workers and to 100% for sedentary women.

Similar proportions of subjects with vegetarian and non vegetarian diet were detected to have compromised bone health.

Percentage of women with sound bone mineralization, increased consistently from 53.24% to 95.65% as daily sun exposure rose from under one hour to more than an hour (Table 3).

For the purpose of statistical analysis we divided the women in the study into two groups, based on their BMD results. Women with normal BMD were classified as group I and those with low BMD (osteopenia or osteoporosis) were classified as group II. Student's t-test was carried out to study the effect of continuous variables on BMD. The mean weight, BMI and Serum Vitamin D concentrations were higher in group I as compared to group II, the difference being statistically significant. With respect to Age, Height, Serum Calcium, PTH, FSH and TSH levels, there was no statistically significant difference observed between the means of group I and group II (Table 4).

On Chi Square analysis of categorical variables, daily physical work (p value = 0.000) and daily sun exposure (p value = 0.003) were found significantly associated with BMD on this analysis, with severe physical work and daily sun exposure (>1h) less inclined towards a low BMD (Table 5).

Multiple logistic regression analysis showed light daily physical work (OR = 5.455; 95% CI = 1.836–16.208), inadequate daily sun exposure (OR = 4.288; 95% CI = 1.006–18.280) and insufficient serum vitamin D concentrations (OR = 0.939; 95% CI = 0.893–0.987) to be significant predictors of low BMD (Table 6).

Table 3
Profile of life style factors in relation to bone mineral density.

	N	Normal	Osteopenia	Osteoporosis
Physical work				
Heavy	44	37 (84.09%)	7 (15.9%)	0
Moderate	53	23 (43.33%)	28 (52.83)	2 (3.77%)
Sedentary	3	0	1 (33.33%)	2 (66.66%)
Total	100	60	36	4
Diet				
Non veg	36	20 (55.55)	13 (36.11%)	3 (8.33%)
Veg	64	40 (62.5%)	23 (35.9%)	1 (1.56%)
Total	100	60	36	4
Daily sun exposure				
<1 h	77	41 (53.24%)	32 (41.55%)	4 (5.2%)
1–5 h	23	22 (95.65%)	1 (4.34%)	0
Total	100	63 (63%)	33 (33%)	4 (4%)

Table 4
Age, anthropometry, biochemical and endocrine profile with respect to bone mineral density.

	Group I mean ± SD	Group II mean ± SD	p value
Age	46.25 (5.53)	46.98 (7.01)	0.566
Weight (kg)	66.87 (9.27)	60.91 (9.67)	**0.003**
Height (cms)	156.45 (6.53)	154.13 (5.69)	0.07
BMI[a]	27.27 (3.18)	25.54 (3.23)	**0.01**
Vit D	29.66 (14.48)	23.01 (11.36)	**0.016**
Calcium	8.88 (0.62)	8.77 (0.72)	0.426
PTH[b]	40.32 (20.40)	44.79 (30.31)	0.380
FSH[c]	40.57 (35.68)	48.98 (38.09)	0.264
TSH[d]	3.19 (1.1)	3.06 (1.8)	0.689

Bold values represent significance of p value ≤ 0.05.
[a] Body mass index.
[b] Parathyroid hormone.
[c] Follicle stimulating hormone.
[d] Thyroid stimulating hormone.

Table 5
Association of life style, endocrine and history based factors with bone mineral density.

Factors	Group 1 N (%)	Group 2 N (%)	p value
History of parental fracture			
Yes	9 (15)	3 (7.5)	0.258
No	51 (85)	37 (92.5)	
Physical work			
Sedentary	2 (3.3)	1 (2.5)	
Moderate	21 (35)	32 (80)	0.000
Severe	37 (61.7)	7 (17.5)	
Sun exposure			
>1h	40 (66.7)	37 (92.5)	0.003
<1 h	20 (33.3)	3 (7.5)	
Diet			
Vegetarian	40 (66.7)	24 (60)	0.496
Non vegetarian	20 (33.3)	16 (40)	
Menopause			
Perimenopausal	33 (45)	21 (47.5)	0.806
Postmenopausal	27 (55)	19 (52.5)	
History of chronic disease			
Yes	10 (16.7)	7 (17.5)	0.913
No	50 (83.3)	33 (82.5)	

Table 6
Multiple logistic regression analysis.

Risk factors	OR	95% CI	p value
Weight	0.932	0.845, 1.027	0.156
BMI[a]	1.042	0.784, 1.386	0.776
Vitamin D	0.939	0.893, 0.987	0.013
Physical work	5.455	1.836, 16.208	0.002
Sun exposure	4.288	1.006, 18.280	0.049

[a] Body mass index.

Discussion

Our study reports on the prevalence of low bone mineral density in women above 40 years of age, visiting the gynecology outpatient department. We found prevalence of osteopenia and osteoporosis to be 36% and 4% respectively, the overall prevalence being 40%. This is comparable to many other Indian studies [12–15]. Another report from the city of Jaipur in Rajasthan, has shown that the mean Indian BMD is about 2 SD lower than the western BMD [15]. Researchers from South America, found the prevalence of low BMD to be 33% and 28.8% [16,17]. Those from Iran report it to be 42% [18]. Kidambi et al. have published a prevalence of 33% in African Americans [19]. These studies and ours, imply that low bone mineral density is a widely encountered phenomenon in women above 40 years. The prevalence of osteoporosis is not only higher in Asian countries as compared to western the deterioration in bone health also tends to present itself at a relatively younger age.

The prevalence of osteopenia and osteoporosis increased from 34.21% to 3.94% in women below 50 to 41.66% and 4.16% in those above this age. The association with age, however, was not found to be significant (p value = 0.566). A negative correlation between age and low BMD has also been reported by other research scholars from India [8,14] and abroad [18,20]. Oxidative stress is a common factor in the pathogenesis of degenerative diseases associated with aging, including osteoporosis, leading to decreased bone formation and increased bone resorption with advancing age [21]. Published data from India have shown lower BMD among young Indian women as compared to those established by the NHANES III reference database in women aged 20–29 years [8,15].

Basal metabolic index has shown positive correlation with bone mineral density in our study and the association has been found significant (p value = 0.01). This corroborates with numerous other studies from different parts of the globe. Unni et al. from Pune reported a similar association, though it was not found to be statistically significant [12]. Naz et al. from Iran and Kim et al. from Korea have also highlighted the correlation between BMI and BMD [18,22].

Recently many articles have reported on low BMI being an independent risk factor for fracture mediated by low BMD [23]. An inverse U shaped curve relationship was reported between BMI and BMD in a study from Italy, thereby meaning that in morbidly obese women the protective effect of BMI was lost [24]. Similar findings were recently reported from North India as well [7]. Probably a smaller sample size explains why these findings were not observed in our study.

Menopausal status and time since menopause have both been unequivocally linked to worsening bone mineral density [12]. In our study, even though a similar percentage of women experienced osteopenia in both the perimenopausal as well as the postmenopausal category, all four cases with osteoporosis were past menopause. On statistical analysis, however the association of menopausal status with poor bone health was not found significant (p value = 0.264). This implies that deterioration in bone health begins early on in the perimenopausal phase and targeting women in this phase for screening would be instrumental in better pick up of cases that are still in the potentially treatable condition. The study however has a small sample size to draw a definite conclusion regarding this association. Finkelstein et al. studied 3302 women and found that BMD loss accelerates substantially in the late perimenopause and continues at a similar pace in the first few postmenopausal years [25].

Fifty-eight percent of women in our study were found to have insufficient levels of Vitamin D. 75% of our cases with osteoporosis and 77.77% of those with osteopenia were encountered to have low levels of serum Vitamin D concentrations. The association of Vitamin D insufficiency with low BMD was found to be statistically significant (p value = 0.016). On logistic regression analysis (OR = 0.939; 95% confidence interval 0.893–0.987) it was found to be an independent risk factor for the development of osteopenia and osteoporosis. In a multinational study spanning 18 nations, the prevalence of hypovitaminosis D was determined to be 64% [26]. 84.9% postmenopausal osteoporotic women from Middle East were found to be Vitamin D deficient, as reported by Marie-Hélène Gannagé-Yared et al. [27] A Columbian study reported the prevalence of low serum Vitamin D to be 54.3% in women with osteoporosis [28].

Four cases had hyperparathyroidism in our study, out of which two were detected to have osteopenia and one had osteoporosis making 75% of them suffer from low bone mineral density in all. Many researchers have reported on the frequent association of hyperparathyroidism and low BMD [29,30].

Eight percent of our cases had thyroid abnormalities. 100% cases of hypothyroidism and 75% cases of hyperthyroidism had T scores below −1.0. Lopez et al. from Spain have reported the prevalence of osteopenia to be 87% and osteoporosis 14% in subjects with subclinical hypothyroidism [31]. In hyperthyroidism the cycle of bone remodeling is shortened to about a hundred days leading to a 9.6% bone loss rate per cycle. The consequence of low BMD is mediated via negative calcium balance, hypercalcemia and hypercalciuria. The ambiguous relationship between thyroid status and mineralization of bone is still a matter of ongoing study [32].

Our study had four cases complicated by diabetes mellitus, out of which 50% were suffering from osteopenia and 25% from osteoporosis. Diabetes mellitus as well as hypertension were significantly associated with low BMD in a study from Jordan [33]. In a systematic review Sugimoto et al. concluded that diabetes is an independent risk factor for the development of fracture in the Asian population. However, the relationship between diabetes and low BMD was equivocal [34].

50% women with rheumatoid arthritis were suffering from osteopenia in the present study. A report from Iran showed 16.2% women with rheumatoid arthritis having osteopenia at the site of femoral neck [35]. Others from UK have arrived at 29.9% prevalence of osteoporosis in patients with this disorder [36].

33% of our subjects had hypertension associated with osteopenia. In a study of metabolic factors and low BMD, hypertension was found to be associated significantly with poor T-scores. A link between these two diseases mediated via low dairy product intake has been proposed by Varenna et al.[37].

Inadequate sun exposure and sedentary life style have been postulated to contribute to low BMD, even in tropical countries [38].

The association between these risk factors and poor T-scores was found to be statistically significant in our study. Similar findings have been reported by other workers as well [5]. Conservative clothing, more pigmented skin and mostly indoor activity have been postulated to be responsible for this. The impact of these factors continues even in subjects who have migrated to geographical locations remote from tropics [38].

No association was found between vegetarian or non vegetarian diet and bone mineral density in our study.

Limitation

We chose the gynae out patient department as our source of patients. This limited our study to only those women who were visiting the hospital for gynae complaints. Taking the sample from the general public or at least a wider population base such as all patients visiting the hospital OPDs in all departments, could have generated a more representative sample but could not be possible due to logistic constraints and a time bound protocol for the study. Many other factors affecting BMD, such as parity, time since menopause, calcium and vitamin D supplementation should also be studied. This being a time bound project may be considered as a pilot study to raise awareness among the masses about this disorder.

Summary

Average age of the study population was 46.54 years and BMI 26.58. The prevalence of osteopenia in the study was 36%, and that of osteoporosis, 4%; the overall prevalence of low bone mineral density being 40%. Proportion of women with low BMD increased with advancing age and menopausal status. On endocrine evaluation, 53.44% cases with insufficient vitamin D, 62.5% with hyperparathyroidism, 100% with hypothyroidism, 75% with hyperthy roidism suffered from low BMD.

Among chronic diseases, 75% women with diabetes, 33.3% with hypertension, 25% with deranged liver function and 50% with rheumatoid arthritis were found to have low BMD. 46.75% women with sun exposure less than one hour daily had poor bone mineralization. The proportion of women with normal BMD decreased

from 84.09% to 43.33% with decrease in daily physical work from heavy to moderate or sedentary.

On logistic regression analysis, insufficient serum vitamin D concentrations, moderate to sedentary physical work and inadequate exposure to sunlight were factors found to be significantly and independently associated with low BMD.

Conclusion

Low bone mineral density is not a disorder confined to postmenopausal women alone. It is widely prevalent in women above 40 years of age. Sedentary life style, inadequate sun exposure and insufficient vitamin D concentrations are independently associated with this disorder. Screening women above 40 in the absence of any high risk factors has the potential of nipping this silent killer in the bud.

Suggestions

- Age for screening for BMD should be reduced especially in Indian women.
- A national program to screen for women above 40 years for BMD and secondary causes of osteoporosis should be devised.
- Community based programs to raise awareness about this largely preventable disorder should be launched.
- A study with a larger sample size is suggested to confirm the associations found in this pilot study.

Conflict of interest

The authors have no conflict of interest relevant to this article.

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