VITAMIN D LEVELS AND ITS RELATIONSHIP WITH BONE MINERAL DENSITY AMONG POSTMENOPAUSAL WOMEN IN CENTRAL INDIA
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ABSTRACT

BACKGROUND
To determine vitamin D (25OHD) status and its relationship with bone mineral density (BMD) in 100 postmenopausal women.

MATERIALS AND METHODS
Postmenopausal women were included according to inclusion and exclusion criteria and serum 25OHD and a peripheral DXA scan of the forearm (distal radius) and calcaneum were taken.

RESULTS
Mean±SD of serum 25OHD levels were 18.0±8.07 ng/ml. The prevalence of vitamin D deficiency was 62%. Patients with hypovitaminosis D had a lower BMD at the distal radius and at calcaneum (p<0.05%).

CONCLUSION
We found a high prevalence of hypovitaminosis D and osteoporosis in postmenopausal women. Age, body mass index and vitamin D levels were correlated with bone mineral density at both sites (i.e. at distal radius and at calcaneum).

KEYWORDS
Vitamin D; Osteoporosis; Bone Mineral Density.

HOW TO CITE THIS ARTICLE: Godara A. Vitamin d levels and its relationship with bone mineral density among postmenopausal women in central India. J. Evid. Based Med. Healthc. 2017; 4(18), 1037-1041. DOI: 10.18410/jebmh/2017/203

BACKGROUND
Vitamin D plays an important role in skeletal development and maintenance. In relation to vitamin D, research has shown that inadequate vitamin D intakes over a long period of time can lead to bone demineralization. Vitamin D deficiency leads to decreased calcium absorption and ultimately the release of calcium from the bones in order to maintain circulating calcium concentrations. Continuous bone turnover and resorption weakens the architecture of bones and increases fracture risk via secondary hyperparathyroidism ultimately leading to the development of osteomalacia and osteoporosis.1 Increased age has especially been associated with lower 25 (OH) D levels owing to changes in lifestyle factors such as clothing habits and decreased outdoor activities, and owing to reduced cutaneous vitamin D synthesis capacity and dietary intake of vitamin D. It has also been reported that serum 25 (OH) D levels decline with age earlier in women than in men.2

It has been estimated that 1 billion people worldwide have Vitamin D deficiency or insufficiency. Kuchuk NO et al showed a high prevalence of low 25 (OH)D in postmenopausal women with osteoporosis worldwide.3 Vitamin D deficiency (<20 ng/ml) is quite common in India as reported by various studies and the prevalence was found to be around 64.3%.4,5 Recently a very high prevalence of vitamin D deficiency was found in another study carried out in India.6 Vitamin D deficiency, a preventable disorder is a common and important public health problem for female gender and for elderly disabled women living in the community. Hypovitaminosis D is widely prevalent in India and is a formidable issue especially in postmenopausal women. Osteoporosis is a skeletal disease characterized by decreased bone strength and increasing the risk of fractures. Osteoporosis is silent disorder similar to hypertension and dyslipidaemia. Various factors are responsible for osteoporosis such as race, family history, body weight, low calcium intake and low vitamin D levels apart from oestrogen deficiency (menopause). Amongst these all risk factors, the oestrogen deficiency is the most common factor associated with postmenopausal osteoporosis.6 Osteoporosis affects about 30% of postmenopausal white women in USA and the proportion rises to 70% in women over age of 80 years. WHO has predicted Asians to be largely affected by the year 2050.7 In India, the precise figures on the prevalence of osteoporosis are not available at present. However, it is estimated that more than 61 million Indians have osteoporosis and of 80% patients are females.8 Gandhi et al reported incidence of 34% osteopenia and 8% osteoporosis in Indian women.9 Singh et al reported a high incidence of osteoporosis and osteopenia (44.34% and 28.69%).
between 41-65 years of age in Indian women. Bone loss in postmenopausal women occurs in two phases. A primary postmenopausal accelerated phase with high bone turnover mediated primarily by oestrogen loss and an ensuing phase of slower bone loss, as a result of both sex steroid deficiency and secondary hyperparathyroidism due to vitamin D impaired metabolism and low intestinal calcium absorption. Oestrogen deficiency is a significant cause of accelerated bone loss after menopause. In women bone loss begins to accelerate approximately 2 to 3 years before the last menses, and this acceleration ends 3 to 4 years after menopause. For an interval of a few years around menopause, women lose 2% of bone annually. Afterward, bone loss slows to about 1% to 1.5% per year. Lower oestrogen levels were implicated as the cause for approximately two thirds of the bone loss and some of the decline can be attributed to age related factors. Bone densitometry is the only technology available for accurately measuring bone mass and predicting fracture risk. This unique ability of bone densitometry to predict fracture risk makes it an important tool for disease prevention. Bone Mineral Density (BMD) measurement may help an individual to start therapies depending on the density and clinical factors. Women are more likely to initiate preventive measures for osteoporosis if they are aware of the presence of low bone mass. In general, a bone density test and vitamin D levels can be an extremely powerful tool for patient education and compliance with lifestyle modification and drug therapy.

The study intends to estimate the prevalence of vitamin D deficiency among postmenopausal women with osteoporosis. Prevention and early detection of hypovitaminosis D is the key to reduce the incidence of osteoporosis among postmenopausal women.

MATERIALS AND METHODS
This was a cross-sectional study, which involved hundred postmenopausal women evaluated on an outpatient and inpatient basis at Kasturba Hospital, Sevagram. After giving informed consent, 100 postmenopausal women were included who attained menopause by ≥2 years. The exclusion criteria adopted were as follows: patients on drugs that known to lead to bone loss, such as glucocorticoids and anticonvulsants, patients on anti-osteoporotic medication therapy; and those with diseases that affect bone metabolism, contributing to osteoporosis, such as diseases of the kidney or liver, malabsorption diseases, primary hyperparathyroidism and uncontrolled hypo- or hyperthyroidism. For determining the diagnosis and extent of osteoporosis WHO criteria were used. The study protocol was approved by the Ethics Committee of Kasturba hospital, Sevagram, MUHS University, Nashik.

Vitamin D Measurements
25-hydroxyvitamin D was measured in the serum by Thyrocare, Advia centaur machine which works on CLIA (Chemiluminescent Immunoassay) principle and measures total 25 (OH) Vitamin D. The standardized value used by the machine to classify serum vitamin D levels was as follows:- Normal vitamin D level-more than 30 ng/ml, Insufficiency of vitamin D -20 ng/ml to 30 ng/ml, Deficiency of vitamin D – less than 20 ng/ml.

Determination of bone mineral density: BMD was measured by the Dual Energy X-ray Absorptiometry (Osteosys EXA-3000 bone densitometer) at the Distal radius and calcaneum. The results are expressed in standard deviation T-score. We used WHO classification to categorized the BMD values.

<table>
<thead>
<tr>
<th>World Health Organization Definition based on Bone Mineral Density levels</th>
<th>Level</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>T-score above or equal to -1.0</td>
<td></td>
</tr>
<tr>
<td>Osteopenia</td>
<td>T-score between -1.0 and -2.5</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>T-score below or equal to -2.5</td>
<td></td>
</tr>
</tbody>
</table>

Statistical Analysis
Data collection tool contains the information on basic sociodemographic factors, anthropometric measurements like height and weight, investigations like serum vitamin D, serum calcium, bone mineral density (BMD) at distal radius and calcaneum. Data was entered and analysed using Epi Info version 3.5.4. Initially frequencies of all variables were taken to check the completeness. X² test was used to test the association. Pearson correlation coefficient was applied to measure Correlation between BMD Indices and other parameters wherever necessary.

RESULTS
The mean±SD age was 58.82±8.42 years with majority (52%) of the women were between age group of 51-60 years followed by 61-70 years (23%). (Table 1)

<table>
<thead>
<tr>
<th></th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>58.82±8.42</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>24.6±4.4</td>
</tr>
<tr>
<td>BMD Distal radius</td>
<td>-2.40±1.45</td>
</tr>
<tr>
<td>BMD Calcaneum</td>
<td>-2.12±1.35</td>
</tr>
<tr>
<td>25-OH (ng/ml)</td>
<td>18.0±8.07</td>
</tr>
</tbody>
</table>

Table 1. Mean Values of Studied Variables for 100 Postmenopausal Women

SD = standard deviation; BMI = body mass index; BMD = bone mineral density.

When we consider the participants according to their socio-economic status (modified Kuppuswami scale), we have found that 46% were from middle socio-economic status followed by 29% from low socioeconomic status and 25% from high Socio-economic status. In present study out of 29 postmenopausal women who belong to low socioeconomic status, 22 (75.9%) have osteoporosis & out of 46 postmenopausal women from middle socioeconomic status, 21 (45.7%) had osteoporosis (by measuring BMD at distal radius) and by measuring BMD at calcaneum out of 29
postmenopausal women who belong to low socioeconomic status, 22 (75.9%) have osteoporosis and out of 46 postmenopausal women from middle socioeconomic status, 20 (43.5%) had osteoporosis which was found to be statistically significant (p<0.05). Mean body mass index was 24.6±4.4 kg/m² in the study and majority (58%) of postmenopausal women had normal BMI (18.5-24.9 kg/m²) followed by 22% were overweight (25-29.9 kg/m²) by using WHO classification for BMI. Out of 16 postmenopausal women who had high BMI (>30 kg/m²), 9 (56.3%) postmenopausal women had normal BMD at distal radius and out of 58 Postmenopausal women who had normal BMI (18.5-24.9 kg/m²), 37 (63.8%) had osteoporosis. Likewise by measuring BMD at calcaneum, out of 16 postmenopausal women who had high BMI (>30 kg/m²), 6 (37.5%) postmenopausal women had normal BMD and out of 58 Postmenopausal women who had normal BMI (18.5-24.9 KG/M2), 33 (56.9%) had osteoporosis. It was found that with increase in body mass index there was an increase in bone mineral density at distal radius and calcaneum (p<0.05). By using the Pearson’s correlation coefficient it was found that there was a positive correlation between body mass index and BMD, at both sites (i.e. at distal radius and calcaneum (r=0.0281, r=0.365).

Out of 55 Hypocalcemic post-menopausal women, 56.4% had osteoporosis and out of 45 postmenopausal women with normal serum calcium levels, 51.1% was osteoporosis and it was found to be statistically not significant (p>0.05 & r=0.061).

Mean serum 25OHD was 18.0 ± 8.07 ng/ml and 62% postmenopausal women had vitamin D deficiency and 30% postmenopausal women had vitamin D insufficiency. Majority of postmenopausal women (54.0%) had osteoporosis followed by 28.0% had osteopenia by measuring BMD at distal radius and 49% of postmenopausal women were osteoporotic, followed by 36% had osteopenia by measuring BMD at calcaneum in the study. Out of 62 postmenopausal women who had vitamin D deficiency 38 (61.3%) had osteoporosis and 16 (25.8%) had osteopenia at distal radius (Table 2) and 8 (100.0) had osteoporosis and 21 (33.9%) had osteopenia at calcaneum (Table 3) and it was statistically significant (p<0.05).

### Table 2. Distribution of Postmenopausal Women According to Serum Vitamin D and Bone Mineral Density at Distal Radius

<table>
<thead>
<tr>
<th>Serum Vitamin D Level</th>
<th>Normal</th>
<th>Osteopenia</th>
<th>Osteoporosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>6 (75.0)</td>
<td>2 (25.0)</td>
<td>0 (0.0)</td>
<td>8 (100.0)</td>
</tr>
<tr>
<td>Vitamin D Insufficiency</td>
<td>4 (13.3)</td>
<td>10 (33.3)</td>
<td>16 (53.3)</td>
<td>30 (100.0)</td>
</tr>
<tr>
<td>Vitamin D Deficiency</td>
<td>8 (12.9)</td>
<td>16 (25.8)</td>
<td>38 (61.3)</td>
<td>62 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>18 (18.0)</td>
<td>28 (28.0)</td>
<td>54 (54.0)</td>
<td>100 (100.0)</td>
</tr>
</tbody>
</table>

(Figures in parenthesis denotes percentages) (x² Value = 21.06 at 4 df p<0.02.).

### Table 3. Distribution of Postmenopausal Women According to Serum Vitamin D and Bone Mineral Density at Calcaneum

<table>
<thead>
<tr>
<th>Serum Vitamin D Level</th>
<th>Normal</th>
<th>Osteopenia</th>
<th>Osteoporosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>5 (62.5)</td>
<td>3 (37.5)</td>
<td>0 (0.0)</td>
<td>8 (100.0)</td>
</tr>
<tr>
<td>Vitamin D Insufficiency</td>
<td>3 (10.0)</td>
<td>12 (40.0)</td>
<td>15 (50.0)</td>
<td>30 (100.0)</td>
</tr>
<tr>
<td>Vitamin D Deficiency</td>
<td>7 (11.3)</td>
<td>21 (33.9)</td>
<td>34 (54.8)</td>
<td>62 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (15.0)</td>
<td>35 (35.0)</td>
<td>50 (50.0)</td>
<td>100 (100.0)</td>
</tr>
</tbody>
</table>

(Figures in parenthesis denotes percentages) (x² Value = 17.67 at 4 df p<0.05).

By using Pearson’s correlation coefficient it was found that there was a positive correlation between serum vitamin D level and BMD at both sites (r=0.081, r=0.179).

### DISCUSSION

Osteoporosis is a major public health issue in Postmenopausal women. If left untreated it can lead to fragility fractures with high morbidity. Low serum vitamin D status and serum calcium further aggravates osteoporosis because of chronic secondary Hyperparathyroidism associated bone resorption, a problem well documented in Indian population. Overall prevalence of osteoporosis among postmenopausal women were found to be 54% and 49% according to measured bone mineral density at distal radius and calcaneum respectively. Other studies had also reported high prevalence of osteoporosis in their studies. In present study we found that BMD (T-score) of postmenopausal women had a significant correlation with increasing age. Similar findings were reported by some other studies suggesting that chances of osteoporosis increases with increase in age.

### Socioeconomic Status and BMD

75.9% of participants from low socioeconomic status had low BMD (osteoporosis) at both sites i.e. distal radius and calcaneum and it was found to be statistically significant (p value<0.05).We observed that majority of osteoporotic postmenopausal women were from low socioeconomic status. Similar results were found in other studies. Lower socioeconomic status might limit adequate consumption of calcium intake and subsequently contribute to poor bone health.

### Body Mass Index (BMI) and Bone Mineral Density (BMD)

In postmenopausal women, increased body weight has various effects on mature bone and extra skeletal collagen containing tissues, resulting in increased bone mineral content. Prevalence of osteoporosis was noted higher with normal BMI (63.8% at distal radius and 56.9% at
calcaneum) and then followed by overweight (45.5% each at both sites i.e. distal radius and calcaneum) and obese (25% at distal radius and 18.8% at calcaneum) in the postmenopausal women. Present study shows a statistically significant positive correlation between body mass index and bone mineral density (BMD) at both sites i.e. distal radius and calcaneum (p value <0.05). Results were comparable with other studies. However a study conducted by Kataria et al reported no correlation between BMD and BMI. Overweight may protect postmenopausal women against bone loss. This caring effect may be due to mechanical support and higher oestrogen synthesis in adipose tissue. Thus BMI can prevent bone loss by increasing the BMD.

Serum calcium and BMD
Out of total 100 postmenopausal women 55% had serum calcium values below 9 mg/dl and 45% had serum calcium values in normal range of 9-11 mg/dl. However the findings of other studies from different settings are not found consistent with the findings of our study, the reason might be due to small sample size, single center study with hospital based population and lack of randomization. Likewise Kuchuk et al studied on 7,441 post-menopausal women from 29 countries and found a strong positive correlation between Vitamin D and BMD at both the sites i.e. distal radius and calcaneum (p=0.05). Our results were comparable with various studies. Likewise Kuchuk et al studied on 7,441 post-menopausal women from 29 countries and found a strong positive correlation between Vitamin D and BMD. However some other study shows no correlation of BMD with vitamin D and BMD at both the sites i.e. distal radius and calcaneum and obese individuals. Therefore it seems to be due to different population and lack of randomization. Small sample size, single center study with hospital based population and lack of randomization. Likewise Kuchuk et al reported no correlation between BMD and BMI. Overweight may protect postmenopausal women against bone loss. This caring effect may be due to mechanical support and higher oestrogen synthesis in adipose tissue. Thus BMI can prevent bone loss by increasing the BMD.

Vitamin D and Bone Mineral Density
In our study the vitamin D deficiency is considered to be present when serum vitamin 25 (OH) D levels are <20 ng/ml. The prevalence of vitamin D deficiency and insufficiency found in present study was 62% and 30% respectively. We found statistically significant positive correlation between vitamin D and BMD at both the sites i.e. distal radius and calcaneum (p<0.05). Our results were comparable with various studies. Likewise Kuchuk et al studied on 7,441 post-menopausal women from 29 countries and found a strong positive correlation between Vitamin D and BMD. However some other study shows no correlation of BMD with vitamin D and BMD at both the sites i.e. distal radius and calcaneum. The differences among these studies might be due limited due to change in demographic features of the study population.

CONCLUSION
In conclusion, we found a high prevalence of vitamin D deficiency and low BMD among healthy postmenopausal women who were seen for routine medical evaluation irrespective of age group. It emphasize the critical role of advancing age, low socioeconomic status, low BMI and low serum vitamin D level as a significant predictors for osteoporosis. So, serum vitamin D levels, socioeconomic status, anthropometry can be used as a risk factors to identify high-risk patients of osteoporosis and because effective interventions exist, many of further complications secondary to osteoporosis are now preventable. It is therefore necessary to create awareness among women from Indian subcontinent, irrespective of their geographic location, about the risk of osteoporosis and educate those regarding preventive measures to avoid future fractures secondary to osteoporosis. Because replacement therapy is expensive, simple, and safe a widespread screening for vitamin D insufficiency and the normalization of vitamin D status should alter our routine medical practice and have important public health implications. Limitations of our study was a small sample size, single center experience with study population not reflective of the general population at large and lack of randomization in the recruitment of patients as most of our subjects were hospital based. However, we feel that our single center experience would give a way for a longitudinal multicenter study involving larger number of patients to confirm or negate our observations. There is also a need for large community based studies so that high-risk population can be picked up and early interventions like adequate calcium intake, vitamin D supplementation, and other life style changes can be planned.


