Vitamin D deficiency (VDD) has been documented across all age groups and both sexes from India and different parts of world. However there is paucity of data on vitamin D status in population more than 50 years of age. Vitamin D deficiency is associated with low bone mass, muscle weakness, and increases the risk of fracture. It has also been linked to infection, cardiovascular disease, malignancy, and autoimmunity which are commonly seen in the elderly, as are fragility fractures. Hence this population study was under taken to assess the vitamin D status and its impact on bone mass in individuals above 50 years of age.

Material and Methods:
The study was carried in 1346 healthy subjects more than 50 years of age residing in Delhi, India. These subjects, who were divided in two groups: Group-1 (50 - <65 years) and Group-2 (≥65 years), underwent anthropometric, biochemical and hormonal evaluation for vitamin D status Bone mineral density was measured by dual X-ray absorptiometry.

Results:
There were 643 males and 703 females, with a mean age of 58.0 ± 9.5 years (range 50-84 years). Vitamin D deficiency [VDD, serum 25(OH)D levels < 20 ng/ml] was present in 1228 (91.2%) and Vitamin D insufficiency [VDI, serum 25(OH)D levels 20-<30 ng/ml] in 92 (6.8%). There was no significant difference in prevalence of either VDD or VDI between two age groups and sexes. Serum 25(OH)D levels were negatively correlated with PTH levels (r = -0.027, p < 0.00001) and BMI (r = -0.128, p 0.05). Prevalence of secondary hyperparathyroidism increased from 14.1% to 43.1% from VDI to severe VDD. PTH levels started rising at vitamin D level < 30 ng/ml. However, more than 50% of subjects with severe VDD had PTH levels within normal range. High prevalence of osteopenia (50.2%) and osteoporosis (31.2%) was observed in this population.

Conclusion:
Hypovitaminosis D is universal above the age of 50 years in north India. Absence of a PTH response was observed in more than 50% of individuals with VDD, the cause of which merits further evaluation. Normal bone mass was observed in only 18.6% of study subjects.

Vitamin D deficiency (VDD) has been documented across all age groups and both sexes from India and different parts of world. However there is paucity of data on vitamin D status in population more than 50 years of age. Vitamin D deficiency is associated with low bone mass, muscle weakness, and increases the risk of fracture. It has also been linked to infection, cardiovascular disease, malignancy, and autoimmunity which are commonly seen in the elderly, as are fragility fractures. Hence this population study was undertaken to assess the vitamin D status and its impact on bone mass in individuals above 50 years of age.

Material and Methods:
The study was carried in population more than 50 years of age in Delhi, India (latitude 28.35º). A total of 1346 individuals were recruited from resident welfare associations and senior citizen associations from different locations in Delhi. Subjects with hepatic, renal, dermatological disorders, alcoholism, and receiving medication likely to adversely affect vitamin D status, were excluded from the study. Demographic, anthropometric and clinical data were ascertained and a detailed physical examination conducted. Individuals taking calcium (minimum 500 mg/day) and Vitamin D (200-400 IU) for >6 months were considered as taking supplements. Fasting blood samples were drawn for the estimation of serum 25(OH)D, intact parathyroid hormone, total and ionic calcium, inorganic phosphorus, and alkaline phosphatase. The study was approved by the ethics committee of the Institute of Nuclear Medicine and Allied Sciences and all subjects gave written informed consent.

Biochemical estimations were carried out using automated analysers (Hitachi 902; Roche, Manheim, Germany) and commercial kits (Roche). The normal range for serum total calcium, (8.8-10.2 mg/dl), ionized calcium, (1.12-1.32 mmol/L), inorganic phosphorus (2.7-4.5 mg/dl), and alkaline phosphatase were (females: <240 U/L; males: <270 U/L). The serum concentrations of 25(OH)D (reference range: 9.0-37.6 ng/ml) and PTH (reference range: 10-65 pg/ml) were measured by RIA (Diasorin, Stillwater, MN) and electrochemiluminescence assay (Roche diagnostics, GMDM-Manheim, Germany) respectively. Serum 25(OH)D level of 20.0 - <30.0 ng/ml was classified as vitamin D insufficiency (VDI) and severe < 20 ng/ml were classified as vitamin D deficiency (VDD). VDD was further categorized based on Lips classification as mild (10.0 – <20.0 ng/ml), moderate (5.0-<10.0 ng/ml) and severe (< 5.0 ng/ml). Secondary hyperparathyroidism was defined by serum PTH level of >65pg/ml.

Bone mineral density (BMD) at anteroposterior (AP) lumbar spine (L1–L4), femur (femoral neck, Ward’s triangle, and trochanter) and forearm (total, ultra distal and 33% radius) was measured using the Prodigy Oracle (GE Lunar Corp., Madison, WI) according to standard protocol. Quality control procedures were carried out in accordance with the manufacturer’s recommendations. Instrument variation was determined regularly using a phantom supplied by the manufacturer and mean coefficient of variation was <0.5%. For in vivo measurements, mean coefficients of variation for all sites were <1%. The WHO classification was used to define osteopenia (T score between -1 and -2.5) and osteoporosis (T score < -2.5). DXA was also used to measure percentage body fat.

Statistical analysis was carried out using STATA 9.0 (College Station, TX). Data were presented as mean ± SD or number (%) unless specified. All unpaired parametric data were analysed by student’s t-test and non parametric data by chi-square test.
Table 1: Anthropometric, Biochemical and Vitamin D Status (All Subjects)

<table>
<thead>
<tr>
<th>Variable/Age Group</th>
<th>50-65 (995)</th>
<th>&gt;65 (351)</th>
<th>P – Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometric Parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.3±9.3</td>
<td>160.3±9.3</td>
<td>0.037</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>25.9±4.1</td>
<td>25.9±4.1</td>
<td>0.00001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>38.6±9.0</td>
<td>38.6±9.0</td>
<td>0.00001</td>
</tr>
<tr>
<td>Biochemical Parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. Calcium (mg/dl)</td>
<td>9.8±0.4</td>
<td>9.8±0.4</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Ionic Calcium (mmol/L)</td>
<td>1.1±0.05</td>
<td>1.1±0.05</td>
<td>0.306</td>
</tr>
<tr>
<td>S. Phosphorus (mg/dl)</td>
<td>3.5±0.5</td>
<td>3.5±0.5</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>211±61</td>
<td>211±61</td>
<td>0.0021</td>
</tr>
<tr>
<td>PTH (ng/ml)</td>
<td>54.7±34.9</td>
<td>54.7±34.9</td>
<td>0.085</td>
</tr>
</tbody>
</table>

Pearson’s correlation was calculated to assess the strength of relationship between 25(OH)D levels and other parameters. A p value of < 0.05 was considered statistically significant.

Results

In this cross-sectional study 1346 subjects were studied. Mean age of subjects were 58.0±9.5 years (median 50.1 years, range 50-84 years). There were 643 males and 703 females. These subjects were divided in two groups: Group-1 - those 50 - <65 years (as all females were postmenopausal in this group) and Group-2 - those with 65 years or above (as senile osteoporosis in after 65 years of age).

Anthropometric and Biochemical Data

Weight, BMI and percentage of total body fat significantly decreased with age (Table 1). Height decreased significantly in females with age (153.7±6.6 vs. 156.2±6.3, p = 0.037) but not in males (165.9±6.2 vs. 166.3±6.4, p = 0.48). Serum phosphorus decreased significantly in males with age (3.5±0.4 vs. 3.3±0.5, p < 0.00001) compared to females (3.8±0.4 vs. 3.8±0.4, p = 0.68). There was no difference in intact PTH level between age groups and sexes.

Vitamin D Status

VDD was present in 1228 (91.2%) and VDI in 92(6.8%) among all (Table 1). There was no significant difference in prevalence of either VDD or VDI between two age groups (Table 1). There was no difference in prevalence of VDD (91.3% vs. 91.2%, p = 0.58) and VDI (7.3% vs. 6.4%, p = 0.26) between sexes (Table 2). There were almost equal distributions of severity of VDD among all and both sexes (Table 2). The only statistically significant correlation of serum 25(OH)D levels on multivariate analysis was a negative correlation with PTH levels, ALP and BMI (Table 3).

Discussion

Wide spread VDD has been recognised in Indians of all age groups and both sexes.3,5,9 The present study extended the assessment of vitamin D status in older age groups where there was limited data and showed that 91.2% subjects more than 50 years of age had VDD and an additional 6.8% subjects had VDI. Varying prevalence of VDD in the elderly has been reported...
where approximately 90% people above the age of 65 years had

States (blacks, Hispanics, and Asians) UK, and Saudi Arabia

has been also observed in elderly population 18 on admission to

moderate (5-<10 ng/ml) 57.8±31.3 (52.69) 31.7%

Vitamin D Insufficiency

mild (10-<20 ng/ml) 53.35±33.34 (48.9) 21.5%

(20-<30 ng/ml)

Vitamin D Deficiency

Normal 43.89±12.43 (42.95)

globally. One of the highest prevalence among postmenopausal

women >50 years reported in recent times have been from Croatia10 and France,11 where 92.5% and 89.9% had VDI. A high

prevalence of VDI and VDD has also been reported from United

States (Blacks, Hispanics, and Asians) UK, and Saudi Arabia

where approximately 90% people above the age of 65 years had

depression. Similar observation has been made by us in previous

study among healthy young paramilitary personnel, where vitamin D and PTH levels were not statistically different between those with osteopenia or osteoporosis.16

Our study, from North India, confirms the high prevalence

of VDD in both men and women in older age groups. The mean 25(OH)D level observed by us in this population of older

subjects was 9.79±7.61 ng/ml. We and other investigators have

earlier reported similarly low levels in different age of healthy

individuals in north India, mean 25(OH)D level ranging from

4.5 ng/ml15 – 20.85 ng/ml. In contrast, higher serum 25(OH)D

levels, 25.3±7.4 ng/ml in females in summer and 18.4±5.3 ng/ml

in males in winter have been observed in paramilitary personnel

who as a consequence of their professional duties have greater

sunlight exposure.18

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sunlight exposure.18

Studies from South India, while showing a high prevalence

of VDD, have consistently reported higher mean serum 25(OH)

D levels than those observed in north India. Harinarayan et

al reported vitamin D level of 14.6±2 and 20.85±6.3 ng/ml in

postmenopausal women in the age group of 50-67 years.13 The

present study was carried out at a latitude of 28.35° whereas

study from south was done at latitude of 12.55° and 13.4°, which

may explain the difference in serum 25(OH)D levels at these two

sites. An additional contributor to the low serum 25(OH)D levels

in Delhi is the atmospheric pollution. In an earlier study, Agarwal

et al19 have shown a significantly higher level of serum 25(OH)

D levels in infants from an area of lower atmospheric pollution

compared to their peers from Delhi.

Serum 25(OH)D level was negatively correlated with PTH

levels, ALP and BMI in multivariate analysis. Serum PTH levels

have strong negative correlation with vitamin D levels2 and a

negative correlation between ALP and vitamin D levels has been

reported3. A negative correlation between 25(OH)D and PTH

has been also observed in elderly population4 on admission to

nursing home with fracture. Serum PTH levels plateau at 25(OH)

D level of 20 ng/dl in this population. However SIVIMAX study

observed rising trends in PTH at 25(OH)D value <30 ng/dl5 in

young adult, whereas such threshold was observed at 10 ng/dl

in population >70 year of age.6 This can be interpreted as with

increasing age there is decrease in threshold for rise in PTH in

relation to 25(OH)D level.

VDD and VDI has been reported to be associated with increased

risk of fracture,7 however there are conflicting reports in the

literature.7 Serum 25(OH)D were not significantly different

among those with or without history of fracture in both age

groups and sexes. However age of occurrence of fracture, and

the degree of trauma associated with the fracture were not

ascertained in this study, limiting the interpretation of this

information. In a study from the UK, patients with hip fracture

were shown to have lower serum 25(OH)D levels compared with

controls. This difference was not observed in case of fractures at

other sites.8 In our study, there was no difference in prevalence

of osteopenia or osteoporosis among subjects with VDD or

VDI. However, there was a trend of increasing prevalence of

osteoporosis progressively as one progressed from mild to severe

degree of vitamin D deficiency. Similar observation has been

made by us in previous study among healthy young paramilitary

personnel, where vitamin D and PTH levels were not statistically

different between those with osteopenia or osteoporosis.16

There was no correlation of BMD at different sites with serum

25(OH)D levels in the present study. No consistent relationship

has been reported between 25(OH)D levels and BMD in cross-

sectional studies. A recent meta-analysis confirms the lack of

a consistent association between 25(OH)D and BMD, with a

consistent observable effect only present in older age groups.21

A correlation has been reported between 25-OHD levels and hip

BMD in subjects of South Asian descent.21,22 However in other

studies involving subjects of South Asian ethnicity, including

those conducted by us in healthy young subjects and school

girls, there was no correlation between 25(OH)D levels and BMD

at any site.16,24-26

More than half of subjects in this study were taking calcium

and vitamin D supplements, but there was no difference in

serum 25(OH)D levels between those who took and did not take

supplements. A lack of difference in serum 25(OH)D levels

between those receiving and not receiving vitamin D supplements

was also reported in an audit from Belfast.20 Most

of the subjects were taking between 200-400 IU of vitamin D3

(cholecalciferol), which is insufficient to normalize serum 25(OH)

D levels in a vitamin D deficient population. One study from

North India15 reported requirement of 60,000-120,000 IU per

month to achieve vitamin D level > 30 ng/ml. In another study27

reported correction of vitamin D level to normal after 8 weeks

supplementation with weekly supplementation of 60,000 IU.

Both these studies highlight the need of regular supplementation

of at least 2000 IU/day vitamin D supplementation to maintain

normal vitamin D levels.

Serum PTH levels progressively increased from VDI to

varying severity of VDD. Serum PTH levels were within normal

range among subjects with serum 25(OH)D levels ≥30 ng/

ml. However, PTH levels above the upper limit of normal

(superior hyperparathyroidism, SHPT) were present in less

than half of subjects with severe vitamin D deficiency (<5 ng/

ml). The possible explanations for this phenomenon include

probable adaptation to vitamin D deficiency or other associated

genetic, nutritional or environmental factors which preclude an

elevation of serum PTH levels. A study of vitamin D receptor

polymorphism from this geographical region did not reveal any

abnormality or increase expression explaining adaptability to

VDI.28 However decreased expression of calcium sensing

receptor has been observed with vitamin D deficiency in rat

and human parathyroid glands.29,30 This may limit the ability of

calcium and calcitriol to regulate PTH secretion in individuals

with long standing vDD.31 variation in calcium intake and other

dietary factor can lead to variation of VDD on PTH.32

Table 4 : PTH Levels According to Vitamin D Status

<table>
<thead>
<tr>
<th>Vitamin D Deficiency</th>
<th>PTH Levels (Median)</th>
<th>PTH % Increase</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (&lt;5 ng/ml)</td>
<td>67.2±81.57 (59.6)</td>
<td>53.3%</td>
<td></td>
</tr>
<tr>
<td>Moderate (5–&lt;10 ng/ml)</td>
<td>57.8±31.3 (52.69)</td>
<td>31.7%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mild (10–&lt;20 ng/ml)</td>
<td>53.35±33.34 (48.9)</td>
<td>21.5%</td>
<td></td>
</tr>
<tr>
<td>Vitamin D Insufficiency (20–&lt;30 ng/ml)</td>
<td>48.29±27.78 (44.85)</td>
<td>10.0%</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>43.89±12.43 (42.95)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5 : Secondary Hyperparathyroidism According to Vitamin D Status

<table>
<thead>
<tr>
<th>Vitamin D Status</th>
<th>Secondary PHPT</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDD Severe (&lt;5ng/ml)</td>
<td>162 (43.1%)</td>
<td>214 (56.9%)</td>
</tr>
<tr>
<td>VDD Moderate (5–10ng/ml)</td>
<td>153 (33.5%)</td>
<td>304 (66.5%)</td>
</tr>
<tr>
<td>VDD Mild (10–&lt;20ng/ml)</td>
<td>93 (23.5%)</td>
<td>302 (76.5%)</td>
</tr>
<tr>
<td>VDI (20–&lt;30ng/ml)</td>
<td>13 (14.1%)</td>
<td>79 (85.9%)</td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>26 (100.0%)</td>
</tr>
</tbody>
</table>
serum PTH. However, all the subjects recruited for this study were mobile and had physical activity commensurate with their age. Nonetheless, the absence of an anticipated PTH response to low serum 25(OH)D levels is an observation, which merits further study.

Conclusion

Vitamin D deficiency is nearly universal above the age of 50 years in northern part of India, with no difference among those with and without a history of fractures or with and without intake of vitamin D supplements. The study highlights the inadequacy of a daily vitamin D intake of 200-400 IU in normalizing serum 25(OH)D levels in this population, which is consistent with recent observations which indicate that a daily intake of 2000 IU cholecalciferol would be required for this. The absence of PTH elevation despite severe vitamin D deficiency is an area for future research.

Acknowledgements

This study was funded through Project No INM305, from the Defence Research and Development Organisation, Ministry of Defence, Government of India. The authors would like to acknowledge the assistance provided by Ms Kalaivani Mani,

References


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