Abstract

Background: To assess vitamin-D deficiency in Northern Pakistan in order to provide inputs towards developing effective preventive and remedial strategies.

Methods: A total of five thousand six hundred and ninety three (n=5693) adult patients of both genders were screened for serum Vitamin D-3 levels over the period of six years.

Results: Mean serum Vitamin D3 levels among males and females were in insufficient range and showed no significant difference (P>0.05). In study population 56.5% (n=3216) of patients were Vitamin D-3 deficient (<20 ng/ml), 18.2% (n=1037) showed insufficient levels (20-30 ng/ml) and 25.3% showed sufficient levels (>30 ng/ml). Significant difference was observed on gender stratification with female population showed higher percentage of deficient levels (79.7%) versus males (20.3%) (p<0.05). Age based stratification also showed significant difference with age groups younger than 50 years showed higher percentage of deficient levels than in patients older than 50 years (P<0.05).

Conclusion: There is a high prevalence of vitamin D deficiency in population of Rawalpindi and Islamabad regions.

Key Words: Vitamin D; Vitamin D deficiency; Vitamin D3

Introduction

Vitamin D is a hormone precursor which has an important function in bone metabolism and immunomodulation. Decreased vitamin D levels are associated with various critical diseases like cardiovascular, cancer, diabetes, tuberculosis and osteoporosis. Low vitamin D can cause obesity and restrict bone growth and bone health in children and adults. Vitamin D is naturally found in the form of Ergocalciferol (Vitamin D2) & Cholecalciferol (Vitamin D3). Ergocalciferol is present in plants, and few fish, while Cholecalciferol is synthesized in the skin when exposed to the sunlight. Almost 50% of the global population affected by the Vitamin D insufficiency based on the measurement of 25-hydroxy D (25[OH]D) below 20ng/ml. It has been estimated that 1 billion people worldwide, across all ethnicities and age groups, have a vitamin D deficiency (VDD). The factors that contribute in high prevalence of VDD may include lack of proper diet, poor calcium intake, social customs and remaining confined to the four walls of primitive housings that deprives the elderly, children and female population of the benefit of the sunlight.

The emergence of VDD as a global pandemic has made it a topic of increasing importance in recent research, and studies from all across the globe testify to the prevalence of VDD in a significant proportion of their population. Pakistan as a region spanning latitude 24° 35' north and longitude 61° East to 78° East, gravelly suffers from increased VDD despite its abundant sunshine. Studies showed that 50-90% of Pakistani population especially females are vitamin D deficient. Poor socioeconomic status and lack of proper attention on diet may be the contributing factors for VDD in Pakistan. Awareness of the significance of vitamin D in the regulation of normal physiology as well as the consequences of its deficiency among general population is the need of the hour to save them from widespread bone and other disorders related to VDD.

Patients and Methods

It was a retrospective cross-sectional study carried out at Nuclear Medicine, Oncology and Radiotherapy Institute (NORI), Islamabad, Pakistan. Data collected over a period of six years (Jan 2010 to December 2015) was analyzed. Study design was approved by the hospital ethical committee. Data of all the adult patients irrespective of gender who presented at our institute for their vitamin D analysis was gathered and analyzed. Mean levels were calculated among males and females. The levels of 25-hydroxivitamin D levels were defined as deficient: < 20 ng/ml; insufficient: 20-
30 ng/ml and sufficient: > 30 ng/ml. The results were further stratified with respect to age and gender. Chi-square test was applied as a test of significance and a P-value ≤ 0.05 was considered significant.

**Results**

A total of five thousand six hundred and ninety three (n=5693) adult patients of both genders were screened for serum Vitamin D-3 levels.

Table 1: Gender and Age distribution in study sample

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>Mean age (years)</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>1236</td>
<td>41.6</td>
<td>21.7</td>
</tr>
<tr>
<td>Females</td>
<td>4457</td>
<td>43.7</td>
<td>15.6</td>
</tr>
<tr>
<td>Total</td>
<td>5693</td>
<td>43.2</td>
<td>17.2</td>
</tr>
</tbody>
</table>

Table 2: Mean serum Vitamin D3 levels in study sample

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean vitamin D3 levels (ng/ml)</th>
<th>Std. Deviation</th>
<th>p-value T-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>24.3</td>
<td>20.2</td>
<td>0.494</td>
</tr>
<tr>
<td>Females</td>
<td>23.8</td>
<td>22.4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>23.9</td>
<td>21.9</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Frequency of vitamin D3 deficiency in study sample

<table>
<thead>
<tr>
<th>Serum vitamin D-3 levels</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sufficient</td>
<td>1440</td>
<td>25.3</td>
</tr>
<tr>
<td>Insufficient</td>
<td>1037</td>
<td>18.2</td>
</tr>
<tr>
<td>Deficient</td>
<td>3216</td>
<td>56.5</td>
</tr>
<tr>
<td>Total</td>
<td>5693</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mean age of study population was 43.2 years, with 43.7% females (Table 1). Mean serum Vitamin D3 levels in overall study subjects were in insufficient range (23.9 ± 21.9 ng/ml) with no significant difference among males and females (p>0.05) (Table 2). As per our operational definition 56.5% (n=3216) of patients were Vitamin D3 deficient (<20ng/ml), 18.2% (n=1037) showed insufficient levels (20-30 ng/ml) and 25.3% showed sufficient levels (>30ng/ml) (Table 3&4). Significant difference was observed on gender stratification with female population showed higher percentage of deficient levels than in patients older than 50 years (P<0.05) (Table 4&5).

Table 4: Gender Based stratification

<table>
<thead>
<tr>
<th>Serum vitamin D3 levels</th>
<th>Gender</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>305(21.2%)</td>
<td>1440(100%)</td>
</tr>
<tr>
<td>Females</td>
<td>1135(78.8%)</td>
<td>1037(100%)</td>
</tr>
<tr>
<td>Total</td>
<td>1440(100%)</td>
<td>1037(100%)</td>
</tr>
</tbody>
</table>

Table 5: Age Based stratification

<table>
<thead>
<tr>
<th>Serum vitamin D3 levels</th>
<th>Age-groups (years)</th>
<th>Total</th>
<th>P-value Chisquare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sufficient</td>
<td>18-30</td>
<td>31-40</td>
<td>41-50</td>
</tr>
<tr>
<td>Insufficient</td>
<td>20.6%</td>
<td>13.9%</td>
<td>25.1%</td>
</tr>
<tr>
<td>Deficient</td>
<td>23.2%</td>
<td>16.5%</td>
<td>23.7%</td>
</tr>
<tr>
<td>Total</td>
<td>26.6%</td>
<td>19.2%</td>
<td>23.9%</td>
</tr>
</tbody>
</table>

Discussion

VDD has been implicated as a risk factor for rickets, birth defects, osteoporosis, osteoarthritis, osteomalacia, chronic pain and muscle pain.17 Recent research has associated VDD deficiency as a contributing factor in diseases, such as heart disease, hypertension, neurological disorders, autoimmune disease, depression and cancer.18 The major cause of VDD is the lack of appreciation that sun exposure in moderation is the major source of vitamin D for most humans. Very few foods naturally contain vitamin D and foods that are fortified with vitamin D are often inadequate to
Vitamin D insufficiency affects almost 50% of the population worldwide and is becoming an important public health issue. Situation in Pakistan is even worse where published data is scarce and most data are based on relatively smaller sample size. In this study, we gathered data over the period of six years and a total of five thousand six hundred and ninety three (n=5693) adult patients of both genders were screened for serum Vitamin D-3 levels during this period. Our results showed that mean serum Vitamin D3 levels among males and females were in insufficient range and showed no significant difference (P>0.05). As per our operational definition 56.5% (n=3216) of patients were Vitamin d-3 deficient (<20 ng/ml), 18.2% (n=1037) showed insufficient levels (20-30 ng/ml) and 25.3% showed sufficient levels (>30 ng/ml). Significant difference was observed on gender stratification with female population showed higher percentage of deficient levels 79.7% versus 20.3% in males (P<0.05). Age based stratification also showed significant difference with age groups younger than 50 years showed higher percentage of deficient levels than in patients older than 50 years (P<0.05). Our results are comparable with one of the largest sample sized study conducted in Pakistan. Hassan S et al estimated the burden of VDD in people from different geographical areas of Pakistan. Out of the total, 40279 (66.1%) subjects were vitamin D-deficient. The minute apparent difference (66.1% vs 56.5%) may be explained by geographical difference. We published data exclusively of Rawalpindi/Islamabad region and they reviewed data of Karachi. In another large sample size study Riaz H et al published data of 4830 randomly selected citizens reported 53.5% had vitamin D deficiency and 31.2% had insufficient vitamin D, our results are quite similar. When we compare our results with a study conducted in the same geographic region by Khan H et al, they reported 56.2% subjects were vitamin D deficient. The results are quite similar with our study results. Earlier Khan AH et al, in 305 community-dwelling females reported, 90.5% of females had vitamin D deficiency. Dar FJ et al, reported vitamin D deficiency and insufficiency in 82.8 and 16.1 %, respectively in 174 healthy premenopausal females. Junaid K et al, reported among 215 participants at Lahore, 156 (73 %) were vitamin D deficient. Mansoor S et al, determined the prevalence and significance of vitamin D deficiency and insufficiency among apparently 123 healthy adults subjects reported 69.9% were deficient and 21.1% had insufficient levels of 25-OHD. Khan AH et al, reported results of 305 premenopausal females in a cross-sectional study in randomly selected communities of Karachi, Pakistan, 90.1% showed to be vitamin D deficient. Sheikh A et al, determined the prevalence of VDD and insufficiency in 300 asymptomatic adult population of Karachi, Pakistan and reported a total of 253 (84.3%) respondents had low levels (<30 ng/dL) of 25OH vitamin D. These high figures are likely due to sample size effect as sample size in these studies is much smaller. In other studies on patients with some known disease, Parveen S et al, determined the vitamin D insufficiency in sixty patients with B-chronic lymphoid leukemia. The frequency of vitamin D insufficiency was found to be 56.7%. Naqvi KZ et al, estimated the prevalence of Vitamin D deficiency in 360 pregnant women at term. Majority (69.6%) females were found to be deficient.

Vitamin D deficiency is also an important health problem in our neighboring country. It is surprising to see so much of VDD in a country with ample sunshine where one would assume it to be nonexistent. Increased pigmentation due to which more prolonged exposure to sun is required, use of sun block, purdah observation and possibly the reason that women in general do not go outside the home may be the likely reasons for VDD in Pakistani population. The two main sources of vitamin D are food and sunlight and generally natural food sources have low vitamin D content and therefore require fortification. Insufficient dietary supplies of vitamin D in Pakistan where food stuffs are not fortified, leads to generally low dietary intake of vitamin D and calcium. Inadequate dietary intake of calcium associated with high phytate/calcium ratio also reduces the bioavailability of calcium in the gut. This then induces increased parathyroid hormone (PTH) level and increases bone turnover and catabolism of 25OHD resulting in reduced serum levels. Multiple indicators inflating VDD have been widely reported such as food habits, sociocultural and religious taboos, restricted sun exposure, unavailability of fortified diets, age, season, gender, and lack of vitamin D supplementation, skin pigmentation and genetic factors. The question remains that are we not getting enough sun exposure or it is due to low dietary intake or are we breaking down this vitamin more rapidly. More detailed studies are required to unravel the cause of VDD in community settings. VDD is becoming a public health issue in Pakistan and enormous efforts need to be done by public health authorities to educate the general population about the prevention and
consequences of VDD. Strategies entailing mandatory food fortification, practical implementation of vitamin D supplementation program, developing awareness on health damaging effects and role of judicious sun exposure with global support to persuade the government, program managers of non-governmental organizations and consumers, need to be framed executed and followed.

Conclusion
1. There is a high prevalence of vitamin D deficiency in population of Rawalpindi and Islamabad regions.
2. Vitamin D deficiency is becoming a public health issue in Pakistan and strategies necessitating health education of masses, mandatory food fortification and vitamin D supplementation programs need to be formulated on national level.

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References

Authorship: 12 Conceived the study and sample collection 3 Data tabulation Wrote the manuscript 4 Consulted the references and formatted the article as per journal requirement