Vitamin D3 Deficiency and Body Mass Index in Females Living at a High Altitude Area

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Abstract

Objective: To assess the magnitude of vitamin D3 deficiency and the correlation between body mass index (BMI) and vitamin D3 serum level among females living in Abha, Southwestern of Saudi Arabia.

Patients and Methods: This study comprised two groups, who were recruited over the period from March to August, 2011. The study group included 78 females who were permanent inhabitants of Abha (A highland city), while the control group included 78 age- and body mass index-matched non-Saudi females who were residents of low-land areas. All participants in both groups were apparently healthy with no evidence of acute or chronic illness. Participants were divided into four groups according to their BMI. Serum Vitamin D3, parathormone, calcium, phosphorus and alkaline phosphatase were measured. Pregnant and lactating females and patients with diabetes mellitus, renal impairment or thyroid dysfunction were excluded. Serum vitamin D3 levels of <20ng/mL were considered as low.

Results: Serum vitamin D3 levels of all included females were low (8.57±4.35ng/mL). There was significant inverse relation between BMI grade and vitamin D3 serum level (p=0.019 in the study group and p=0.044 in the control group). Secondary hyperparathyroidism was evident in 86.6% of the studied group with strong correlation with serum levels of phosphate (p=0.01) and alkaline phosphatase (p=0.019).

Conclusions: In the high altitude area of Abha, where females are used to cover their whole skin, vitamin D3 deficiency was evident in all the studied group of females with significant association with BMI grade. Hypophosphatemia and elevated alkaline phosphatase levels in patients with vitamin D3 deficiency are highly associated and indicative for development of secondary hyperparathyroidism.

Key Words: Vitamin D3 — Body mass index — High altitude — Parathormone — Hypophosphatemia — Alkaline phosphatase.

Introduction

RECENT reports suggest that the amounts of vitamin D required for optimal health are probably much higher than previously reported. While severe vitamin D deficiency manifests as rickets and fractures in children and osteomalacia among adults, less severe deficiency has also been associated with long term injurious skeletal consequences, including secondary hyperparathyroidism, increased bone turnover, enhanced bone loss, and fracture risk [2,3].

Over the past decade, the importance of vitamin D in maintaining health and function of the immune, reproductive, muscular, skeletal, and integumentary systems of people of all ages and races has come to the forefront [4]. Evidence supports the strong association between vitamin D status and the risk of chronic diseases [5].

Currently, a pandemic of vitamin D deficiency/insufficiency has been reported [6-8] with significantly lower serum vitamin D3 in obese people than non-obese individuals [9]. Serum 25—hydroxyvitamin D (25OH) is the most sensitive index for the assessment of vitamin D status. Moreover, it is generally accepted that 25(OH)D3 concentrations of at least 20ng/mL are needed to prevent high parathyroid hormone (PTH) levels and maintain skeletal health [5,10-12].

Because vitamin D has many physiological functions beyond bone, experts have suggested that 25(OH)D concentrations higher than 30ng/mL should be maintained to ensure vitamin D adequacy to meet calcemic and noncalcemic requirements [5,13-15]. In addition, it was supported by several reports that serum 25(OH)D of 30ng/mL or greater is associated with better cardiometabolic and functional outcomes [14-17].

The major source of vitamin D is through its endogenous production in the skin as a result of
sunlight exposure [18]. So, lack of sun exposure is an important cause of vitamin D deficiency.

The aim of our study is to assess the magnitude of vitamin D3 deficiency and to study the relationship between vitamin D3 level and body mass index in females living in Abha, a high-altitude city in the south-western region of Saudi Arabia.

**Patients and Methods**

This study comprised two groups, who were recruited over the period from March to August, 2011. The study group included 78 females who were permanent inhabitants of Abha (A highland city). Age of subjects ranged from 18 to 50 years. The control group included 78 age- and body mass index- (BMI) matched non-Saudi females who were residents of low-land areas. All participants in both groups were apparently healthy with no evidence of acute or chronic illness.

**Exclusion criteria included:** Thyroid dysfunction, diabetes mellitus, pregnancy, lactation, renal impairment, malignancy, liver disease and immobility. Clinical examination was done.

Height and weight were measured by a stadiometer and a balance scale, respectively, and the BMI was calculated as weight in kilograms divided by square the height in meters (kg/m²). Then, participants were divided into four groups according to their BMI as follows: Group 1 (BMI: 18.5-24.9 kg/m²), Group 2 (BMI: 25-29.9 kg/m²), Group 3 (BMI: 30-34.9 kg/m²), and Group 4 (BMI >35 kg/m²).

For all subjects in the study group, serum vitamin D3, calcium, phosphorous, alkaline phosphatase and parathyroid hormone were measured. For participants in the control group, serum vitamin D3 levels were measured. All measurements were performed in the fasting state between 8-10 am.

Vitamin D3 was assayed by Cobas e 601 & Elecsys 2010 using liquid chromatography-tandem Mass Spectrometry [19]. A serum vitamin D3 level of 20ng/mL was considered as the cut-off value below which vitamin deficiency was diagnosed [10-12]. Intact parathyroid hormone (iPTH) assay was done by a two-site Sandwich immunoassay using direct chemiluminometric technology [20].

Descriptive statistics were applied to all study variables (i.e., frequency, percentage, mean and standard deviations). Tests of significance (i.e., t-test or χ²) were applied accordingly. The Pearson's correlation coefficient (r) between quantitative variables was calculated. A significant level was considered when p<0.05.

**Results**

All subjects in the study group were deficient in 25(OH)D3 (i.e., <20ng/mL), with a mean value of 8.75±4.35ng/mL. A significant negative association between vitamin D3 level and BMI was found (p=0.019 in the study group and p=0.044 in the control group), i.e., the higher the body mass index the lower the vitamin D3 serum level. Participants in the control group showed significantly higher vitamin D3 serum levels than the study group (Table 1 & Fig. 1).

The mean serum calcium was 9.25±0.51mg/dL with significant correlation with vitamin D3 (r=0.229; p=0.043). The mean serum PTH level was high (113.57±71.18pg/mL). Secondary hyperparathyroidism (i.e., >65pg/mL) was evident in 86.6% of subjects with no significant correlation between serum levels of PTH and 25(OH)D serum levels (r=-0.145; p=0.178), serum levels of PTH and serum calcium (r=0.035; p=0.759). However, PTH was significantly and directly correlated with serum alkaline phosphatase (r=0.266; p=0.019) but inversely with both serum vitamin D3 (r=-0.145, p=0.178) and serum phosphorus (r=-0.158;p=0.166). Secondary hyperparathyroidism was more prevalent among subjects with higher. However, this association was not statistically insignificant (p0.519), as shown in Tables (2-5).

**Table (1): Vitamin D3 serum levels (ng/mL) according to BMI group in the study and control groups.**

<table>
<thead>
<tr>
<th>BMI Groups</th>
<th>Study Group</th>
<th>Control Group</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean±SD</td>
<td>No.</td>
</tr>
<tr>
<td>Normal BMI (&lt;25 kg/m²)</td>
<td>16</td>
<td>11.19±5.40</td>
<td>17</td>
</tr>
<tr>
<td>Overweight (25-29.9 kg/m²)</td>
<td>23</td>
<td>8.82±3.53</td>
<td>25</td>
</tr>
<tr>
<td>Obesity Class 1 (30-29.9 kg/m²)</td>
<td>25</td>
<td>7.74±3.96</td>
<td>24</td>
</tr>
<tr>
<td>Obesity Class 11 (&gt;35 kg/m²)</td>
<td>14</td>
<td>6.63±3.76</td>
<td>12</td>
</tr>
<tr>
<td>p-values</td>
<td>0.019</td>
<td>0.044</td>
<td></td>
</tr>
</tbody>
</table>

**Table (2): Mean serum levels of biochemical markers.**

<table>
<thead>
<tr>
<th>Biochemical markers</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parathyroid hormone</td>
<td>113.57</td>
<td>71.18</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>96.75</td>
<td>48.84</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.49</td>
<td>0.60</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.25</td>
<td>0.51</td>
</tr>
<tr>
<td>Vitamin D3 (ng/mL)</td>
<td>8.57</td>
<td>4.35</td>
</tr>
</tbody>
</table>
Table (3): Correlation matrix between studied biochemical markers in the study group.

<table>
<thead>
<tr>
<th>Biochemical Markers</th>
<th>Vitamin D3</th>
<th>Calcium</th>
<th>Phosphates</th>
<th>Parathormone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$p$</td>
<td>$r$</td>
<td>$p$</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>0.229</td>
<td>0.043</td>
<td>0.083</td>
<td>0.470</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.083</td>
<td>0.470</td>
<td>0.049</td>
<td>0.672</td>
</tr>
<tr>
<td>Phosphates</td>
<td>-0.145</td>
<td>0.178</td>
<td>0.035</td>
<td>0.759</td>
</tr>
<tr>
<td>Parathormone</td>
<td>0.115</td>
<td>0.318</td>
<td>0.027</td>
<td>0.811</td>
</tr>
</tbody>
</table>

Table (4): Frequency and percentage of BMI groups according to PTH serum levels in the study group.

<table>
<thead>
<tr>
<th>Parathormone Serum Levels</th>
<th>BMI Groups</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>High*</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Normal</td>
<td>4</td>
<td>25.0</td>
</tr>
<tr>
<td>Overweight</td>
<td>4</td>
<td>17.4</td>
</tr>
<tr>
<td>Obesity Class 1</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>Obesity Class 11</td>
<td>2</td>
<td>14.3</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>15.4</td>
</tr>
</tbody>
</table>

p=0.519 * >65 pg/mL.

Table (5): Mean values of different variables according to PTH serum levels in the study group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>PTH level Mean±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>30.03±7.72</td>
<td>0.205</td>
</tr>
<tr>
<td>High*</td>
<td>33.14±7.77</td>
<td></td>
</tr>
<tr>
<td>Vitamin D3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>9.20±5.00</td>
<td>0.589</td>
</tr>
<tr>
<td>High*</td>
<td>8.45±4.25</td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>109.00±58.62</td>
<td>0.348</td>
</tr>
<tr>
<td>High*</td>
<td>95.52±47.03</td>
<td></td>
</tr>
<tr>
<td>Phosphates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3.90±0.64</td>
<td>0.010</td>
</tr>
<tr>
<td>High*</td>
<td>3.42±0.56</td>
<td></td>
</tr>
</tbody>
</table>

* >65 pg/mL.

Discussion

The prevalence of serum 25(OH)D deficiency reportedly varied between 30% and 93% in different studies [21-28]. Typically, the prevalence of low 25(OH)D serum levels has been reported in approximately 36%, otherwise healthy, young adults, aged 18-29 years [24]; 42% in black women aged 15-49 years [25]; 41% in outpatients aged 49-83 years [9]; while up to 57% in general medicine inpatients in the US [29].

The picture is much worse in Europe, where 28-100% of healthy adults and 70% of all hospitalized adults have such 25(OH)D values [26-28]. Despite the significant role of sunlight in vitamin D synthesis, the studies carried out in the last two decades have shown a high prevalence of 25(OH)D deficiency in tropical countries, such as China, India, Iran, and Saudi Arabia [30-34].

In our study the prevalence of vitamin D3 deficiency (i.e., <20ng/mL) was 100% with mean values of 25(OH)D of 8.57±4.35ng/ml. Several hypotheses may explain the 25(OH)D deficiency among Asians mainly related to altered metabolism and decreased intake. Awumey et al. [35] showed a higher activity level of 24-hydroxylase in skin fibroblasts of South Asians. Therefore, increased 25(OH)D catabolism may cause 25(OH)D deficiency in Asians. Moreover, our study was conducted on a specific population of females, those who are living in Abha, which is a high-altitude city, where all women are completely veiled and mostly kept indoors. Consequently, this type of population is characterized by having significantly higher fat mass and fat mass index when compared with lowland inhabiting women with the same body mass index [36].

Although 25(OH)D3 production is more at higher than lower altitude habitats [37], populations such as our study group whose costume dictate that the whole body is completely covered definitely lose this beneficial effect [38]. Having high body fat and the tradition of whole body covering add to the explanation of the universal vitamin D3
deficiency in this area. This may also be explained by their lower consumption of vitamin D-containing foods, such as fortified cereals and oily fish [3].

This study also revealed statistically significant association between vitamin D3 level and body mass index (p=0.019). Serum vitamin D3 levels were inversely proportionate to BMI. This finding is in agreement with those reported in several studies in this field [39,40].

Multiple mechanisms have been proposed to explain the association of obesity with hypovitaminosis D, including lack of sunlight exposure due to physical inactivity [24] and sequestration of vitamin D in subcutaneous fat depots [41].

Wortsman et al., reported that the capacity of the skin to produce vitamin D is not altered in obesity. However, the increase in serum vitamin D after sun exposure was 57% less in obese compared with non-obese subjects suggesting a decreased bioavailability of vitamin D because of its deposition in body fat compartments, given that vitamin D is fat soluble [42].

The Heart Framingham Study revealed that the relation of 25(OH)D3 with adiposity was present even among healthy, lean individuals who might otherwise not be considered at risk for vitamin D deficiency. Lower serum 25(OH)D3 was associated with greater regional adiposity, a finding that was not attributable to differences in physical activity or vitamin D intake. The association between 25(OH)D3 and adiposity was stronger for visceral than subcutaneous abdominal adiposity, and significant across the spectrum of body size. This may indicate that specific patterns of adiposity promote vitamin D deficiency, that depletion of vitamin D stores contributes to specific patterns of adiposity, or that both are the product of another primary process [43]. Vitamin D3 level was also found to be inversely correlated with body fat index in women with normal body mass index or only over weight [44].

In our study, there was a secondary hyperparathyroidism in 86.6% of participants, although its level was not significantly correlated with vitamin D3 level, with a tendency to be more prevalent in subgroups with higher BMI.

Several studies showed that parathyroid hormone is a sensitive indicator for vitamin D deficiency [45,46], while others revealed secondary hyperparathyroidism to be more common in obese than lean persons with vitamin D deficiency [47,48]. Absence of statistical significance in our research may be due to the small sample size and the fact that blood extraction for biochemical analysis was done in one occasion only.

This study showed that mean serum calcium level was within the normal range (9.25±0.51mg/dL), which is accepted especially when compensatory secondary hyperparathyroidism is present as evidenced in a high percentage in our study group. A high serum level of parathyroid hormone normalizes serum calcium level by several mechanisms including mobilization of calcium from bone leading to osteomalacia [3,49,50].

Serum calcium was significantly and directly correlated with vitamin D3 level, while alkaline phosphatase was significantly and directly proportionate with PTH level, without any significant correlations with any of the other variables. Analysis of biochemical data in females who had secondary hyperparathyroidism in comparison with those who did not have hyperparathyroidism showed no significant difference except for mean serum phosphate level which was significantly lower in hyperparathyroid group (p<0.01) than that group with normal PTH. The association hypophosphatemia with hyperparathyroidism was also found in other studies [51]. High PTH level has phosphaturic effects that can explain hypo-phosphatemia while the presence of vitamin D3 deficiency with high PTH level has its effect on bone metabolism interpreted in the form of elevation of alkaline phosphatase level [52,53].

Our finding indicates that presence of hypophosphatemia and elevated alkaline phosphatase level in persons with vitamin D3 deficiency are reliable clues to the development of secondary hyperparathyroidism.

In conclusion, there are several factors which determine the state of vitamin D3 level toward which due consideration should be paid. At the high altitude area of the City of Abha, the prevalence of vitamin D3 deficiency is quite very high. The customs and traditions of whole body covering and being home-bound with limited chance for sun exposure, and the specific characteristics of females living in this area regarding high body fat content and body fat index (as evidenced in other studies) may have a considerable role in such very high prevalence of vitamin D deficiency. Vitamin D3 level incurs significant inverse association with BMI. Serum calcium is directly proportionate to vitamin D3 level although it may be within normal range even with severe deficiency due to compensatory hyperparathyroidism. Parathyroid hormone
is a sensitive marker for vitamin D3 deficiency. The presence of hypophosphatemia with elevated alkaline phosphatase may indicate the development of secondary hyperparathyroidism in persons with vitamin D3 deficiency.

So, inhabitants of Abha should be continuously informed about the importance of sun exposure, and types of foods rich in vitamin D3. Paying attention to the symptomatology of hypovitaminosis D and screening of vitamin D even in apparently healthy individuals is highly recommended in this population.

References


