Prevalence of Vitamin D Deficiency and Insufficiency in Kosovo Population

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Abstract

BACKGROUND: Vitamin D deficiency is a global health problem, but it is not known about its status in the Kosovo population.

AIM: The purpose of this study is to determine the status of Vitamin D deficiency and insufficiency in our population.

MATERIALS AND METHODS: Data collection was done from January 2020 to July 2021, during which period blood samples were collected. The sampling was done for 769 selected subjects and statistical data (frequency, mean values, and standard deviation) have been analyzed for 25-hydroxyvitamin D [25(OH)D] concentration. They were categorized by age group, gender, and level of 25(OH)D. The prevalence and percentage of Vitamin D deficiency and insufficiency in the study population were evaluated.

RESULTS: The mean concentration of 25(OH)D in the serum of the study group was 18.3 ng/ml. The mean value was significantly lower for females when compared for that of males (17.89 and 19.58 ng/ml, respectively), with p < 0.0035, but there was no significant difference between age groups. The level of 25(OH)D less than 20 ng/ml was observed in 62% of the cases in our study population with a slight difference between female (63.6%) and male (57.2%) group. The age group of >60 had 25(OH)D deficiency in 62% of cases when compared to other age group respectively, and 40.1% of males had Vitamin D insufficiency.

CONCLUSION: The mean values of 25(OH)D in the study population are relatively low, which corresponds to significant Vitamin D deficiency and insufficiency in all age groups, and which may also have serious implications for their overall health.

Introduction

Vitamin D and its metabolites are well known for their role in calcium homeostasis and bone mineralization process. In the past, it was believed that a significant proportion of the problems caused by Vitamin D deficiency were rickets in children and osteomalacia and osteoporosis in adults [1], [2], [3]. Now, the role of Vitamin D is known better and it has been described that its deficiency is not only associated with skeletal diseases but also with cardiovascular disease [4], [5], cancer [6], [7], [8], and infection [9], [10].

Vitamin D deficiency is also associated with autoimmune diseases including type 1 diabetes, insulin resistance and beta-cell dysfunction, rheumatoid arthritis, and multiple sclerosis [11], [12], [13]. As well, data suggest that the antimicrobial response is dependent on Vitamin D [14]. Another prospective study has documented an increase in mood after Vitamin D intake and a reduced risk of cancer [15]. Thus, Vitamin D administration has helped and reduced the incidence of these diseases as well as the mortality rate [16], [17], [18].

Regular administration of Vitamin D is recommended as daily intake is good for bone health. Vitamin D administration in amounts of 200IU/day is recommended from birth to age 50, then 400 UI/day for ages 51–70 and over 71 years 600 UI/day [19].

Taking into consideration, the above-mentioned data on the importance of Vitamin D and its deficiency, we came up with an idea of our study to observe to what extent we have Vitamin D levels in our population.

The purpose of this study is to determine the status of Vitamin D deficiency and insufficiency in our population.

Materials and Methods

We collected our data from January 2020 until July 2021, from the patients who presented at the Clinic of Medical Biochemistry at the University Clinical Center of Kosovo and Akumed Laboratory. Our study population includes 769 subject aged between 1 and
89 years, where the concentration level of 25(OH)D was measured.

The subjects were divided by gender and categorized in four age groups, as follows: Age group 1–19 years, 20–39 years, 40–59 years, and age group >60 years.

To determine Vitamin D levels, we have used the electrochemiluminescence method in the Roche Diagnostic Elecsys 2010 system. This assay is for the quantification of 25-hydroxyvitamin D in human serum and plasma, and is used as an auxiliary method in assessing Vitamin D sufficiency, deficiency, and insufficiency. Blood sampling was performed in the morning. Blood was taken with a closed system on Sarstedt monovette and then, serum was separated. Serum Vitamin D is stable for 8 h at 18–25°C, 4 days at 2–8°C, and 24 weeks at −20°C. The working method of this test is based on three incubations (I: Incubation of 15 µL of serum sample and pre-treatment reagent 1 and 2; II: Incubation of samples pre-treated with ruthenium Vitamin D-binding protein; and III: Incubation with streptavidin and biotin) and aspiration of mixed reaction, removal of substances unrelated to ProCell/ProCell M. After this, voltage is applied to electrodes which involves chemiluminescence emission and is measured by photomultiplier. In the end of this procedure, we obtain the result.

For statistical processing of our data, we have used InStat3 and we have done ANOVA for data comparison.

Initially, we calculated the percentage of cases that were below the reference values of vitamin 25(OH) D as per sex and age group. Then, it was calculated the overall prevalence of Vitamin D deficiency and insufficiency, as well we calculated the prevalence according to gender and age group.

The mean values of Vitamin D [25(OH)D] levels were calculated for all mentioned groups and then were compared by sex and age group.

Results

We have classified patients based on serum 25(OH)D cutoff values as follows: Normal serum levels of Vitamin D-25(OH)D of our study subjects are considered to be 30–70 ng/ml. Serum Vitamin D-25(OH) D values of 20–30 ng/ml are considered as Vitamin D insufficiency. Serum Vitamin D-25(OH)D values below 20 ng/ml are considered as Vitamin D deficiency.

The mean age of the study group is 46.55 years with a significant difference between the mean age of females and males (47.41 and 43.88 years, respectively). The two-tailed p = 0.0208 is considered statistically significant.

The mean value of 25(OH)D vitamin is 18.30 ng/ml with a statistically significant difference (p < 0.0352) between the mean 25(OH)D values of females (17.89 ng/ml) and males (19.58 ng/ml) (Table 1).

However, when the age group comparison took place, we found no statistically significant difference in mean values of 25(OH)D vitamin, although there was a gradual decrease in 25(OH)D vitamin level. Thus, the age group of 1–19 years had the mean values of 25(OH)D=20.56 ng/ml, the age group of 20–39 years had 25(OH)D=18.82 ng/ml, age group of 40–59 years had 25(OH)D=17.95 ng/ml, and the age group of older than 60 years had the average value of 25(OH) D=17.66 ng/ml.

The values of vitamin 25(OH)D compared to referent levels are shown in Figure 1. It was found that 88.3% of our study subjects had Vitamin D levels below normal values. There was difference in percentages between males and females having 25(OH)D values below the normal level (89.0%, respectively, and 86.1%). The same Figure 2 shows 25(OH)D values for the age groups compared to the referent level. From this, we can reckon that the prevalence of insufficiency and deficiency for the age groups of 1–19 years and >60 years is really high at 87.9%.

Except reference levels, we have analyzed Vitamin D insufficiency and deficiency in our population group with 25(OH)D values below 20 ng/ml considered as deficient and values of 25(OH)D between 20 and 30 ng/ml considered as insufficient.

About 62.7% of the subjects are Vitamin D deficient, while Vitamin D insufficient is 25.6% of our subjects. It is evident that Vitamin D deficiency is mostly found in the age group of 40–59 years (65.9%), concurrently, the least deficient is the age group of 1–19 years presenting with only 6.1%. The high prevalence of Vitamin D insufficiency was found in the age group of 1–19 years in 30.3% of cases and in the age group of 20–39 years in 28.3% of cases.

There was a gender difference between
subjects below the reference level of vitamin 25(OH)D values in all age groups with the age group of 1–19 years (females 92.7% and males 7.3%) being the most prominent difference. About 64.3% of women and 57.8% of men are deficient in Vitamin D. According to gender and age group, we have found that the highest prevalence of Vitamin D deficiency among women and men is in the age group of 40–59 years old, with 66.4% of females in this age group being Vitamin D deficient and 63.5% of males in this group being deficient. The least deficient age groups were 1–19 years and 20–39 years, but in the same age groups, we observed the biggest difference between genders. The cross-tabulation below represents our findings graphically.

Figure 2: Gender and age group in relation to Vitamin D levels

Vitamin D insufficiency was more common in males than in females when all age groups were compared. About 28.3% of males were Vitamin D insufficient, concurrently, 24.7% of females were Vitamin D insufficient. While in every age group, the insufficiency was more prominent in males, it was only in the age group of 1–19 years where the female percentage of vitamin D insufficiency was higher.

Table 2 shows the cross-tabulation for number of subjects in each of our study category, gender, and age group as layered for Vitamin D levels.

Table 1: Statistical parameters for Vitamin D values as per gender

<table>
<thead>
<tr>
<th>No.</th>
<th>Statistical parameters</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No of Patients</td>
<td>769</td>
<td>582</td>
<td>187</td>
</tr>
<tr>
<td>2</td>
<td>Mean</td>
<td>18.30</td>
<td>17.89</td>
<td>19.58</td>
</tr>
<tr>
<td>3</td>
<td>Std. deviation</td>
<td>9.56</td>
<td>9.58</td>
<td>9.40</td>
</tr>
<tr>
<td>4</td>
<td>Lower 95% CI</td>
<td>17.63</td>
<td>17.11</td>
<td>18.23</td>
</tr>
<tr>
<td>5</td>
<td>Upper 95% CI</td>
<td>18.98</td>
<td>18.67</td>
<td>20.93</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>p&lt;0.0352</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Referent value of Vitamin D 30–70 ng/ml

The two-tailed p = 0.0352 is considered statistically significant.

It has been calculated that normal Vitamin D values are when we have the concentration of 25(OH)D ≥75 nmol/L (>30 ng/ml) [22]. Concentration levels 50–75 nmol/L (20–30 ng/ml) are considered as Vitamin D insufficiency. 25(OH)D values <50 nmol/L (<20 ng/L) are considered as Vitamin D deficiency and these levels have negative bone repercussions. 25(OH)D values <30 nmol/L (<12 ng/ml) are assessed as severe Vitamin D deficiency, whereas 25(OH)D values <20 nmol/L (<8 ng/ml) cause serious disorder of bone metabolism (rickets or osteomalacia) and myopathy. We have done our classification of Vitamin D normal values as well as insufficiency and deficiency based on the above-mentioned data and the data of other authors [23], [24], [25], [26], [27].

Table 2: Cross-tabulation for gender, age groups, and Vitamin D Levels

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age Group</th>
<th>Count</th>
<th>Deficient</th>
<th>Insufficient</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>1–19</td>
<td>20</td>
<td>18</td>
<td>13</td>
<td>41</td>
<td>78</td>
</tr>
<tr>
<td>F</td>
<td>20–39</td>
<td>25</td>
<td>55</td>
<td>55</td>
<td>135</td>
<td>215</td>
</tr>
<tr>
<td>F</td>
<td>40–59</td>
<td>47</td>
<td>113</td>
<td>81</td>
<td>241</td>
<td>341</td>
</tr>
<tr>
<td>F</td>
<td>&gt;60</td>
<td>46</td>
<td>59</td>
<td>60</td>
<td>165</td>
<td>261</td>
</tr>
<tr>
<td>F</td>
<td>Total</td>
<td>123</td>
<td>247</td>
<td>212</td>
<td>582</td>
<td>769</td>
</tr>
<tr>
<td>F</td>
<td>1–19</td>
<td>2</td>
<td>12</td>
<td>12</td>
<td>25</td>
<td>46</td>
</tr>
<tr>
<td>F</td>
<td>20–39</td>
<td>11</td>
<td>17</td>
<td>24</td>
<td>52</td>
<td>82</td>
</tr>
<tr>
<td>F</td>
<td>40–59</td>
<td>4</td>
<td>28</td>
<td>20</td>
<td>52</td>
<td>78</td>
</tr>
<tr>
<td>F</td>
<td>&gt;60</td>
<td>15</td>
<td>19</td>
<td>24</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td>F</td>
<td>Total</td>
<td>32</td>
<td>75</td>
<td>80</td>
<td>187</td>
<td>293</td>
</tr>
<tr>
<td>M</td>
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<td>7</td>
<td>31</td>
<td>28</td>
<td>66</td>
<td>100</td>
</tr>
<tr>
<td>M</td>
<td>20–39</td>
<td>36</td>
<td>72</td>
<td>79</td>
<td>187</td>
<td>393</td>
</tr>
<tr>
<td>M</td>
<td>40–59</td>
<td>51</td>
<td>141</td>
<td>101</td>
<td>293</td>
<td>445</td>
</tr>
<tr>
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<td>&gt;60</td>
<td>61</td>
<td>78</td>
<td>84</td>
<td>223</td>
<td>363</td>
</tr>
<tr>
<td>M</td>
<td>Total</td>
<td>155</td>
<td>322</td>
<td>292</td>
<td>769</td>
<td>1146</td>
</tr>
</tbody>
</table>

Vitamin D insufficiency and deficiency are associated with suboptimal health. The prevalence of Vitamin D insufficiency and deficiency maybe in a rise and population-based trends are uncertain. We have tried to evaluate the prevalence of Vitamin D insufficiency and deficiency in Kosovo population, having in mind that the prevalence data of Vitamin D in our population and the subgroups are limited.

It has been documented that there is a high worldwide prevalence of Vitamin D deficiency that may require public health actions [28].

Discussion

Vitamin D deficiency is diagnosed by measuring the concentration of calcidiol (25-hydroxyvitamin D) in the blood, which is a precursor to the active form of 1,25-dihydroxyvitamin D (calcitriol). According to a systematic review, the following categories were set for hypovitaminosis D: Normal values 75–250 nmol/L (30–100 ng/mL) and insufficiency values 25–74 nmol/L (10–29.6 ng/mL) [20]. 1.0 nmol/L equals 0.4 ng/mL according to “Dietary Supplement Fact Sheet: Vitamin D” [21].

Data on Vitamin D prevalence are important for the development of public health policies and reduce the risk for potential health consequences of an inadequate Vitamin D status [29].

Our study included 769 cases or 0.03% of the Kosovo population (approx. 1.7 million inhabitants). We calculated the mean value of 25(OH)D and evaluated Vitamin D deficiency and insufficiency in our population, similar to the study of 32,252 persons or 0.01% of the American population (221 million inhabitants) [30], as well similar to the 0.019% of Canadian population [31].

The aim of our research was to measure the rate of Vitamin D insufficiency and deficiency in the Kosovo population and to assess the differences by age and sex. This study also had limitations because it failed to analyze other Vitamin D-related phenomena that were associated with the season, sunlight exposure, and diet.

The mean value of 25(OH)D was 18.3 ng/ml, with minimum and maximum values between 3.0 and 68.0 ng/ml in our research subjects. In 195 studies conducted in 44 countries involving more than 168,000 participants, mean values of 25(OH)D differed significantly across studies (ranging from 4.9 nmol/l to 136.2 nmol/l), where 37.3% of studies reported average Vitamin D values below 50 nmol/l or 20 ng/mL [29].

A study which took place in the United States was done at two different time periods (including 18.883 and 13.369 participants, respectively), with the aim to determine the mean values for all those included. The mean value of 25(OH)D was 30 ng/ml, respectively, and 24 ng/ml in the two period times (1994–1998 and 2001–2004). The same study found gender differences in mean values of 25(OH)D for females at 28 ng/mL and for males at 32 ng/mL [30]. We have reported similar results in our study as well.

Studies in the Canadian population report for mean values of 25(OH)D concentrations at 67.7 nmol/L (27.08 ng/mL) [31]. In our study population, the mean values of 25(OH)D concentrations were 18.3 ng/mL.

Vitamin D status in Europe varies by gender, season, and skin pigmentation. As observed in various studies, serum 25(OH)D level is higher in North Europe than in South Europe and higher in West Europe than in East Europe [32], [33].

Multicenter studies report high levels of 25(OH)D in North Europe 25 years ago [34]. High levels of 25(OH)D in Norway and Sweden are probably due to high consumption of fatty fish. Low levels of Vitamin D in Spain, Italy, and Greece could be due to increased pigmentation of the skin and avoidance of sunlight penetration [35].

Low levels of 25(OH)D are found in various regions of Asia, for example, in Asian part of Russia [36], in Mongolia [37], in China, and in India, meanwhile, Vitamin D status was better in Malaysia and Japan [38], [39].

Vitamin D deficiency is more common in vulnerable groups, especially in pregnant women and their newborns [40], [41], [42]. Higher risk of low levels of Vitamin D was observed in dark-skinned women and their newborns, as well lower levels were observed in obese and adolescent children [43], [44].

Low levels of Vitamin D in children and adolescents may be due to reduced intake of Vitamin D3 (e.g., minor bowel disorders), reduced synthesis, or increased degradation of 25(OH)D or 1.25 (OH) 2D (e.g., chronic liver or kidney disease) [45].

The elders have lower levels of Vitamin D synthesis in the skin, especially those living in a nursing home who are rarely exposed to the sun [46].

It is pointed out that Vitamin D deficiency has a high prevalence rate worldwide, and not only in the risk groups such as young children, pregnant women, the elderly, and immigrants but also in other groups who are not exposed to the sun, have pronounced skin pigmentation, those who use sun protect lotions, or use cloths that cover the whole body, and poor diets with fish and dairy products [35].

We found that the prevalence of Vitamin D deficiency in our study was 89.4% for the age group of 40–59 years. Studies conducted in other countries show lower prevalence of 25(OH)D for similar group (43.3%) [47]. The mean value of 25(OH)D in the 1–19 age group was 20.56 ng/ml. Similar data are reported by other authors [47] who reported mean values of 25(OH)D vitamin at 25.82 ng/ml. The mean value of 25(OH)D in subjects older age groups is steadily declining. The age group of 20–39 years recorded mean values of Vitamin D at 18.82 ng/ml, age group of 40–59 years recorded values at 17.95 ng/ml, and the eldest age group over 60 years recorded values of 25(OH)D at 17.66 ng/ml.

**Conclusion**

The mean values of 25(OH)D in our study group are low which correspond to Vitamin D deficiency and insufficiency in all age groups. Our findings suggest that there is a need for public health intervention and health promotion to prevent further decline of Vitamin D values which may have serious implications for population overall health. There is a need for continuous and seasonal Vitamin D levels measurement in our population as well-conducting studies which would find association between Vitamin D deficiency and related health problems.

**References**

1. Hasegawa Y, Miyai K, Takeda R. Updates on rickets and osteomalacia: Pathogenesis and pathophysiology of rickets.
PMid:19307527

PMid:20426226

PMid:20332246

PMid:20204667

PMid:7616799

PMid:21872807

PMid:16328605

PMid:15252862

PMid:15331337

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