Abstract

Background. The recent studies have demonstrated that hypovitaminosis D is extremely common in various regions around the world. The territory of Ukraine occupies several latitudes, thus cholecalciferol synthesis turns out to be somewhat different when comparing one region to another.

Objectives: to determine the frequency of vitamin D deficiency and insufficiency in a representative sample of the population of Ukraine across age groups, geographical localization, and seasons; and to assess the iPTH levels against the vitamin D deficiency.

Methods. 1575 people aged 20–95 yrs. residing in various regions of Ukraine were examined. 25(OH)D and iPTH levels were evaluated using electrochemiluminescence method (Elecsys 2010, Roche). Vitamin D deficiency was defined as 25(OH)D below 50 nmol/L, and vitamin D insufficiency as a 25(OH)D of 50–75 nmol/L.

Results. Vitamin D deficiency was registered in 81.8% persons, 13.6% of examined had vitamin D insufficiency. There was a determined negative correlation between iPTH and 25(OH)D (r = −0.16, p < 0.0001). Secondary hyperparathyroidism was diagnosed in 11.9% patients. The mean level of 25(OH)D was proved to be significantly higher in the south of the country (p < 0.001), especially during summer (p < 0.05).

Conclusions. High level of vitamin D deficiency (81.8%) and secondary hyperparathyroidism (11.9%) make doctors search for the effective treatment and prevention methods of revealed disorders.

Key words: vitamin D deficiency/insufficiency, age differences, seasonality, secondary hyperparathyroidism

Introduction

The problem of osteoporosis and vitamin D deficiency (VDD) does not lose its relevance worldwide. The frequency of VDD differs in different countries [1–6]. In particular, from 2 to 30% of the adult population of Europe have a level 25(OH)D in serum below 25 nmol/l, but this figure could increase to 75% and higher in the elderly and in patients of hospices and nursing homes [7].

According to the estimates made in the USA, Canada and Europe, 20–100% of non-institutionalized elderly women and men have a vitamin D deficiency. The risk of VDD and insufficiency is equally high for children as well as for young and middle age adults [8–10].

An epidemiological randomized study, which involved 367 residents of Estonia aged 25–70 years, showed a high frequency of VDD and seasonal fluc-
tuations in 25(OH)D. Thus, in winter VDD (25(OH)D below 50 nmol/l) was registered in 73% of patients and severe deficit in 8%, while in summer these figures were 29% and 1%, respectively [11].

In Hungary, independent epidemiological observations have not been conducted. However, the city Monor was included into SENECA epidemiological study. The concentration of 25(OH)D was studied during 1988–1989 years. The study has revealed that the VDD (25(OH)D below 30 nmol/l) was registered in 33% of men and 52% of women [7].

As for nowadays, there are no completed epidemiological studies on the prevalence of VDD in Eastern Europe. Conducted cross-sectional epidemiological study among postmenopausal women aged 45–83 years in Moscow revealed VDD in 47.3% of patients, and severe deficiency (25(OH)D below 25 nmol/l) in 17.6% of cases [12, 13]. In their research, Professor A. M. Lyesnyak, et al. investigated the level of 25(OH)D in 97 elderly citizens of Yekaterinburg. They have found that the average level of 25(OH)D was 28.1 nmol/l, the incidence of secondary hyperparathyroidism was 47% [14].

In the population of western regions of Belarus the average level 25(OH)D is 44.2 nmol/l. In people with diseases of the cardiovascular system it ranges from 20.4 to 29.9 nmol/l [15].

In Ukraine the VDD study is of great importance. Lack of systematic epidemiological observations for deficiency and insufficiency of vitamin D in the population of Ukraine necessitated the further research. The territory of Ukraine occupies several latitudes, thus cholecalciferol synthesis turns out to be somewhat different when comparing one region to another. The northern extremity of Ukraine lies close to the village of Gremyach in Chernihiv region (52°22’ N). The southern extremity is at the Sarych cape in the Crimea (44°23’ N). The distance between these two extremities is 893 km (and 1316 km from the western to eastern extremity of Ukraine).

The aim of the study was to determine the frequency of vitamin D-deficiency and insufficiency in a representative sample of the population of Ukraine across geographical localization, age groups, and seasons; and to assess the iPTH levels against the vitamin D deficiency.

Because of the territorial considerations and taking into account the fundamental principles of epidemiology studies, subjects from various regions of Ukraine were involved. In order to assess the influence of age and seasonal factors on 25(OH)D level, the sampling was done throughout the year in various age groups.

**Subjects and methods**

Serum samples were obtained from 1575 subjects aged from 20 to 95 years old. Because of the territorial considerations and taking into account the fundamental principles of epidemiology studies, subjects from various regions of Ukraine were involved. In order to assess the influence of seasonal factors on 25(OH)D level, the sampling was done throughout the year. The vast majority of those subjects were women (86.3%), with the mean age of 58.61 ± 0.37 years; mean age for men was 54.93 ± 1.09 years. Subjects’ distribution according to their age and place of residence is presented in Tables 1 and 2.

**Table 1. Subjects’ distribution according to their age**

<table>
<thead>
<tr>
<th>Age groups, years</th>
<th>Number of subjects</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–34</td>
<td>117</td>
<td>7.4</td>
</tr>
<tr>
<td>35–44</td>
<td>140</td>
<td>8.9</td>
</tr>
<tr>
<td>45–59</td>
<td>521</td>
<td>33.1</td>
</tr>
<tr>
<td>60–74</td>
<td>670</td>
<td>42.5</td>
</tr>
<tr>
<td>75–95</td>
<td>127</td>
<td>8.1</td>
</tr>
</tbody>
</table>

**Table 2. Subjects’ distribution according to the region of residence**

<table>
<thead>
<tr>
<th>Region of Ukraine</th>
<th>Number of subjects</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>West</td>
<td>209</td>
<td>13.3</td>
</tr>
<tr>
<td>East</td>
<td>227</td>
<td>14.4</td>
</tr>
<tr>
<td>North</td>
<td>842</td>
<td>53.5</td>
</tr>
<tr>
<td>South</td>
<td>50</td>
<td>3.2</td>
</tr>
<tr>
<td>Center</td>
<td>247</td>
<td>15.6</td>
</tr>
</tbody>
</table>

All subjects had been assessed for the level of 25(OH)D and intact parathyroid hormone (iPTH) in blood serum. Patients receiving calcium and/or vitamin D supplements within 6 months prior to the study entry were excluded from the study.

25(OH)D and iPTH levels were evaluated by electrochemiluminescent method (Elecsys 2010 analytical system (Roche Diagnostics, Germany)) and test-systems cobas. This is considered to be the most highly-sensitive method which allows for very precise evaluation within a wide range of possible research samples.

Subsequent assessment of vitamin D status was performed according to the latest classification [10], where vitamin D deficiency is defined as a 25(OH)D
50 nmol/L, and vitamin D insufficiency as a 25OHD of 50.0–75.0 nmol/L.

Statistical analysis of the research data was done using the software package of STATISTICA 6.0. Data presentation corresponded to the character of their distribution: in normal distribution (Lilliefors test) the data were expressed as mean values ± standard deviation (M ± SD), in others variants – as median (Me) and interquartile range [LQ–UQ]. In the normal distribution to test our hypothesis about the equality of two groups’ averages we used a Student t-test (t). In case of non-normal distribution, comparison of two independent groups of the variables was done with the help of Mann-Whitney U test. The null hypothesis was rejected at p < 0.05 for each of the tests employed.

Results

Only 4.6% of the Ukrainian citizens were found to have normal 25(OH)D values, whereas 13.6% were diagnosed with a vitamin D insufficiency, and 81.8% with vitamin D deficiency. It must be noted that a severe VDD ((25(OH)D level is below 25 nmol/l) was registered in 37.3% of the subjects (Fig. 1). Finally, as many as 12.2% of the study subjects have had 25(OH)D levels below the lower sensitivity threshold of the analytical system (Fig. 2).

![Fig. 1. Frequency of vitamin D deficiency and insufficiency among Ukrainian population](image)

![Fig. 2. Distribution of vitamin D levels among 1575 examined subjects](image)

Table 3. Comparison of vitamin D status according to the age groups

<table>
<thead>
<tr>
<th>Age groups / vitamin D status</th>
<th>Persons 20–34 yrs (n = 117)</th>
<th>Persons 35–44 yrs (n = 140)</th>
<th>Persons 45–59 yrs (n = 521)</th>
<th>Persons 60–74 yrs (n = 670)</th>
<th>Persons &gt; 75 yrs (n = 127)</th>
<th>Total group (n = 1575)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of vitamin D insufficiency</td>
<td>20 (17.1%)</td>
<td>19 (13.6%)</td>
<td>78 (15.0%)</td>
<td>83 (12.4%)</td>
<td>14 (11.0%)</td>
<td>214 (13.6%)</td>
</tr>
<tr>
<td>Prevalence of vitamin D deficiency</td>
<td>84 (71.8%)</td>
<td>117 (83.6%)</td>
<td>420 (80.6%)</td>
<td>561 (83.7%)</td>
<td>107 (84.3%)</td>
<td>1289 (81.8%)</td>
</tr>
<tr>
<td>Prevalence of severe vitamin D deficiency (&lt;25 nmol/L)</td>
<td>35 (29.9%)</td>
<td>67 (47.9%)</td>
<td>194 (37.2%)</td>
<td>237 (35.4%)</td>
<td>51 (40.2%)</td>
<td>584 (37.1%)</td>
</tr>
</tbody>
</table>

* Difference in 25(OH)D level when compared with the age group of 20–34 yrs. (p < 0.05);
* Difference in 25(OH)D level when compared with the age group of 35–44 yrs. (p < 0.05);
* Difference in 25(OH)D level when compared with the age group of 20–34 yrs. and the group of 20–34 yrs (p < 0.01).
iPTH was found to have a weakly positive correlation with age ($r = 0.17$, $p < 0.0001$) (Fig. 3A). However, there was no correlation identified between 25(OH)D and age (Fig. 3B).

As a vitamin D synthesis is largely dependent on the geographical latitude, the epidemiological studies of 25(OH)D values were conducted in different regions of Ukraine. The analysis showed that 25(OH)D level was significantly higher in those subjects living in the southern regions ($p < 0.0001$). There were no statistically significant differences across the other regions in that regard (Fig. 4).

The influence of seasonal factors has also been considered. It was determined that the median 25(OH)D level of the examined subjects during the summer season was significantly higher ($36.32$, [23.68; 52.27]) nmol/L, ($p < 0.001$) compared with the observed people’s levels in winter ($28.96$, [16.07; 40.15]), spring ($28.29$, [16.23; 40.77]) and autumn ($30.04$, [15.88; 43.87]) nmol/L. A considerably higher 25(OH)D concentration was distinguished in August ($p < 0.00001$) at a significant difference from other months (Fig. 5). The lowest data were registered in February, especially in the age group of those over 75 yrs., whose mean level of 25(OH)D was $12.36 \pm 2.13$ nmol/L (Fig. 6).

The indices of 25(OH)D level in each of the age groups are demonstrated in Table 4. Significant difference was observed among the young (20–34 yrs.) and old (60–74 yrs.) people.
To determine the frequency of vitamin D deficiency according to the seasons, all people were divided into two groups – the first group consisted of the examined during the winter period (from November to April) and the second group included subjects observed in the summer period (from May to October). It was determined that a normal level of 25(OH)D was registered only in 3.1% cases and vitamin D deficiency was reported in 85.8% cases observed in winter. During the summer period the frequency of vitamin D deficiency decreased to 79.5% of examined subjects (Fig. 7).

<table>
<thead>
<tr>
<th>Age groups, years</th>
<th>Winter</th>
<th>Summer</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>25(OH)D</td>
<td>n</td>
</tr>
<tr>
<td>20–34</td>
<td>41</td>
<td>28.62</td>
<td>[14.88; 39.98]</td>
</tr>
<tr>
<td>45–59</td>
<td>207</td>
<td>31.60</td>
<td>[19.37; 47.68]</td>
</tr>
<tr>
<td>60–74</td>
<td>235</td>
<td>27.91</td>
<td>[15.61; 38.13]</td>
</tr>
<tr>
<td>75 and older</td>
<td>39</td>
<td>25.78</td>
<td>[14.70; 36.50]</td>
</tr>
<tr>
<td>Total</td>
<td>579</td>
<td>28.62</td>
<td>[16.16; 40.98]</td>
</tr>
</tbody>
</table>

NS = No significant difference (p > 0.05).

1235 patients had been assessed for the level of iPTH in blood serum. 147 (11.9%) subjects were diagnosed with higher-than-normal iPTH values: in 92.5% of those cases the concomitant vitamin D deficiency was registered (Fig. 8), thus effectively proving the onset of secondary hyperparathyroidism [11].

There is an inverse and significant correlation between 25(OH)D and iPTH levels (Fig. 9). The iPTH level is increasing along with the progression of vitamin D deficiency, thus representing the onset of secondary hyperparathyreosis with the subsequent resorbition of the bone tissue.

Fig. 7. Frequency of vitamin D deficiency and insufficiency according to the season of examination. The Figure 6A demonstrates the frequency of vitamin D deficiency in examined people during the winter period (from November to April); the group consists of 579 subjects. The Figure 6B shows the frequency of vitamin D deficiency observed during the summer period (from May to October), the group included 996 subjects.

Fig. 8. Distribution of iPTH levels among 1235 examined subjects. 11.9% of examined subjects were registered with higher-than-normal iPTH values.
A low serum vitamin D level (below 50 nmol/L) is a worldwide predicament, ranging from 30% to over 80% in various populations [16–18]. Recent studies show that this problem is not limited to sun-deprived areas of the world but is also common in sunny regions such as Florida (USA), Turkey, Australia, India, Israel, etc. [19–22]. In accordance, our study has found that a significant proportion of Ukrainian population has suboptimal vitamin D serum levels, and 81.8% are vitamin D deficient. This figure is slightly higher than the European average data which indicate the VDD in 2 to 30% of the adult population, but is close to the results of Estonian and Romanian authors which confirm the presence of VDD in 73% and 83.5% respectively [24, 25].

Traditionally population that is considered at risk for VDD is the elderly, especially postmenopausal women. But some of the recent studies demonstrate the lack of a clear age gradient in vitamin D insufficiency and deficiency occurrence [25]. In this study we observed almost the same trend: the total VDD prevalence in the population was high, ranging from minimal 71.8% in the age group 20–34 yrs. to a maximum of 84.3% in older, than 75 yrs. group. We consider it can be due to the lowering of vitamin D levels in the younger general population.

Comparing the vitamin D levels between subjects residing in different areas of Ukraine, we have noticed that 25(OH)D level was significantly higher in those living in the southern regions. It corresponds with the data gathered in high-latitude countries, where undetectable amounts of ultraviolet radiation in the winter (due to the distance from the equator) significantly lower vitamin D serum levels [26]. Our results also suggest that there is a significant seasonality in vitamin D levels in Ukraine. Remarkable is the fact that seasonal differences are clearly evident in young adults (mean 25(OH)D levels 28.62 and 40.69 nmol/l in the winter and summer respectively) and almost absent with ageing. This can be due to better general metabolism in younger population.

While analyzing the correlation between 25(OH)D and iPTH levels, we have determined that the iPTH level is increasing along with the progression of vitamin D deficiency, thus representing the onset of secondary hyperparathyreosis with the subsequent resorption of the bone tissue.

Conclusions
Only 4.6% of Ukrainians have been proved to have 25(OH)D values within the normal limits; 13.6% are suffering from vitamin D insufficiency, while 81.8% were registered with vitamin D deficiency. 11.9% of the study subjects were identified to have increased iPTH levels. Significantly higher 25(OH)D level was registered in younger age group (20–34 years) as compared to other age groups (p < 0.05–0.01). The subjects living in the southern regions of Ukraine were found to have significantly higher 25(OH)D levels (p < 0.001 and p < 0.01). At the same time, it was confirmed that those values were higher throughout the summer with a peak in August (p < 0.00001). High level of vitamin D deficiency (81.8%) and secondary hyperparathyroidism (11.9%) make doctors search for the effective treatment and prevention methods of revealed disorders.

References


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VITAMINO D TRŪKUMAS UKRAINOE: DEMografinė
IR SEZONINĖ ANALIZĖ

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Santrauka
Mokslinių tyrimų rezultatai rodo, kad vitamino D stoka yra paplitusi visame pasaulyje. Ukrainos teritorijoje yra kelios geografinės platumos, todėl cholekalciferolio sintezė skiriasi skirtinguose šalies rajonuose.

Tyrimo tikslas – nustatyti vitamino D trūkumo ir nepakankamumo dažnumą Ukrainos populiacijoje, vitamino D koncentracijos kraująje amžiaus, geografinių bei sezoniškių ypatumų; nustatyti intaktinio parathormono (iPTH) koncentraciją esant vitamino D trūkumui.

Tyrimo metodai. Į tyrimą įtraukti 1575 asmenys, kurių amžius buvo nuo 20 iki 95 metų. Tyrime gyveno skirtingose Ukrainos rajonoje. 25(OH) vitaminas ir iPTH buvo ištirti taikant elektrochemioliuminiscentinį metodą (Elecsys 2010, Roche). Mažesnė negu 50 nmol/l 25(OH) vitamino D koncentracija kraująje buvo vertinama kaip vitamino D trūkumas, o nuo 50 iki 75 nmol/l – kaip vitamino D nepakankamumas.

Rezultatai. Vitamino D trūkumas nustatytas 81,8 proc., vitamino D nepakankamumas – 13,6 proc. tirtų asmenų. Intaktinis PTH neigiamai koreliavo su 25(OH) vitaminu D (r = –0,16, p < 0,0001). Antrinė hiperparatirozė nustatytas 11,9 proc. tirtų pacientų. Pietiniuose šalies rajonuose nustatyta statistiškai reikšmingai didesnė vidutinė 25(OH) vitaminų koncentracija, lyginant su kita Ukrainos rajons, ypatingas variaus metu (p < 0,05).

Išvada. Vitamino D trūkumo (81,8 proc.) ir antrinės hiperparatirozės (11,9 proc.) didelis dažnumas skatina dievių ir gydytojų ieškoti efektyvių nutrikimų prevencijos ir gydymo metodų.

Raktažodžiai: vitamino D trūkumas / nepakankamumas, amžiaus ypatumai, sezoniškumas, antrinė hiperparatirozė