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СТАТУС ВИТАМИНА D У ЖИТЕЛЕЙ РОССИЙСКОЙ ФЕДЕРАЦИИ, ЕГО ВОЗРАСТНЫЕ ОСОБЕННОСТИ И ВЗАИМОСВЯЗЬ С УРОВНЕМ ПАРАТИРЕОИДНОГО ГОРМОНА

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Vitamin D Status Among Residents of the Russian Federation and Its Relation with Age and Parathyroid Hormone

Резюме

Цель: оценить статус витамина D (25(OH)D) в различных регионах Российской Федерации (РФ), а также установить взаимосвязь между уровнем 25(OH)D, возрастом и уровнем паратиреоидного гормона (ПТГ). **Материалы и методы:** оценка статуса витамина D проводилась у жителей различных регионов РФ (Северно-Западного федерального округа (СЗФО), Центрального (ЦФО), Южного (ЮФО) и Дальневосточного (ДФО)) в период с 2012 по 2017 г. Всего в кросс-секционном исследовании проанализировано 115694 анонимных образцов, предоставленных независимой коммерческой лабораторией. Для определения уровня 25(OH)D использовался хемилюминесцентный иммуноанализ. **Результаты:** Выявлена повсеместная распространенность низких уровней 25(OH)D: дефицит (<20 нг/мл) — 33,16 %, недостаточность (≥20 и <30 нг/мл)-37,11 %, которая значительно не отличалась в зависимости от региона проживания (ЮФО (76,3 %), ЦФО (69,2 %), СЗФО (67 %) и ДФО (63 %), p>0,05). В летние месяцы медиана уровня витамина D оказалась выше, чем в зимние (25,3 нг/мл [18,3; 33,5] vs 24 нг/мл [16,7; 32,5], p=0,006). Уровень 25(OH)D<30 нг/мл чаще всего встречался у участников младше 20 лет и старше 80 лет (75 % и 81 %, соответственно). Также в группе младше 20 лет количество участников с целевыми уровнями витамина D (>30 нг/мл) оказалось низким, что было сопоставимо с группой старше 80 лет (22,6 % и 18 %, соответственно, p=0,1). Подтверждена отрицательная обратная связь между уровнями витамина D и ПТГ (r=-0,11, p=0,002). Выявлена слабая положительная корреляция между возрастом участников и уровнями ПТГ (r=0,18, p=0,000). **Заключение:** Полученные данные свидетельствуют о широкой распространенности низких уровней 25(OH)D среди всех возрастных групп в РФ. Выявлены статистически значимые различия в статусе витамина D в зависимости от возраста и времени года. При этом географические факторы не оказали значимого влияния на уровни 25(OH)D. Отмечена высокая распространенность выраженного дефицита витамина D у лиц младше 20 лет и старше 80 лет. Установлена слабая положительная корреляция между возрастом и уровнем ПТГ, что вместе с высокой частотой низких концентраций витамина D в старшей возрастной группе, требует адекватной своевременной коррекции данного состояния и дальнейшего динамического наблюдения, с целью предотвращения потенциальных негативных влияний дефицита витамина D на костную ткань.

Ключевые слова: *витамин D, паратиреоидный гормон, статус витамина D, дефицит витамина D, распространенность, возраст*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Соответствие принципам этики

Исследование представляет собой анализ анонимных образцов, которые были предоставлены добровольно без какой-либо идентифицирующей информации лицом, не принимающим никакого участия в этой работе. Основные положения Хельсинской декларации нарушены не были. В рамках данного исследования медицинское вмешательство участникам не проводилось, и участие не несло никаких потенциальных рисков, поэтому работа не считается исследованием на человеке и не требует заключения этического комитета.

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Abstract

Objective: to study the vitamin D (25(OH)D) status in various regions of the Russian Federation (RF), and to determine the relation between age, levels of 25(OH)D and parathyroid hormone (PTH). **Methods:** The vitamin D status was investigated in residents of various regions of the Russian Federation (Northwestern Federal District, Central Federal District, Southern Federal District and Far Eastern Federal District) between 2012 and 2017. In this cross-sectional study 115694 anonymous samples were analyzed. All samples were provided by an independent commercial laboratory. Serum levels of vitamin D (25(OH)D) were measured using chemiluminescent assay. **Results**: The prevalence of low levels of 25(OH)D was widespread in the Russian Federation: deficiency (<20 ng/ml) — 33,16 %, insufficiency (≥20 and <30 ng/ml) — 37,11 %, which did not significantly differ between various regions (Southern Federal District (76,3 %), Central Federal District (69,2 %), Northwestern Federal District (67 %) and Far Eastern Federal District (63 %), p>0,05). The median level of vitamin D was higher in the summertime than in the winter months (25,3 ng/ml [18,3; 33,5] vs 24 ng/ml [16,7; 32,5], p=0,006). Levels of 25(OH)D<30 ng/ml were most common in the age group younger than 20 years and in the age group older than 80 years (75 % and 81 %, respectively). Also in the age group younger than 20, the number of participants with vitamin D levels in target range (>30 ng/ml) was low, which was comparable to the age group over 80 years (22,6 % and 18 %, respectively, p=0,1). A negative inverse correlation between vitamin D and PTH levels was confirmed (r=-0,11, p=0,002). There was a weak positive correlation between the age of participants and PTH levels (r=0,18, p=0,000). **Conclusion:** The obtained data indicate the high prevalence of 25(OH)D deficiency among all age groups in the Russian Federation. Vitamin D levels were statistically differed depending on age and season. Geographic factors did not have a significant impact on vitamin D status in different regions of the Russian Federation. The highest prevalence of severe D deficiency was observed in age group younger 20 years and over 80 years. A weak positive correlation was established between age and PTH levels. Consideringthe high frequency of low vitamin D concentrations in the elderly age group, this condition rerequires adequate correction and further follow-up in order to prevent the negative effects of vitamin D deficiency on bones.

Key words: *vitamin D, parathyroid hormone, vitamin D status, vitamin D deficiency, prevalence, age*

Conflict of interests

The authors declare no conflict of interests

Sources of funding

The authors declare no funding for this study

Conformity with the principles of ethics

The study is an analysis of anonymous samples that were provided voluntarily without any identifying information by a person not involved in any way with this work. The main provisions of the Helsinki Declaration were not violated. There were no medical interventions performed on participants in this study, and there were no potential risks associated with participation, so the work is not considered human research and does not require an ethics review

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FEFD — Far Eastern Federal District, PTH — parathyroid hormone, RF — Russian Federation, NWFD — North-Western Federal District, CFD — Central Federal District, SFD — Southern Federal District

Relevance

Low vitamin D concentrations are observed in the populations all over the world [1]. The precursor of the active vitamin D (25-hydroxyvitamin D, 25(OH) D) is synthesised in the liver induced by enzymes CYP2R1 and CYP27A1 from vitamin D3, which forms in the skin exposed to UV radiation, and can also enter the body with food. Exposure to the sun, which directly impacts the synthesis of endogenous vitamin D, depends on the geographical latitude and climate in the place of residence. In the regions lying above 40° of the north latitude, exposure to the sun in winter is inadequate for the body to have a sufficient amount of vitamin D [2]. Therefore, a major part of the population in the Northern Hemisphere is at risk of vitamin D deficiency. Data of epidemiological studies confirm that fact: the incidence of vitamin D deficiency (25(OH)D < 20 ng/mL) in Europe varies from 30 % to 60 % [3].

In addition to geographical factors, vitamin D status can be impacted by lifestyle, skin colour, clothes, less time spent in the sun, and a wide use of sunscreens [4]. In the Middle East, vitamin D deficiency can be as high as 90 %, despite a lot of sun during the year, because of their lifestyle [5].

Without timely correction of low vitamin D concentrations, levels of parathyroid hormone (PTH) rise to compensate the deficit, causing more intense bone resorption [6]. Also, severe vitamin D deficiency usually has direct negative impact on bones, impairing calcium phosphate deposition in new bone tissue and causing osteoid mineralisation defects. All these factors can compromise the quality of the bone tissue and increase the risk of fractures, especially in elderly [7].

The Russian Federation (RF) is located between 77° and 41° of northern latitude; the climate, number of sunny days in a year and UV index differ. In addition to climatic factors, regions of Russia differ in culture and traditions of their populations. Therefore, vitamin D status of the RF citizens can vary depending on the region. Due to geographic factors, a major part of the population in Russia is at risk of vitamin D deficiency, this fact being confirmed by study results. For example, in a study by P. Lips et al. (2019), vitamin D deficiency was observed in 39.7 % of samples, while low vitamin D levels were diagnosed in 36.5 % [3]. A study by E.A. Pigarova et al. (2020) also demonstrated a high incidence of low vitamin D concentrations in Russia: 84.3 % of subjects had 25(OH)D < 30 ng/mL [8].

Since the vitamin D status depends on geographic and demographic factors, as well as quality of life, dynamic monitoring of vitamin D levels in various regions of Russia is required to prevent its deficiency and potentially negative impact of low levels of 25(OH)D on the bone tissue.

The objective of this study was to evaluate the extent of vitamin D deficiency and insufficiency among the population of the Russian Federation depending on geographic factors and age, as well as to analyse the correlation between 25(OH)D levels, PTH values and age.

Materials and Methods

The study enrolled 115,694 anonymous samples provided by the independent laboratory INVITRO. The samples were collected over the period from 2012 to 2017 in the regions of Russia located between 43° and 59° of northern latitude: central region (CFD) — 61,772 (53.4 %) participants; north-western region (NWFD) — 10,003 (8.7 %) participants, southern region (SFD) — 18,288 (15.8 %) participants, and Far Eastern region (FEFD) — 25,631 (22.1 %) participants. The study included specimens from patients aged 18 and above years old (the median age was 45 [33; 58] years old): the under 20 years old group included 5,553 (4.8 %) people; 20–39 years old — 39,105 (33.8 %) people; 49–59 years old — 44,658 (38.6 %) people; 60–79 years old — 24,411 (21.1 %) people; and over 80 years old — 1,967 (1.7 %) people. This study did not require any inclusion/exclusion criteria to be met.

Serum 25(OH)D levels were measured by a chemilumescent analysis (Architect 8000, Abbot, USA). The results were evaluated in accordance with the clinical guidelines for the diagnosis, management and prevention of vitamin D deficiency in adults (2016), where an adequate 25(OH)D level was 30–60 ng/mL, 25(OH)D of less than 20 ng/mL is deficiency, while 25(OH)D levels of 20–30 ng/mL is vitamin D insufficiency [9]. In addition to vitamin D levels, blood creatinine, calcium and PTH levels were measured (reference range: 1.6–6.9 pmol/L). The correlation between PTH and vitamin D levels was analysed only for samples, where calcium and creatinine levels were within the reference range (reference calcium values depending on the age: 12–60 years old — 2.1–2.55 mmol/L, 60–90 years old — 2.2–2.55 mmol/L; creatine: 50–98 μmol/L for women and 64–111 μmol/L for men).

Statistical Analysis

Statistical data processing was performed using STATISTICA6.0 package (StatSoftInc., 2001, USA). Data are presented as the median (Me) and quartiles [Q1;Q3]. Quantitative differences between two independent groups were identified using the Mann-Whitney test. The Kruskal-Wallis test was used to identify quantitative differences between three and more independent groups. Frequency differences in groups were evaluated using χ^2. The Spearman's test was used to evaluate the correlation. The level of statistical significance was 0.05.

Results

The median age of participants was 45 [33; 58] years old. The median 25(OH)D concentration for all samples was 23.9 ng/mL [17.0; 31.6]. Vitamin D insufficiency was observed in 42,934 (37.11 %) samples. Vitamin D deficiency (< 20 ng/mL) was diagnosed in 38,364 (33.16 %) participants, including 4,211 (3.6 %) cases of severe deficit. Thus, 70 % of participants had 25(OH)D levels below 30 ng/mL. Target vitamin D levels (30–60 ng/mL) were recorded only in 31,237 (27 %) of participants (Fig. 1).

Given varying daylight duration and number of sunny days in a year, vitamin D status has been evaluated for different federal districts of Russia (Fig. 2). Vitamin D

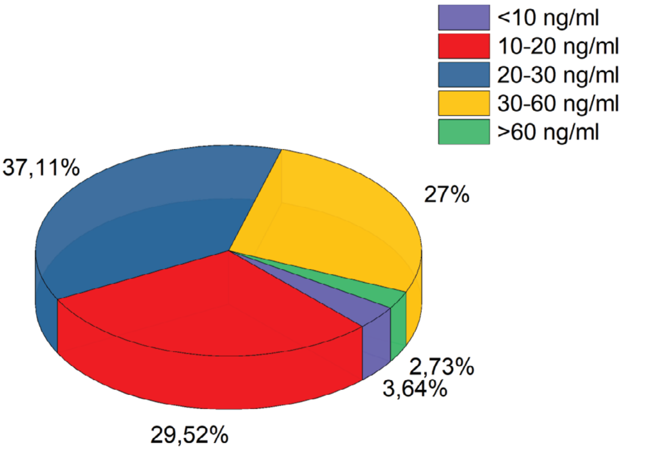

Figure 1. *Vitamin D status from 2012 to 2017 in Russian Federation*

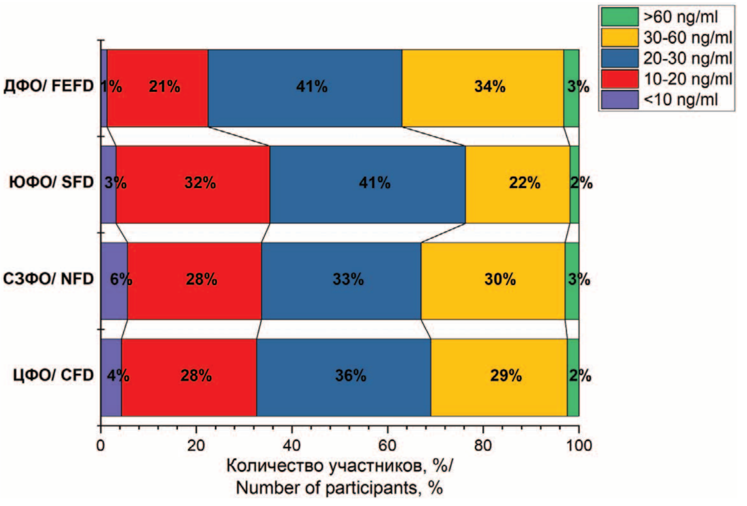

Figure 2. *Vitamin D status among residents of different regions of Russian Federation*

Note. CFD — Central Federal District, NFD — Northwestern Federal District, SFD — Southern Federal District, FEFD — Far Eastern Federal District

deficiency and insufficiency are a common condition among the citizens of Russia, irrespective of a region of their residence: CFD — 33 % and 36.2 %, NWFD — 33.6 % and 33.4 %, SFD — 35.4 % and 40.9 %. There were no significant differences in the number of participants with adequate vitamin D levels in the CFD, NWFD, SFD and FEFD ($p > 0.05$).

The incidence of severe vitamin D deficiency (< 10 ng/mL) was higher in the NWFD — 5.6 % ($p < 0.05$ for all) vs. other federal districts of Russia.

Low vitamin D levels were usually observed during winter. 35 % of samples collected during winter had vitamin D deficiency; it is higher than during summer (30 %) ($p = 0.006$). The data for the CFD demonstrated this trend: in winter, the median vitamin D levels were lower and made 24 ng/mL [16.7; 32.5], while in summer, they were 25.3 ng/mL [18.3; 33.5] ($p = 0.006$). Of note, in the NWFD this trend was not observed: vitamin D levels were similar in winter (24.5 ng/mL [17.2; 33.0]) and summer (26 ng/mL [18.5; 33.9]), $p = 0.244$ (Fig. 3).

The 25(OH)D status was analysed in various age groups (Fig. 4). It has been shown that vitamin D deficiency and severe vitamin D deficiency were most common in participants under 20 years of age — 42 % and 7.7 % vs. other age groups: 20–39 years of age (31.5 % and 3.9 %) and 40–59 years of age (32 % and 3.7 %), $p = 0.000$ for all. At the same time, the number of participants with the target vitamin D levels in the group of under 20 years old was also low and comparable with the group of over 80 years of age (22.6 % and 18 %, respectively, $p = 0.1$). Vitamin D concentrations below 30 ng/mL were predictably common in patients over 80 years old (79 %). Adequate 25(OH)D concentrations were observed in 29.1 % of participants in the age group 20–39 years old, which is statistically higher than in all other age groups ($p = 0.000$ for all).

PTH levels at various vitamin D concentrations were evaluated. At the vitamin D level of below 30 ng/mL, the median PTH value was 5.1 pmol/L [3.9; 6.6], while at the target vitamin D value, the median PTH was 4.7 pmol/L [3.7;6.1], which is statistically lower ($p = 0.002$) (Fig. 5).

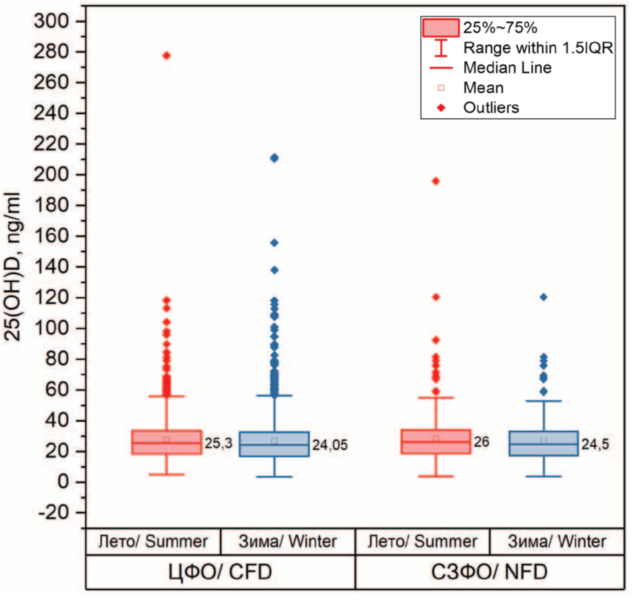

Figure 3. *Vitamin D levels during summertime and winter in the Central and Northwestern regions*

Note. 25(OH)D — vitamin D, NFD — Northwestern Federal District, CFD — Central Federal District

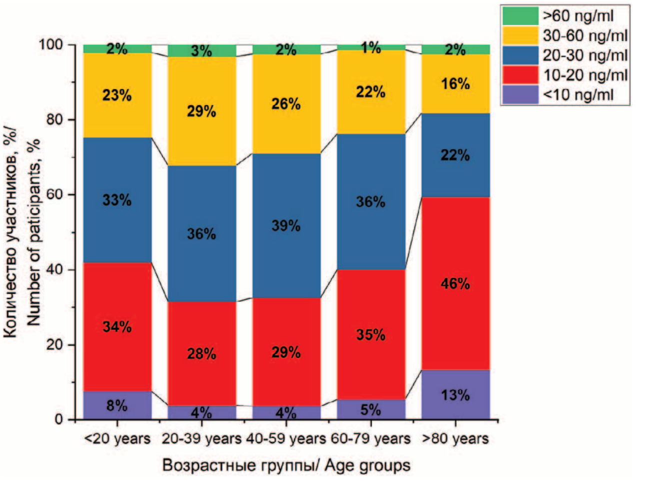

Figure 4. *Vitamin D levels in different age groups*

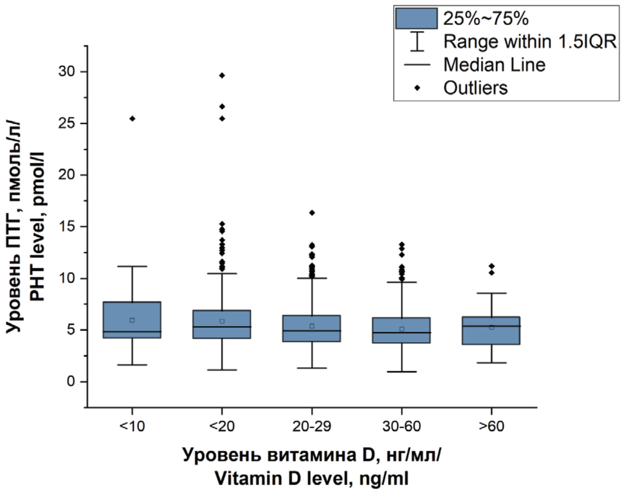

Figure 5. The relation between PTH and vitamin D levels

Note. PTH — parathyroid hormone, <10 ng/ml — severy vitamin D deficiency, <20 ng/ml — vitamin D defiency, 20-29 ng/ml — vitamin D insufficiency, 30-60 ng/ml — optimal levels, >60 ng/ml — above target range

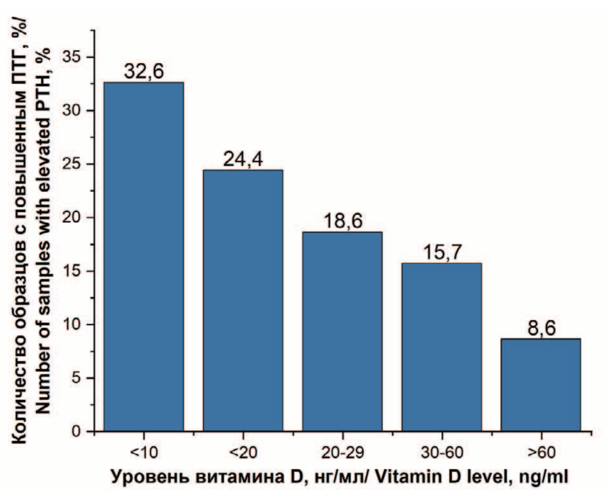

Figure 6. The number of samples with eveleted PTH levels depending on vitamin D levels

Note. PTH — parathyroid hormone, <10 ng/ml — severy vitamin D deficiency, <20 ng/ml — vitamin D defiency, 20-29 ng/ml — vitamin D insufficiency, 30-60 ng/ml — optimal levels, >60 ng/ml — above target range

Among samples with the vitamin D levels of 30–60 ng/mL, higher PTH levels (reference range used in the laboratory: 1.6–6.9 pmol/L) were observed in 15.7 % of samples, whereas with the severe vitamin D deficiency — in 32.6 %; where the 25(OH)D concentration was below 20 ng/mL — in 24.4 % and only in 8.6 % of participants — at the vitamin D levels of above 60 ng/mL ($p = 0.000$ for all) (Fig. 6).

A weak negative reverse correlation between the vitamin D level and PTH ($r = -0.11$, $p = 0.002$) was confirmed. A weak direct correlation between the age and PTH levels ($r = 0.18$, $p = 0.000$) was observed. There was no correlation between the age and the vitamin D level ($r = -0.015$, $p > 0.05$).

Samples with the vitamin D level of 30–60 ng/mL and PTH exceeding the upper reference limit were analysed separately. The median age in the high PTH group was 64 years old [56;70], whereas in the group with the target PTH group, it was 56 years old [47;63], ($p = 0.000$).

Discussion

This study analysed the 25(OH)D status of 115,694 samples from various regions of Russia, and this number is higher than in any similar study in the Russian Federation. Vitamin D insufficiency was recorded in 37.11 % of samples, while deficiency was observed in 33.16 %. Only 27 % of participants had the 25(OH)D level of over 30 ng/mL. The data confirm the high incidence of low vitamin D levels in Russia, which corresponds to other Russian studies [8, 10-14]. A study by Smirnova D. et al. (2022) in 30,040 participants showed that in 2013–2018 the vitamin D deficiency rates were 39.7 %, while the target 25(OH)D levels (> 30 ng/mL) were recorded only in 23.8 % of participants [10].

More strict inclusion criteria can affect the results. E.g. [8] evaluating in 2020 the 25(OH)D status of 500 volunteers living in the regions of Russia located between 45° and 70° north longitude showed that the mean vitamin D level was 20.9 ng/mL. Vitamin D deficiency was observed in 56.4 % of participants, while insufficiency was recorded in 27.9 %. However, in this study we did not have information on any vitamin D preparations taken, comorbidities and reasons to test 25(OH)D levels. At the same time, Pigarova E.A. et al. (2020) did not include participants taking vitamin D preparations, and that could have caused lower 25(OH)D values [8].

An evaluation of the 25(OH)D status of people residing in various regions of Russia showed a high incidence of vitamin D deficiency and insufficiency, even in the areas with a larger number of sunny days and warmer climate. For instance, in the SFD, the adequate vitamin D level was observed only in 21.8 % of samples, while deficiency and insufficiency were observed in 76.3 %. A high incidence of low 25(OH)D levels was also observed in other southern regions of the Russian Federation. In 2013–2015, vitamin D deficiency and insufficiency were recorded in 82 % of the citizens of Rostov-on-Don [11]. In their article Pigarova E.A. et al. [8] describe that the 25(OH)D level below 30 ng/mL among the population of the same region was recorded even in a larger number of cases (92.86 %), while the target vitamin D levels were observed only in 7.14 %.

The incidence of vitamin D deficiency in Moscow (55° north latitude) was 32 %, in Saint-Petersburg (59° north latitude) — 34 %, which was higher than in other countries in the same geographical region. For instance, in Sweden (58° north latitude), 25(OH)D levels of below 20 ng/mL were recorded in 17 % of the population [15] and in Denmark (56° north latitude) — in 23.6 % [16]. These differences in the incidence of low vitamin D concentrations can be associated with differences in the diet. In Russia, food is usually not supplemented with vitamin D, and people eat little fatty fish [17], while in the Nordic countries, food supplementation with vitamin D is a common practice, and the populations in these countries each more fish and seafood [18].

In this article, the geographical distribution is not the major factor impacting the differences in the vitamin D status. At the same time, in a study by Smirnova D.V. et al. (2022) [10], an analysis of the correlation between mean vitamin D values and the latitude revealed a non-linear dependence. In women, the highest 25(OH)D concentrations were observed in mid-latitudes, while the lowest concentrations were recorded in southern and northern regions. In men, the vitamin D concentrations were roughly at the same level (25 ng/mL) in southern and mid-latitudes, with a sharp drop in values in regions located to the north of latitude 69°.

Elderly people are especially susceptible to vitamin D deficiency because of the reduced time spent under the sun, reduced synthetic function of the skin and reduced glomerular filtration rate [19]. As expected, vitamin D deficiency (81 %) and severe vitamin D deficiency (18 %) were recorded in subjects over 60 years of age. In another Russian study analysing the vitamin D status in the Irkutsk Region, the mean vitamin D level in the group of people over 70 years of age was lower than in people of other ages and made 15.13 ± 2.24 ng/mL [13]. In elderly people, low vitamin D levels often cause phosphoric-calcium exchange impairments, as well as contribute to sarcopenia. Sarcopenia in patients is associated with senile asthenia, an increased risk of falls, fractures, thus reducing the quality and length of life. In 2022, in Russia over 33 million of people were people aged 60 and over years old [20]; and this study shows that a majority of them have vitamin D deficiency. This condition requires adequate and timely correction in order to prevent possible negative impact by vitamin D deficiency.

High rates of vitamin D deficiency and severe vitamin D deficiency in people under 20 years of age is of particular interest. In a study by Pigarova E.A. et al. (2020), an analysis of the vitamin D status in 18–50 years olds showed a similar pattern: vitamin D deficiency was observed in 72.2 % of samples collected from people aged 18–25 years old, i.e. higher than in other age groups [8]. It can be assumed that this pattern is a result of a higher demand in vitamin D in this age group. According to Rosstat data for 2022, there are 7 million people aged 15–19 years old [20]. This study shows that vitamin D deficiency is recorded in 42 % of people under 20 years old, i.e. in approximately 3 million young people. Bone mass acquisition starts in childhood and adolescence and peaks at the age of 20–30 years old; therefore, correction of vitamin D deficiency in this age group is crucial for the prevention of poorer bone tissue quality and age-related fractures.

This study confirmed the impact of the sunlight on vitamin D concentrations. 25(OH)D levels were statistically higher during summer than during winter.

Given that a number of articles [21, 22] discuss the significance of vitamin D status accounting when setting reference PTH range, this study evaluated the association between PTH levels and various 25(OH)D values.

Median PTH at the target vitamin D levels was lower than at 25(OH)D < 30 ng/mL. However, the median PTH value at severe vitamin D deficiency was comparable with median PTH at vitamin D levels of 30–60 ng/mL, which can be a result of a small sample size selected for analysis.

The age can also impact the association between PTH and vitamin D levels [23, 24], that is why age-related changes in PTH and 25(OH)D levels were analysed. A weak negative reverse correlation between PTH and vitamin D levels was confirmed. A weak direct correlation between the age and PTH levels was observed. Also for the samples with the target sufficient vitamin D levels, but with higher PTH concentrations, participants were older than for the samples with target PTH and 25(OH) D values. Y. Jiang et al. (2020) demonstrated that, with ageing, parathyroid glands express less vitamin D receptor, 1-alfa-hydroxylase(CYP27B1) and 24-hydroxylase (CYP24A1), and it results in reduced synthesis of the active form of vitamin D (1,25$(OH)_2$D) and higher PTH levels in elderly people [25].

A high incidence of lower vitamin D levels not only in elderly, but also in young people (under 20 years of age) can signify a U-shape correlation between vitamin D levels and age of participants.

This is a large-scale cross-sectional study; however, there were a number of limitations: anthropometric information, including sex and body weight, was missing; comorbidities were unknown; there was no information on medications or biologically active supplements containing vitamin D, which could impact 25(OH)D concentration.

Conclusion

We analysed 115,694 samples collected in 2012–2017. The incidence of vitamin D insufficiency and deficiency was 37.11 % and 33.16 %, respectively. There are statistically significant differences in the vitamin D status depending on age and time of year. At the same time, geographic factors did not have any impact on vitamin D levels. A high incidence of vitamin D deficiency in participants under 20 years of age and over 80 years of age was observed. Since the bone mass is actively acquired up to 30 years of age, correction of 25(OH)D deficiency in young people is essential for normal bone mineralisation in order to prevent fractures. A weak direct correlation between the age and PTH levels was established. Given the low vitamin D levels in elderly people and an increase in PTH levels with ageing, this group of patients needs adequate and timely correction of low vitamin D levels and follow-up.

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Мармалюк Д.А.: анализ и интерпретация данных, написание статьи

Рунова Г.Е.: разработка концепции и идеи статьи, анализ и интерпретация данных, внесение правки с целью повышения научной ценности статьи

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All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Marmalyuk D.A.: participation in data analysis, interpretation of results, writing of the manuscript

Runova G.E.: development of the concept and design of the study, data analysis, interpretation of results, verification of critical intellectual content

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