



## Seasonality of Vitamin D Insufficiency in Children of Moscow

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**Abstract:** The article presents the analysis of vitamin D levels in children of various age groups residing in Moscow and assesses the seasonality of vitamin D variations in this population group. In this work, the results of 25 (OH) D level measurement in 1041 children in the age from 1 month to 18 years collected in the period since 2012 to 2015 have been analyzed. In accordance with the analysis, in spite of the age, the high percentage of vitamin D insufficiency was detected among children in Moscow. The generally accepted optimum level of vitamin D metabolite – calcidiol in blood (>30 ng/ml) was observed only in the small part of the study participants (26%), while the larger part (74%) had the insufficient level of vitamin D of various intensity: 28% - insufficiency (20-29 ng/ml), 33% - deficiency (<20 ng/ml), 13% - severe deficiency (<10 ng/ml). With the age, the insufficiency level was more pronounced. The seasonality analysis showed the significant difference of vitamin D level between summer and winter seasons (p=0.01). The greatest decrease of vitamin D levels was observed in winter (median level of 25(OH)D 17.0 (11.0; 25.0) ng/ml). In summer months, the relative calcidiol gain was fixed (median – 22.9 (18.0; 33.0) ng/ml) which, however, did not achieve the normal level. Children and, in particular, adolescents residing in Moscow need year-round hypovitaminosis D prophylaxis with cholecalciferol products.

**Keywords:** Vitamin D, Cholecalciferol, Hypovitaminosis D, Vitamin D Deficiency, Seasonal Variations of Vitamin D

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## 1. Introduction

Currently, there is a big number of fundamental and clinical studies related to various biological effects of vitamin D and its favorable health effect. If the disorder of phosphorus - calcium metabolism and other bone metabolism disorders were previously considered as the main point of vitamin D therapy, nowadays, the considerable complex vitamin D effect on numerous body systems has become gradually evident. The main differential characteristic of vitamin D in comparison with other vitamins is its steroid chemical structure and presence of the specific receptor to its active metabolite  $1.25(\text{OH})_2\text{D}$  in various body tissues. It allows to consider vitamin D as a steroid hormone. Its functions are mediated by the nuclear receptor (VDR – vitamin D receptor) which induces transcriptional alterations on the genetic level affecting growth and inflammation factor levels, activity of various proteins and hormone levels in blood. It is known that vitamin D affects both directly and indirectly the expression of about 1250 – 5000 genes [1, 2].

The investigators have revealed the relationship of vitamin D deficiency and:

- cardiovascular diseases (arterial hypertension, myocardial infarction, cardiogenic stroke);
- manifestation of autoimmune diseases (1 type diabetes mellitus, multiple sclerosis, Crohn's disease, rheumatoid arthritis, systemic lupus erythematosus);
- higher frequency of acute respiratory infection;
- allergic pathology (bronchial asthma and atopic dermatitis);
- cancer diseases (pancreatic cancer, colorectal cancer, breast cancer) [2, 3, 4].

In the recent years, a favorable effect of the vitamin on nervous system development, neuroprotective and neurotrophic effect on CNS has been proven in children and adolescents [1, 5]. The relationship between the sufficient vitamin D intake and increase of mean population life span has been demonstrated.

The wide range of vitamin D effects on human health, in particular health of a child that acutely needs vitamin D on each stage of his/her development, have been of great interest for scientists and physicians already for several decades. In spite of this fact, the prevalence of D-deficient status remains currently rather high and requires decisive steps to overcome it.

It is known that only 5% of vitamin D is received with food, and the rest of 95% shall be synthesized in skin under exposure of UV-irradiation [6]. However, due to the geographic location of the country – above  $40^\circ$  the north latitude, the residents of the Russian Federation have the increased risk of a lower vitamin D status due to insufficient insolation and reduced epidermal synthesis [7].

There is some rather contradictory data on the presence of seasonal variations of serum calcidiol concentration. For example, the study carried out in Denmark assessed the vitamin D levels in girls aged 11-13 years during winter and summer. The better calcidiol level was detected in summer

months. It was also proven that in case of  $25(\text{OH})\text{D}$  level – 40 ng/ml in summer,  $25(\text{OH})\text{D}$  level of 20 ng/ml may be achieved next winter [8]. In Great Britain, the peak blood level of vitamin D was observed in autumn months [9]. In addition, several works on adults and children have shown that  $25(\text{OH})\text{D}$  level decreases on 24-42% to winter period in comparison with “summer” level [10, 11, 12, 13].

The necessity to develop recommendations for pediatricians on hypovitaminosis D prophylaxis in children and adolescents was the rationale for the series of studies on the determination of vitamin D status in child population.

Despite the divergences in determination of the criterion of normal blood level of vitamin D metabolite (calcidiol) according to various authors, the most prevalent point of view of experts are the following values: in severe vitamin D deficiency, serum  $25(\text{OH})\text{D}$  level was less than 10 ng/ml, in deficiency – less than 20 ng/ml, in insufficiency – in the range 21–29 ng/ml. The target serum calcidiol concentration that characterizes the normal levels corresponds to the level above 30 ng/ml [3, 7, 14]. The concentration allows to achieve positive effects of vitamin D on human body including bone metabolism: the study with flank bone biopsy showed the significant improvement of bone density in patients with  $25(\text{OH})\text{D}$  level above 30 ng/ml, while among patients with the level of 21-29 ng/ml, the amount of biopsies with osteomalacia signs was 21% [15]. Based on the literature data, blood level of vitamin D above 150–200 ng/ml is considered to be excessive which may manifest as development of hypercalcaemia, hypercalciuria or hyperphosphatemia [16].

Study aim: to examine vitamin D provision in children and detect its relationship with the age group and year season among the Moscow residents.

## 2. Study Materials and Methods

The retrospective analysis was made using laboratory values of 1041 children aged from 1 month to 18 years which were supervised in treatment prevention institutions of Moscow in the period 2012 to 2015. 259 patients aged from 2 months to 18 years at the polyclinic at the Presidential Administration, 360 patients aged 10-18 years from municipal polyclinic № 133 and 100 adolescent girls aged 11-17 years from the cadet corps were examined. 322 younger children (1 month – 3 years) were also enrolled to the study that were examined at the base of Z. A. Bashlyaeva Pediatric Municipal Clinical Hospital and polyclinic of Group of companies “Mother and child”.

To assess vitamin D status in blood, the content of the main metabolite of vitamin D was determined –  $25(\text{OH})\text{D}_3$  (25-hydroxyvitamin D or calcidiol). While analyzing the results, we relied on standard serum  $25(\text{OH})\text{D}$  values developed during research studies: over 30 ng/ml - sufficient levels; 21–29 ng/ml – insufficient levels; 10–20 ng/ml - deficiency; less than 10 ng/ml - severe deficiency [3, 17, 18].

For statistical data processing, software package IBM SPSS

Statistics was used (version 20.0.0). The results were processed using generally accepted parametric and non-parametric comparison methods. Quantitative data was presented as median and interquartile range (Me [25Q; 75Q]).

### 3. Study Results

In accordance with the data obtained during the study, the prevalence of vitamin D deficiency in various age groups of the Moscow pediatric population remains very high. Sufficient 25(OH)D level (> 30 ng/ml) was observed in the small part – in 26% patients, while 74% of the population demonstrated hypovitaminosis D of various intensity; 28% had insufficiency (20-29 ng/ml), 33% – deficiency (<20 ng/ml), and 13% – severe vitamin D deficiency (<10 ng/ml).

It should be especially noted that the sufficient calcidiol level in blood was observed only in the group of patients of the first year of life, while already from the age of two years,

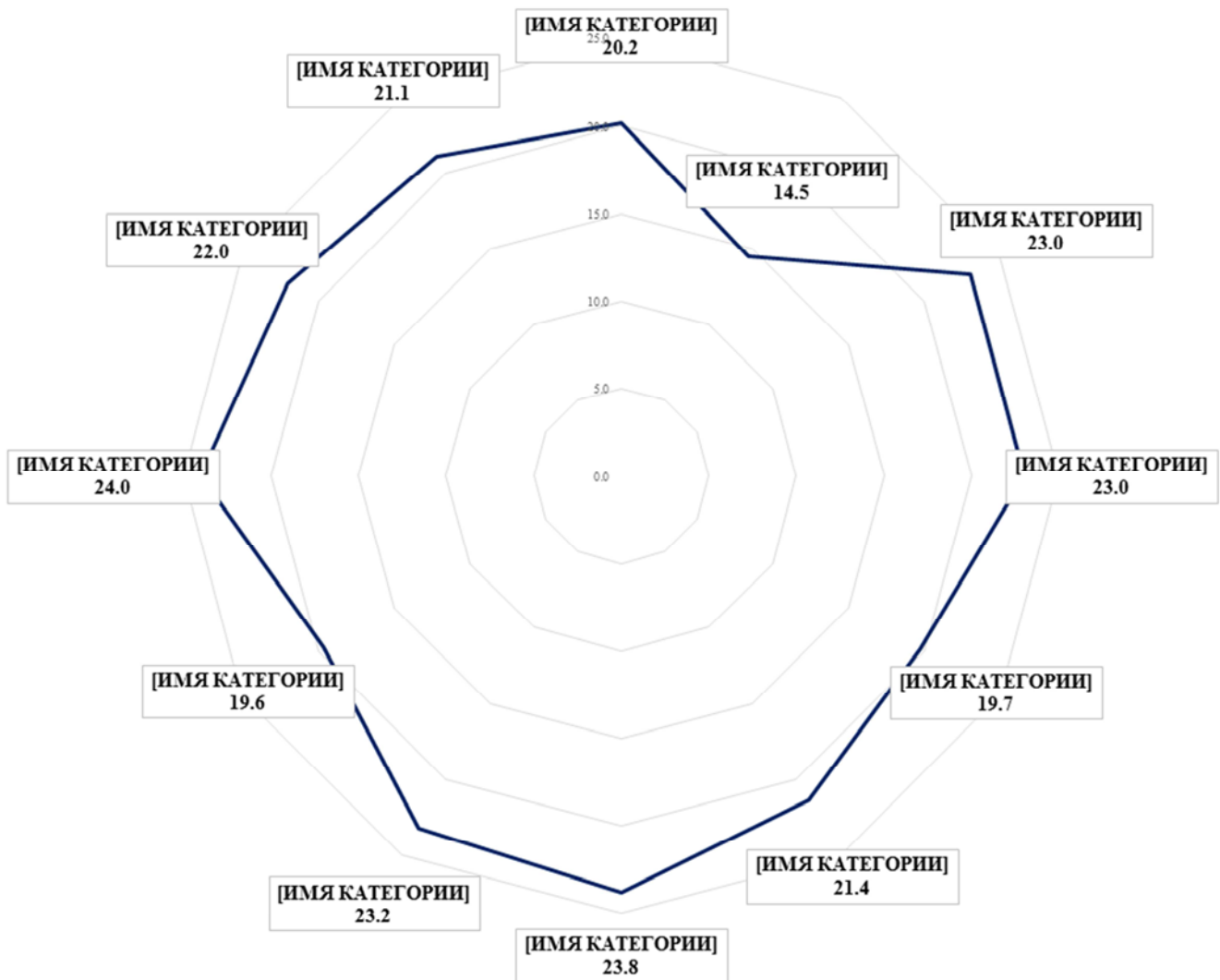
the larger part of the study participants had vitamin D insufficiency and its prevalence only increases with the age (table 1).

*Table 1. Median 25(OH)D level in various age groups.*

Age group	Median level of vitamin D (ng/ml)
up to 1 year	34.2 (25; 51)
1 year	30.5 (21; 45)
2 years	24.0 (20; 38)
3 years	27.0 (23; 36)
4-6 years	25.0 (22; 31)
7-9 years	27.0 (23; 36)
10-12 years	15.0 (11; 22)
13-16 years	17.0 (11; 22)
17-18 years	17.0 (13; 21)

While analyzing variations of blood level of vitamin D depending on the month of measurements, we obtained just small differences in values (figure 1).

**Level of 25(OH)D3 ng/ml in various months**



*Figure 1. Median 25(OH)D concentration in blood per months.*

While comparing vitamin D level in children in various year seasons, we detected the significant difference of

summer and winter seasons: 25(OH)D decrease in winter up to deficiency level – 17.0 [11.0; 25.0] ng/ml and increase in

summer period up to 22.9 [18.0; 33.0] ng/ml (p=0.001). It is evident that despite the significant gain in the higher insolation period, even in summer months, the optimum vitamin D concentration in children residing in Moscow is not achieved.

So the largest decrease up to deficiency level of 25(OH)D<sub>3</sub> in blood was observed in winter period with median – 17 (11; 25) ng/ml, the dominant insufficiency was observed in other

months: in spring period – 22.6 (14; 35) ng/ml, in summer – 22.9 (18; 33) ng/ml, in autumn – 23.0 (16; 31) ng/ml (figure 2).

The analysis of the data presented in figure 2 shows that 25(OH)D median in neither of year seasons achieves the normal level (30 ng/ml), hereby in winter period, it rather naturally decreases up to minimum values corresponding to vitamin D deficiency.

The pooled data per months is graphically shown in figure 3.

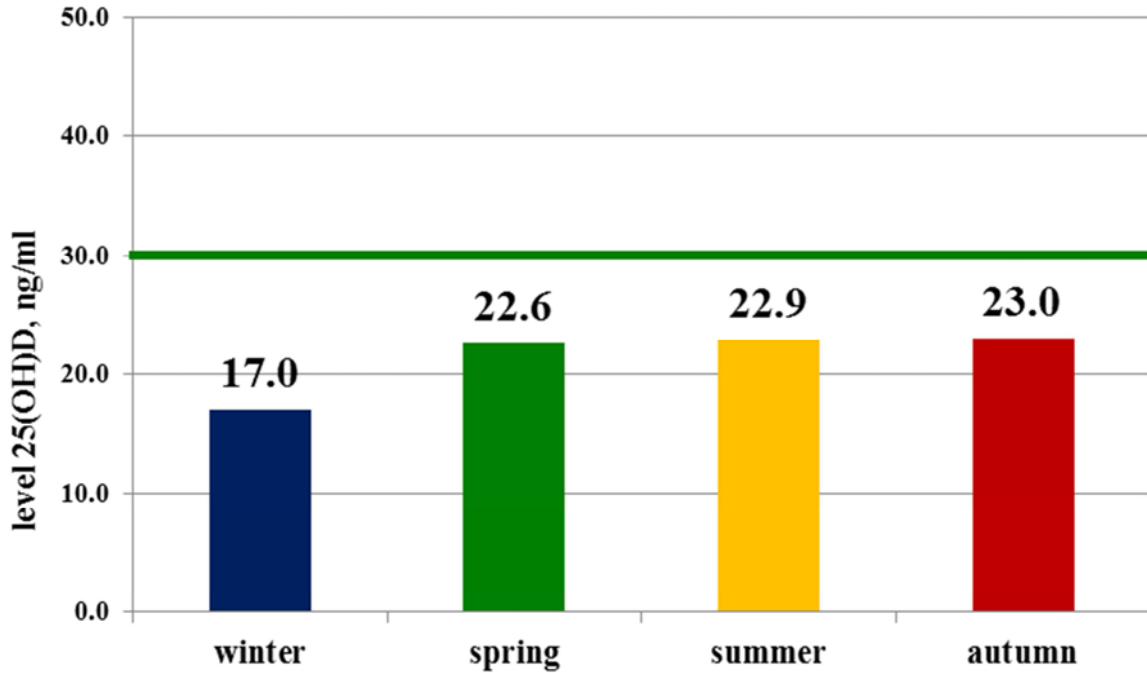


Figure 2. Seasonal variations of 25(OH)D level in children residing in Moscow.

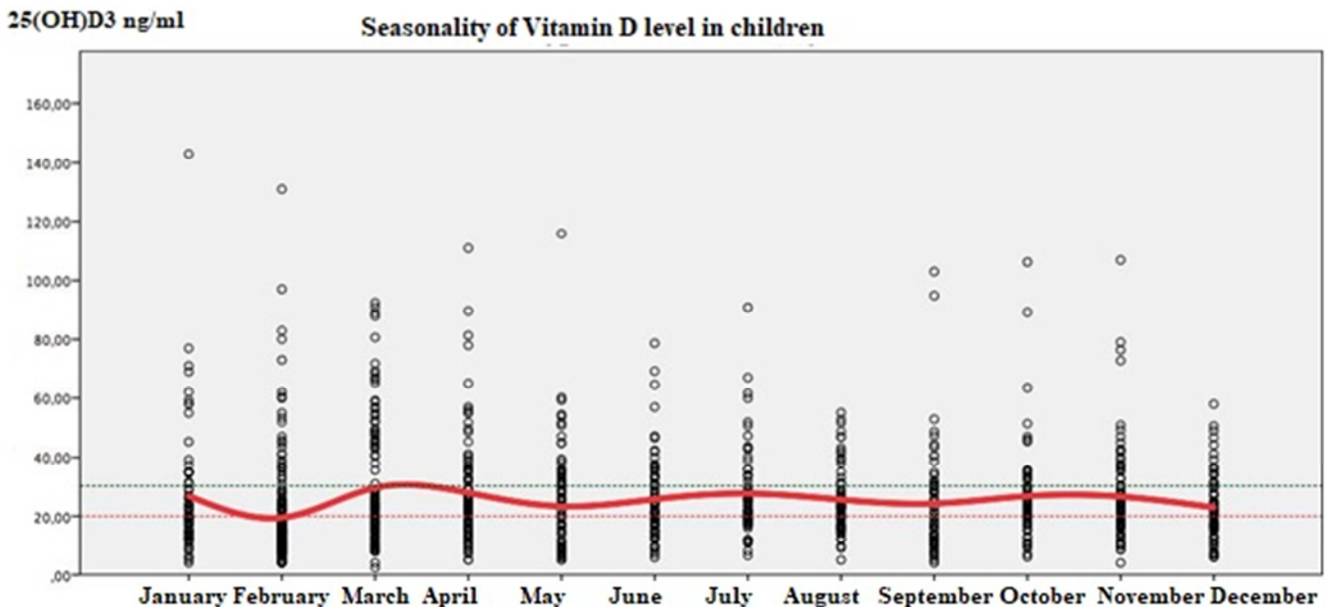
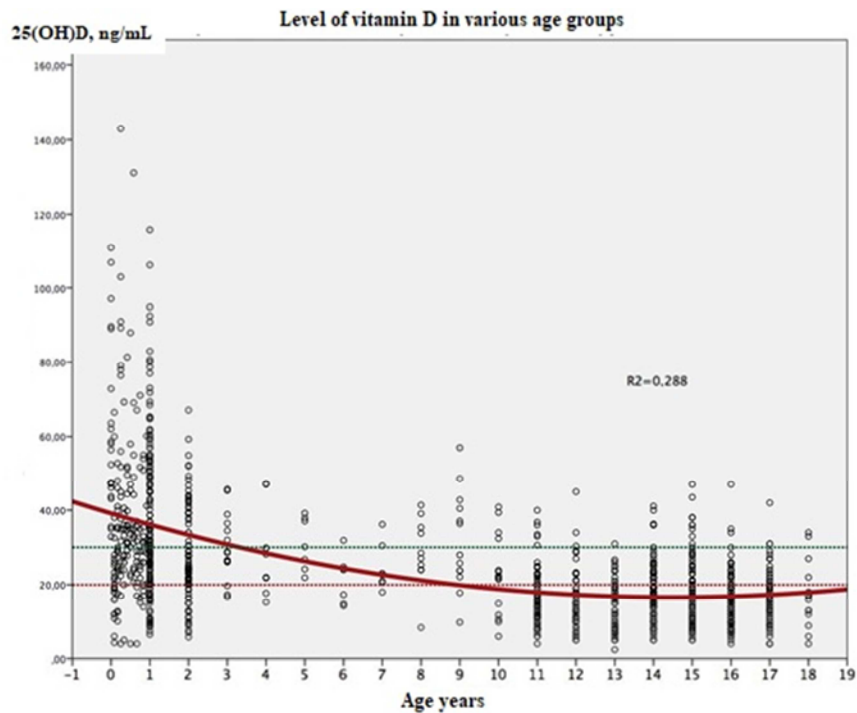


Figure 3. Distribution of 25(OH)D concentrations per months (ng/ml): red line reflects the mean level of vitamin D in each month; green dashed trends shows the optimum value, and red – deficiency threshold.

Figure 4 presents histogram of calcidiol level distribution in children depending on the age.



**Figure 4.** Distribution of 25(OH)D concentrations per age (ng/ml): red line reflects the mean level of vitamin D; green dashed trends shows the optimum value, and red – deficiency threshold.

The consistent decrease of calcidiol level with the age is observed on the flow chart, hereby beginning from the age 10 years, 25(OH)D level is decreased to the deficiency zone (below 20 ng/ml) in which it stays up to 18 years. It is evident that if enteral products (formula, complementary foods) and vitamin D preparations are present in the first year of children's life, then further exogenous intake of cholecalciferol is decreased, and its endogenous synthesis does not allow to provide the normal vitamin D levels in the conditions of limited insolation. The decrease of 25(OH)D level below 20 ng/ml and maintenance of such a low status throughout the adolescent age inevitably reflects rather negatively on health status of the significant part of the child population.

The high prevalence vitamin D deficiency in all age groups except the group of younger children allows to state inefficacy of available prophylactic actions and unanimously shows the necessity of year-round active D-vitaminization of the diet of children and adolescents.

#### 4. Discussion and Conclusions

The presented data demonstrates a rather wide vitamin D deficiency prevalence in all age groups of the child population. This situation described in the Moscow sample of patients confirms the previously published data on the child population of Europe and USA that dictates the necessity of application of new prophylaxis scheme depending on the age [7, 18, 19].

It is important to understand that child's diet which in the parents' opinion is healthy, covers energy needs and consists of natural products, nevertheless, does not provide a child

with sufficient amount of vitamins and micronutrients [20]. The data is especially relevant for vitamin D as its level in the body depends on several conditions and is maintained with the complex regulation system [21, 22].

As confirmed in our data on seasonality of vitamin D deficiency in the mid-latitudes as well as in other literature data, in the conditions of city atmosphere pollution, even a child's stay in the sun in summer months does not allow to liquidate vitamin D deficiency via endogenous synthesis in the skin under effect of UV-rays and achieve its optimum level [14, 23, 24].

Nowadays, the daily vitamin D intake of 400–500 IU/day is recommended for children in Russia during autumn-winter period that according to the large number of clinical studies does not allow to perform effectively mass prophylaxis of hypovitaminosis D [7, 21, 23]. The needs of a child's body are constantly increasing as he/she grows gradually achieving the needs of an adult that explains the need for the increase of prophylactic cholecalciferol dosages in the older age groups.

According to the European authors, the role of vitamin D-oriented nutrition has recently been increasing, hereby diet supplementation promotes maintenance of normal vitamin D levels in children [18, 25].

Therefore, the development of vitamin D insufficiency in children and adolescents residing in Moscow may be prevented with the year-round administration of cholecalciferol in the form of food supplements or vitamin products, while vitamin D intake with food and synthesis in the skin is insufficient for maintenance of its adequate level in a child's body. The necessity of development of new clinical recommendations in prophylaxis and treatment of deficient conditions in children is highlighted.

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