

## Analysis of Vitamin D Levels in Blood Serum in Children

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### Abstract

**Objective:** To analyze the concentrations of vitamin D in the blood serum in children.

**Materials and methods:** Retrospective analysis of vitamin D (25-hydroxycholecalciferol) levels in the blood serum of 2008 children.

**Results:** 41.2% (828) of tests were performed in children under 2 years of age and 58.8% (1180)-for children over 2 years of age. Vitamin D concentrations significantly differ between the groups: 52.1% of children younger than 2 years had an increased concentration of vitamin D and 19.0% had vitamin D deficiency, while the majority (74.0%) of children older than 2 years had the vitamin D deficiency.

**Conclusions:** The intake of vitamin D is not optimal among the children in Lithuania. More than a half of children younger than 2 years receive too high doses of vitamin D, whereas 74% of older children suffer from constant vitamin D deficiency.

**Keywords:** Vitamin D; Vitamin D deficiency; Vitamin D overdose; Children; 25-Hydroxyvitamin D

### Introduction

With the start of testing of vitamin D (25-hydroxycholecalciferol) levels in blood serum in Lithuania, it has been possible to evaluate the sufficiency of this important vitamin in children and therefore precisely recommend the usage of vitamin D supplements. So far, it has been unclear whether the prescribed doses to prevent vitamin D deficiency in babies and children were sufficient enough and if older children, especially teenagers, who were rarely using vitamin D supplements, were getting enough of this vitamin as well as whether Vitamin D usage should be recommended.

It was a common belief that vitamin D deficiency was solely a problem of the Nordic countries. In the current years there has been an increasing amount of studies proving that vitamin D deficiency is at a pandemic level all around the world [1,2]. Even though inadequate exposure to sunlight mainly affects people living in Canada, Ireland, United Kingdom, Scandinavian countries, Baltic countries, Russia and Japan, vitamin D deficiency is found in such countries as Spain, where exposure to sunlight is enough all year round to produce the amount of vitamin D that our body needs [2,3]. Adequate sunlight needed for optimal amount of vitamin D to be made in central Europe occurs from April till the beginning of September [4]. During these months, being outside for 2-3 times a week for 15 minutes from 10 a.m. to 3 p.m. is enough to reach the recommended vitamin D concentration [5]. Unfortunately, increased indoor time, fear of increased risk of skin cancer caused by sunlight, leads to decreased exposure to sunlight, which results in the lack of vitamin D [6]. In Italy and Spain, where ultraviolet B radiation from sunlight is sufficient all year round,

vitamin D deficiency is caused by increased skin pigmentation and active protection from sunlight [2].

The major source of vitamin D for humans is exposure to sunlight or it can be obtained with food and vitamin D supplementation. The best source of vitamin D is considered to be fatty fish, especially salmon [7]. Beef liver, cheese, and egg yolks are also high in vitamin D [8]. Despite the insufficient ultraviolet B radiation from sunlight to produce vitamin D in such countries as Norway or Sweden, there was no vitamin D deficiency found, most likely due to frequent use of fatty fish and fish-oil [2]. 64% of people in Lithuania use fatty fish less than once in a week or do not use it at all [9]. Similar nutritional habits apply to children also-only a third of first grade students (elementary school students) use (consume) fish 1-3 times per week and 44.1%-once or several times a month [10]. Vitamin D concentrations differ among children who use vitamin D supplements and who do not-vitamin D deficiency is more common in children who do not use vitamin D supplements [11].

In the 19th century it was noticed that exposure to the sun decreases the growth retardation and bone deformation related to rickets. In the 20<sup>th</sup> century, after discovering the pathogenesis of rickets, children started being treated with vitamin D supplements. It is known that rickets is the disease of small children, which is the most common in the first two years of children's lives. Due to this reason, in Lithuania the vitamin D is prescribed by doctors and parents only for children under 2 years old.

The perceived wisdom was that vitamin D has an effect only on kidneys, intestinal tract and bones and its main role is maintaining calcium homeostasis and promoting the healthy growth and remodeling of bone. This is now known to be false: after the discovery of vitamin D receptors which were found in the skin, pancreas,

placenta, breasts, prostate, activated T lymphocytes [12], cardiomyocytes, cardio fibroblasts, endothelial cells of the vessels [13], more and more functions of vitamin D are being discovered. Many new vitamin D functions were proved using experimental models with animals, but the number of studies with people is increasing. Vitamin D deficiency is also linked to the immune system [14], insulin secretion and its functions [15].

The number of scientific research in analyzing the vitamin D concentration in blood around the world has increased [16], as well as maps of vitamin D concentration are being comprised [2]. However, there is a growing number of regions where this data is lacking, especially less data is gathered about children [17]. In Lithuania, the amount of comprehensive data on vitamin D concentration in blood for children is small.

### Aims of the study

1. To analyse the results of the tests performed from 2011 to 2016 on the concentration of vitamin D in the blood of children in Lithuania.
2. To compare the test results by sex and age as well as their dependency on a particular season.

### Materials and Methods

Retrospective analysis of vitamin D (25-hydroxycholecalciferol) levels in the blood of 1354 children, hospitalised in Children's Hospital, Affiliate of VULSK between the years 2011 and 2016.

The concentration of 25-hydroxyvitamin D in blood serum is a good indicator showing the reserves of vitamin D in the body. Test result can be measured in nanograms per milliliter (ng/ml) or nanomoles per liter (nmol/l). 1 ng/ml=2.5 nmol/l. Based on Children's Hospital practice vitamin D (25-OH) (nmol/L) tests results were divided into 7 categories:

- Severe deficiency - <25 nmol/L;
- Moderate deficiency - 25-50 nmol/L;
- Mild deficiency - 50-75 nmol/L;
- Optimal concentration - 75-125 nmol/L;
- Increased concentration - 125-250 nmol/L;
- Extremely high concentration - 250-500 nmol/L;
- Toxic concentration - >500 nmol/L.

In order to evaluate the differences of vitamin D levels among children who are being prescribed vitamin D for rickets prevention in Lithuania, and older children, who rarely use vitamin D supplements, children were classified into two groups: group I-children younger than two years, group II-older than two years. The differences between genders and different seasons were also observed.

### Statistical analysis

Data was presented as numbers and frequencies for categorical variables and median values for continuous variables. The continuous

variables were analyzed for normality with Kolmogorov-Smirnov test. Children's age and vitamin D concentration levels were found to have not normal distribution. Categorical variables were compared using chi-square test. Mann-Whitney U and Kruskal-Wallis tests were used to compare vitamin D levels and other factors. A p value less than 0.05 was considered statistically significant. Data analyses were performed using IBM SPSS Statistics version [20].

### Results

Blood tests for vitamin D levels in blood serum have been available at Children's Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos, since 2011. During a 6-year period a total of 2008 tests have been carried out. The annual number of tests grew from 153 performed in the year 2011 to 654 performed in 2016 shown in Figure 1.

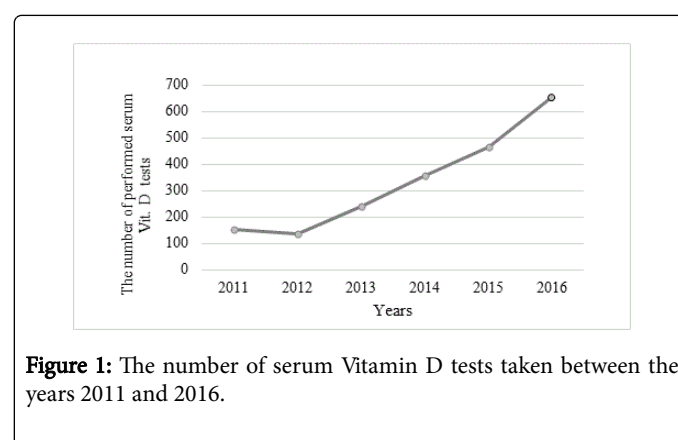


Figure 1: The number of serum Vitamin D tests taken between the years 2011 and 2016.

Of 2008 patients, 41.2% (828) of tests were performed in children under 2 years of age (group I) and 58.8% (1180)-for children over 2 years of age (group II). Out of the targeted, 1130 (56.3%) were boys and 878 (43.7%) were girls. Vitamin D blood levels between boys and girls did not differ significantly ( $p>0.05$ ). The median age of the children was 3.75 year. The largest number of tests were performed in spring (29.6%); the least number of test were conducted in winter-20.4% (410).

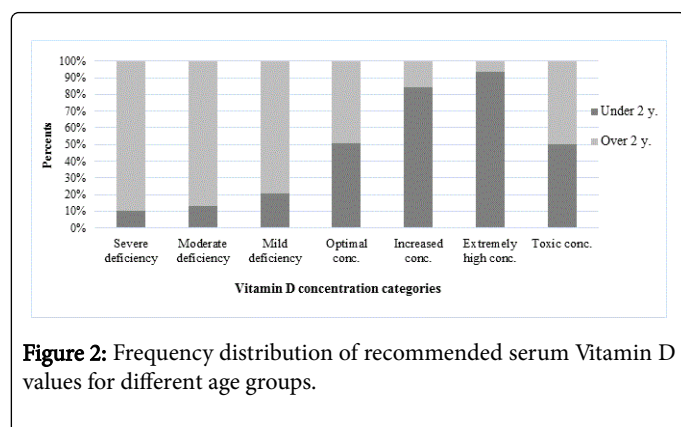
Vitamin D level in blood serum values ranged from 5.5 to 1017 nmol/L, the median value was 72.3 nmol/L. Only 29.0% of children under 2 years of age and only 19.7% of children over 2 years had optimal level of vitamin D. Severe vitamin D deficiency was found in 10.9% (219) of children, moderate deficiency-22.0% (442), mild deficiency-18.4% (369), optimal concentration-23.6% (473), increased concentration-20.9% (419), extremely high concentration-4.0% (80) and toxic concentration was found in 0.3% (6) of children shown in Table 1.

Age groups	Severe deficiency	Moderate deficiency	Mild deficiency	Optimal conc.	Increased conc.	Extremely high conc.	high	Toxic conc.
All children (n=2008)	219	442	369	473	419	80		6

	-10.90%	-22.00%	-18.40%	-23.60%	-20.90%	-4.00%	-0.30%
Children under 2 y. (n=828)	22	59	76	240	353	75	3
	-2.70%	-7.10%	-9.20%	-29.00%	-42.60%	-9.10%	-0.40%
Children over 2 y. (n=1180)	197	383	293	233	66	5	3
	-16.70%	-32.50%	-24.80%	-19.70%	-5.60%	-0.40%	-0.30%

**Table 1:** Vitamin D concentration in the blood serum in different age groups. The results are presented in absolute numbers and as a percentage. Conc.-concentration.

Vitamin D severe deficiency, moderate deficiency and mild deficiency were found statistically significantly more often in Group II (children over 2 years of age), while increased concentration and extremely high concentration-in Group I (children under 2 years) Table 1 and Figure 2. Differences between the groups were significant, i.e., 52.1% of children in group I had an increased concentration of vitamin D and 19.0% had with vitamin D deficiency, while the majority (74.0%) of children in group II had the vitamin D deficiency.



**Figure 2:** Frequency distribution of recommended serum Vitamin D values for different age groups.

Vitamin D concentration differences between seasons have been statistically non-significant in the first group, while the second group showed statistically significant differences between spring and summer ( $p < 0.001$ ), spring and autumn ( $p < 0.001$ ), spring and winter ( $p = 0.01$ ) and between summer and winter ( $p = 0.20$ ), of which lower vitamin D concentrations were present in spring and winter respectively.

## Discussion

Our study showed that only 29.0% of children up to 2 years old (Group I), and only 19.7% over 2 years (Group II), have an optimal vitamin D levels in their blood serum. It was also found that the levels of vitamin D in blood serum differ statistically significantly between Groups I and II. More than half of the children (52.1%) in Group I had increased vitamin D concentrations in their blood serum. Meanwhile, 74% of children in Group II had vitamin D deficiency. This is related to vitamin D prescription traditions, based on an old belief that vitamin D should be used only as a rickets prevention for young kids, as it usually affects children under two years of age [12] and the majority of children receive vitamin D supplements only during the first years of life, and then these supplements are rarely used or not used at all in older age. Our results also confirm that the amounts of

vitamin D that exist in the diet of Group II children is inadequate to keep optimal vitamin D levels in their body and there is insufficient production of vitamin D in skin during exposure to sunlight ultraviolet B radiation.

In our study, more than a half of the children under 2 years were found with higher than optimal vitamin D levels in blood serum and it could be linked to vitamin D supplements overdosing when the amount of vitamin D in high quality adapted formula is not taken into account and/or when non-specific symptoms, such as sweating, restlessness, low muscle tone and/or others are mistaken for vitamin D deficiency symptoms and, without testing vitamin D level in blood serum, vitamin D doses are unreasonably increased.

There was a statistically significant difference in vitamin D levels in blood serum of the older children between the seasons, whilst in younger children this difference was not observed. This showed that in older children, the vitamin D concentration has increased when ultraviolet B radiation from sun was more intense, i.e., in summer and it remains higher during autumn, whilst in spring it is the lowest. Younger children do not experience these variations, as they are using vitamin D supplements, which is reduced in sunny days. Literature of other countries also indicates that the usage of vitamin D supplements decreases the variations of vitamin D concentrations in blood serum between seasons [18] and reduces the risk of getting ill with vitamin D deficiency related diseases [19].

## Conclusion

The intake of vitamin D is not optimal among the children in Lithuania. More than a half (52.1%) of children younger than 2 years age receive too high (excess) doses of vitamin D, whereas 74% of older children suffer from constant vitamin D deficiency. In order to ensure optimal vitamin D concentration in the blood for Lithuanian children, it is necessary to follow the guidelines for the intake of vitamin D supplements.

According to the Central European recommendations for vitamin D supplementation, it is recommended to get from 400 to 600 IU of vitamin D daily for newborns from the first days of life up to 1-1.5 years, while for children over 1-1.5 years of age vitamin D doses should be increased to 600 - 1000 IU of vitamin D per day and this has to be continued during the entire childhood and adolescence [12,20].

Since for light skinned Central Europeans adequate daily vitamin D dose is produced in their skin from April to September, 2-3 times a week for 15 minutes (between the 10<sup>th</sup> to the 15<sup>th</sup> hour) of solar UV radiation affecting about 18% of the body surface (i.e., unveil forearms

and legs) without applying any sunscreen [4], in this period, the prophylactic dose of vitamin D supplements can be skipped.

In case of the doubt on the adequate intake of vitamin D, it is recommended to test its level in blood [12].

### Conflicts of Interest

The authors declare that they have no competing interests.

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