

## Seasonality of vitamin D concentrations and the incidence of vitamin D deficiency in children and adolescents from central Poland

Zmienność sezonowa stężeń witaminy D oraz częstość jej niedoboru u dzieci i młodzieży z regionu Polski Centralnej

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### Abstract

**Introduction:** Vitamin D<sub>3</sub> [25(OH)D] deficiency is a significant problem in Polish children. In many regions of the world, 25(OH)D concentrations show seasonal variation and differences between boys and girls, due to seasonal differences in insolation, as well as different sociological and cultural factors.

**The aim of the study** was to assess the seasonal variations of 25(OH)D concentrations and the incidence of vitamin D deficiency in children from central Poland.

**Material and methods:** The analysis comprised 1275 children, age 3–18 (11.2 ± 4.0) years, with disorders of growing and/or puberty, obesity, and other complaints that could be related to endocrine diseases, except for ones with calcium-phosphorus imbalance, impaired parathyroid hormone secretion, and diseases that may influence vitamin D supply.

**Results:** Seasonal variability of 25(OH)D concentrations was observed with maximal levels in August and minimal in January and close relationship between 25(OH)D levels and insolation in the previous two months. In all the quarters, 25(OH)D concentrations were lower in girls than in boys and in older vs. younger children. The median value of 25(OH)D concentrations was below the lower limit of optimal range during the whole year. High incidence of 25(OH)D deficiency was observed (from 10.7% in August to 80.4% in January) together with low proportion of normal 25(OH)D levels (from 3.6% in January to 42.1% in August).

**Conclusions:** Our results are consistent with previous reports on inadequate vitamin D supplementation in Polish children and adolescents, pointing out the necessity to implement current recommendations concerning vitamin D supplementation and the need for further studies on the consequences vitamin D deficiency for health of children and adolescents, with special attention to the pleiotropic effects of vitamin D.

### Key words:

vitamin D<sub>3</sub> [25(OH)D], vitamin D deficiency, seasonality, vitamin D supplementation.

### Streszczenie

**Wstęp:** Niedobór witaminy D<sub>3</sub> [25(OH)D] jest istotnym problemem w populacji dzieci polskich. W wielu regionach świata stężenia witaminy D<sub>3</sub> wykazują zmienność sezonową oraz różnice wartości u chłopców i dziewcząt związane z sezonowymi różnicami nasłonecznienia oraz uwarunkowaniami natury socjologicznej i kulturowej.

**Cel pracy:** Ocena zmienności sezonowej stężeń 25(OH)D oraz częstości występowania niedoboru witaminy D u dzieci z regionu Polski Centralnej.

**Materiał i metody:** Analizą objęto 1275 dzieci w wieku 3–18 ( $11,2 \pm 4,0$ ) lat z zaburzeniami wzrastania i/lub dojrzewania, otyłością oraz innymi dolegliwościami, które mogły być związane z chorobami gruczołów dokrewnych, z wyłączeniem pacjentów z zaburzeniami gospodarki wapniowo-fosforanowej, nieprawidłowymi stężeniami parathormonu i innymi chorobami, które mogą wpływać na zaopatrzenie w witaminę D.

**Wyniki:** Stwierdzono istnienie zmienności sezonowej stężeń 25(OH)D z najwyższymi wartościami w sierpniu, a najniższymi w styczniu oraz ścisłą zależność pomiędzy stężeniami 25(OH)D i nasłonecznieniem w poprzednich 2 miesiącach. We wszystkich kwartalach stężenia 25(OH)D były mniejsze u dziewcząt niż u chłopców oraz u dzieci starszych niż w młodszych grupach wiekowych. Mediana wartości 25(OH)D pozostawała poniżej dolnej granicy zakresu optymalnego przez cały rok. Stwierdzono dużą częstość niedoboru 25(OH)D (od 10,7% w sierpniu do 80,4% w styczniu), a jednocześnie niski odsetek prawidłowych stężeń 25(OH)D (od 3,6% w styczniu do 42,1% w sierpniu).

**Wnioski:** Uzyskane wyniki są zgodne z wcześniejszymi doniesieniami dotyczącymi niedostatecznego zaopatrzenia w witaminę D populacji dzieci i młodzieży w Polsce, co wskazuje na konieczność adekwatnej suplementacji tej witaminy, jak również na celowość prowadzenia dalszych badań nad konsekwencjami zdrowotnymi niedoboru witaminy D u dzieci, ze szczególnym uwzględnieniem jej działania plejotropowego.

**Słowa kluczowe:**

witamina D<sub>3</sub> [25(OH)D], niedobór witaminy D, sezonowość, suplementacja witaminy D.

## Introduction

It is undisputed that optimal vitamin D supply plays an important role in bone health. In children the first described significant role of vitamin D supplementation was prevention and treatment of rickets. However, in recent years, numerous reports have stressed the pleiotropic effects of vitamin D on different aspects of human health and the role of vitamin D deficiency in the pathogenesis of many diseases [1–5].

The process of vitamin D<sub>3</sub> synthesis from its precursor – 7-dehydrocholesterol – requires adequate skin exposure to sunlight for conversion to previtamin D<sub>3</sub>, and heat for conversion to vitamin D<sub>3</sub> (cholecalciferol). Next, vitamin D<sub>3</sub> must be hydroxylated in the liver to 25-hydroxyvitamin D [25(OH)D] (inactive metabolite) and in kidneys to 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D] (the final active metabolite). The main form of vitamin D in circulation, most widely used for measurement of vitamin D status, is 25(OH)D [2]. Serum 1,25(OH)<sub>2</sub>D is not a reliable marker of vitamin D status because it may be normal or elevated in terms of secondary hyperparathyroidism associated with vitamin D deficiency [6].

The oldest cut-off value for diagnosing vitamin D deficiency, defined based on the reports concerning 25(OH)D levels and development of rickets, was 10 ng/ml [3]. In 1998, this threshold was increased to 20 ng/ml, taking into account the association between vitamin D deficiency and increase of parathyroid hormone (PTH) secretion [7]. Next, the cut-off value was further increased to 30 ng/ml, according to the observations of the higher incidence of secondary hyperparathyroidism in postmenopausal women with lower vitamin D concentrations [8]. Currently, a 25(OH)D concentration of 30 ng/ml is recommended as the threshold for optimal and suboptimal vitamin D supply, while values below 20 ng/ml are considered to be evidence of vitamin D deficiency [5, 6].

Endogenous vitamin D synthesis is closely related to sun exposure and skin pigmentation. In children, seasonality of 25(OH)D concentrations has been reported in studies from different countries with different insolation [9–17]. In countries with

relatively low sun exposure, the problem of vitamin D deficiency on the population level is much more important than the risk of its excess. Thus the exogenous sources of vitamin D, including both natural and fortified foods as well as supplements of diet and pharmaceutical preparations, are very important for its appropriate supply [2].

Studies by Polish authors on vitamin D status in children have pointed out the high incidence of 25(OH)D deficiency in this population [18–21], with marked seasonal variation of 25(OH)D concentrations [19]. Polish recommendations concerning management of vitamin D deficiency were established in 2009 [22], and guidelines for Central Europe in 2013 [5]. However, these recommendations have not been rigorously preserved [4]. In 2018, updated guidelines of vitamin D supplementation were published [23, 24].

The aim of present study was to assess the of seasonal variations of vitamin D concentrations and the incidence of 25(OH)D deficiency in children from central Poland.

## Material and methods

Retrospective analysis included 1275 children (673 boys, 602 girls), age  $11.2 \pm 4.0$  years (mean  $\pm$ SD), range 3–18 years, admitted to the Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital – Research Institute in Lodz in 2014–2017 for diagnostics. The patients were diagnosed due to disorders of growth (short or tall stature), obesity, premature or delayed puberty, irregular menstruation, and/or hirsutism or other complaints that could be related to endocrine diseases. The patients with disorders of thyroid function, pituitary hormone deficiencies (except for those with isolated growth hormone deficiency), disorders of adrenal function, calcium-phosphorus imbalance, and/or impaired PTH secretion, as well as those with other diseases that may influence vitamin D supply (including coeliac disease, other malabsorption syndromes, anorexia nervosa, etc.) were excluded from the

study. The patients did not receive either vitamin D supplementation or any medication that might influence their vitamin D level for at least six months before the assessment.

In all the patients, blood samples were collected during fasting, in the morning hours. Concentrations of 25(OH)D were measured with electrochemiluminescence binding assay (ECLIA), Roche, standardised against LC-MS/MS, range of detection 5.0–60.0 ng/ml. Concentrations over 30 ng/ml were considered normal, concentrations below 20 ng/ml were classified as vitamin 25(OH)D deficiency, and concentrations between 20 ng/ml and 30 ng/ml as suboptimal 25(OH)D supply.

For statistical analysis, the Shapiro-Wilk test was used as the first one for the assessment of distribution of 25(OH)D concentrations in the studied group and in particular subgroups. Due to the lack of normal distribution of 25(OH)D levels, non-parametric tests for independent samples were applied for comparisons between particular groups and subgroups, in-

cluding the Kruskal-Wallis test for multiple samples followed by post-hoc Bonferroni-Dunn test if applicable and Mann-Whitney U test for comparisons between two samples. Statistical significance was defined as  $p < 0.05$ . Finally, the  $\chi^2$  test was applied for comparison of incidences of normal, subnormal, and decreased 25(OH)D levels in particular quarters.

The study was approved by the Committee of Bioethics of the Polish Mother's Memorial Hospital – Research Institute in Lodz, Poland.

### Results

In the studied group the mean 25(OH)D concentration was  $21.6 \pm 8.6$  ng/ml, the median value of 25(OH)D was 20.6 ng/ml, the 25<sup>th</sup> centile was 15.3 ng/ml, and the 75<sup>th</sup> centile was 27.0 ng/ml. Only 17.1% of measured 25(OH)D values were within normal range, 36.2% were suboptimal, and as many as 46.7% confirmed vitamin D deficiency.

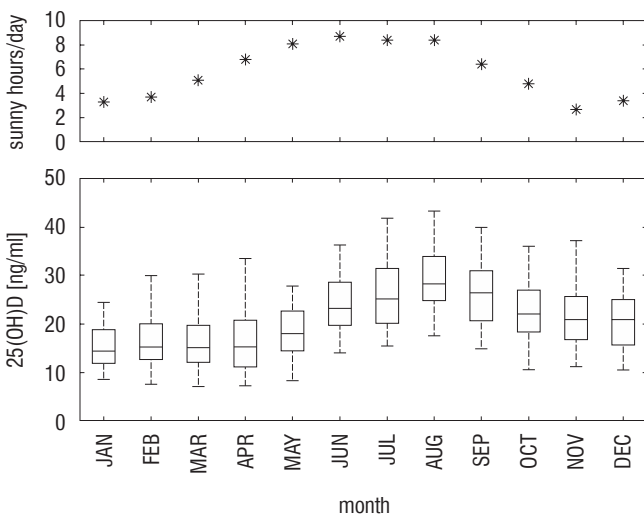
Seasonal variability of 25(OH)D concentrations was observed, with maximal levels in August and minimal in January (Figure 1). Close relationship between 25(OH)D levels and the number of sunny hours in previous months should be noted, with about a two-month shift between maximal insolation and maximal 25(OH)D levels (Figure 1).

Significant differences ( $p < 0.001$ ) in 25(OH)D concentrations in particular quarters (seasons) except for between spring (quarter II – April, May, June) and autumn (quarter IV – October, November, December) were observed, with the highest values in summer (quarter III – July, August, September) and lowest in winter (quarter I – January, February, March; Table I).

In all the quarters, 25(OH)D concentrations were lower in girls than in boys; however, the difference was significant only for the whole year ( $p = 0.03$ ) and not for particular quarters (Table II).

A tendency towards lower 25(OH)D levels in older age groups was marked in particular seasons (Figure 2).

Median value of 25(OH)D concentrations was below the lower limit of optimal range during the whole year (Figure 1). High incidence of 25(OH)D deficiency was observed, ranging from 10.7% in August to 80.4% in January, with a relatively low proportion of patients with normal 25(OH)D levels, ranging from



**Figure 1.** Comparison of number of sunny hours per day, according to www.weatheronline.pl (upper graph), and 25(OH)D concentrations (lower graph) in particular months. Boxes represent median and 25<sup>th</sup>-75<sup>th</sup> centile range, whiskers – minimal and maximal measured values of 25(OH)D concentration

**Table I.** 25(OH)D concentrations in particular quarters (seasons)

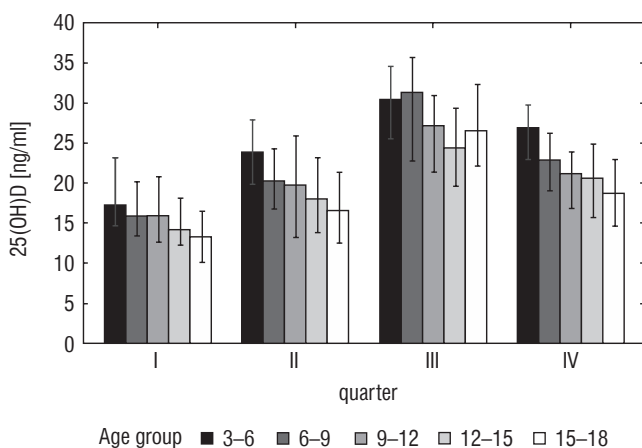
25(OH)D [ng/ml]	Winter (quarter I)	Spring (quarter II)	Summer (quarter III)	Autumn (quarter IV)
median	15.0	19.8	27.0	21.4
25 <sup>th</sup> centile	12.1	14.6	21.9	16.8
75 <sup>th</sup> centile	19.5	24.5	32.5	26.1

Significant differences in Kruskal-Wallis test for quarters:  $p < 0.001$

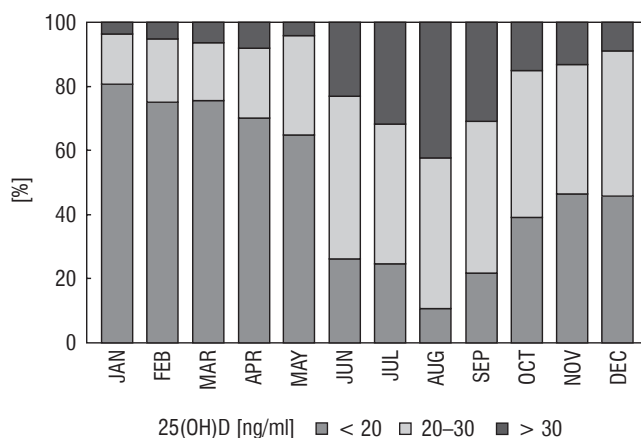
**Table II.** 25(OH)D concentrations in particular quarters (seasons)

25(OH)D [ng/ml]	Boys			Girls		
	median	25 <sup>th</sup> centile	75 <sup>th</sup> centile	median	25 <sup>th</sup> centile	75 <sup>th</sup> centile
whole year	21.6	16.0	27.7	19.9	14.3	26.4
winter (quarter I)	15.8	12.4	20.1	14.2	11.8	19.2
spring (quarter II)	20.2	15.9	25.5	18.7	13.1	24.0
summer (quarter III)	27.4	23.2	32.5	26.4	20.5	32.4
autumn (quarter IV)	22.1	17.7	26.3	20.0	16.3	25.7

Significant difference in Mann-Whitney U test for the whole year:  $p = 0.03$



**Figure 2.** Comparison of 25(OH)D concentrations in boys and girls in particular age groups in 3-year intervals, from 3 to 18 years. Boxes represent median values, whiskers – 25<sup>th</sup> and 75<sup>th</sup> centile of 25(OH)D concentration



**Figure 3.** Distribution of normal, subnormal, and decreased 25(OH)D concentrations in particular months of the year

3.6% in January to 42.1% in August (Figure 3). Significant differences ( $p < 0.001$ ) were found between the incidence of 25(OH)D deficiency in particular quarters, with only 5.1% of children with optimal 25(OH)D concentrations in winter and 35.8% in summer (Figure 4).

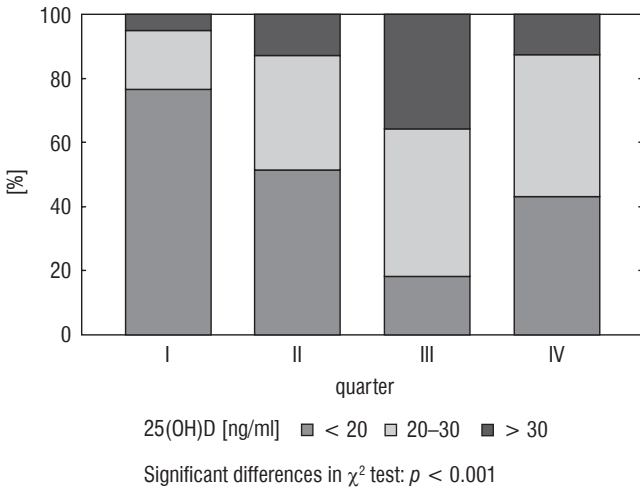
## Discussion

Seasonal variability of vitamin D concentrations, as observed in our study, was also reported in a previous study on Polish children with complaints that might be related to disorders of the skeletal system [19], as well as in numerous reports from regions with different insolation, including countries from Northern Europe [13, 16] and Canada [11], countries from Southern Europe [12, 14, 25, 26], and sunny countries of Asia [10, 15].

In most countries lower vitamin D levels were observed in months with lower insolation; however, the opposite tendency was reported in Saudi Arabia, which might be explained by avoiding excessive sunlight exposure and heat in summer [27].

Significant differences in vitamin D levels between the countries from northern and southern Europe (Ireland, United Kingdom, Netherlands, and Denmark vs. Greece), with similar seasonal variations (more pronounced in southern Greece than in other countries) were reported by O'Neil *et al.* [28].

In European countries, a relatively high incidence of vitamin D deficiency or insufficiency was reported, even in countries with high insolation. In Italian adolescents the incidence of vitamin D deficiency was almost 50%, and an additional 30% of this population presented with suboptimal vitamin D levels [29]. A study on children from the United States [30] revealed 9% incidence of vitamin D deficiency and 61% incidence of its insufficient



**Figure 4.** Distribution of normal, subnormal, and decreased 25(OH)D concentrations in particular quarters of the year

levels, with age-, gender-, and race-related differences. In our study the total incidence of suboptimal 25(OH)D concentrations within the whole year was 82.9%, including 47.6% of 25(OH)D deficiency.

Moreover, a study by Shakeri *et al.* [31] showed that in more than 90% of children with optimal vitamin D concentrations in the end of summer, a significant decrease in vitamin D level was observed in the end of winter, leading to its suboptimal concentrations or deficiency in more than 50% of them.

In Polish children and adolescents, vitamin D concentrations were lower in girls than in boys during the whole year, and in older age groups compared with younger ones. A tendency towards lower vitamin D levels in girls than in boys and in females than in males was also reported in other studies from different countries [26, 30, 32]. A tendency towards lower vitamin D concentrations in older age groups was also observed in a previous report from our region [19]. Similar observations were obtained from the United States [30] and Saudi Arabia [32]. However, such a phenomenon was not confirmed in adolescents from South Africa [9]. It seems that these findings might be explained by lower physical activity of girls (including team games in the field) and less time spent out-of-doors by

children from older age groups and adolescents, especially as the opposite tendency was reported in children with complaints related to the skeletal system that might lead to lower physical activity in them [19]. In Iranian children [10] a difference in vitamin D levels between boys and girls was observed during summer but not in winter. The problem of vitamin D deficiency is especially important in girls and women from Arabian countries, who are fully veiled due to religious reasons [32]. Interestingly, no difference in vitamin D levels between adolescent boys and girls was reported in a study from Italy [29].

In our study the incidence of 25(OH)D concentrations below 30.0 ng/ml was even higher than that observed in children from our region who were hospitalised due to different complaints that might be related to disorders of the musculoskeletal system in the Department of Paediatric Propaedeutics and Bone Metabolic Diseases of the Medical University of Lodz in 2011–2015 [19] (82.9% vs. 71.6%). This finding may be explained by the fact that the patients with problems related to bone health could receive prophylactic vitamin D supplementation (however, none of them was treated with therapeutic doses of vitamin D), while the patients included in our study did not use vitamin D preparations. Nevertheless, in both groups, the addition of vitamin D to food products for younger children and its supplementation in the form of candies or jellybeans should be taken into account.

## Conclusions

Both the present study and previous reports concerning Polish children and adolescents [18, 19] indicate inadequate vitamin D supplementation. It seems very important to implement current recommendations concerning vitamin D supplementation [5, 22] in the Polish paediatric population. Monitoring vitamin D concentrations during its supplementation seem necessary, especially because the data presented by Koflątaj *et al.* [33] have pointed towards the inadequacy of recommended doses of vitamin D to obtain its optimal level and the necessity of individualisation of vitamin D doses as well as of measurement of 25(OH)D concentrations before and during supplementation. The relationships between suboptimal or decreased vitamin D levels and their real consequences for the health of children should also be evaluated with special attention paid to the pleiotropic effects of vitamin D.

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