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ORIGINAL ARTICLE

Evaluation of Vitamin D Levels According to Age, Gender and Seasonal Characteristics in Children and Adolescents

Çocuk ve Adölosanlarda Yaş, Cinsiyet ve Mevsimsel Özelliklere Göre Vitamin D Düzeylerinin Değerlendirilmesi

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ABSTRACT

Objective: Vitamin D is an essential hormone for the health of the musculoskeletal system and acts in immune system, cardiovascular system and metabolic homeostasis. The aim of this study was to determine the vitamin D status of children in the central Anatolia region. Also, the study evaluated the age, gender and seasonal variations in the study population.
Materials and Methods: Children aged 1-17 years who were admitted to a Secondary Maternity and Children Hospital in Konya were included in this study. The medical records of the participants were retrospectively evaluated from the hospital information system between July 2016 and December 2021. All patients were categorized according to age, gender, and season in which their blood samples were obtained.
Results: A total of 3547 children were included in the study. The mean serum level of 25-hydroxyvitamin D in the study population was 16.45±9.39 ng/ml. The number of samples obtained in winter was 1063 (30%) and in summer 756 (21.3%), respectively. Only 7.4% (n=262) of the participants had sufficient vitamin D levels (>30 ng/ml) in the study population. Additionally, severely deficiency of serum 25-hydroxyvitamin D level was mostly measured in winter season (378 patients, 45%). Severely deficiency (352 patients, 41.9%) was most common in children aged 12-17 years. Among all patients, only 7.4% had sufficient serum 25-hydroxyvitamin D levels. Also, 5.2% (103 patients) of the girls and 3.7% (59 patients) of the boys had sufficient 25-hydroxyvitamin D levels. On the other hand, severely deficiency of serum 25-hydroxyvitamin D levels was most common in boys (521 patients, 33.1%) than in girls (137 patients, 6.9%).
Conclusion: Vitamin D deficiency/insufficiency is wide spread among children in the world and in Turkiye. Our study revealed that seasonal variations, age and gender affect the serum levels of 25-hydroxyvitamin D in children. In this context, the importance of vitamin D rich foods or vitamin D supplementation is increasing.

Keywords: Vitamin D, children, adolescent, age, seasonal variation, treatment.

ÖZ

Amaç: D vitamini, kas-iskelet sistemi sağlığı için gerekli bir hormondur ve bağışıklık sistemi, kardiyovasküler sistem ve metabolik homeostazda görev yapar. Bu çalışmanın amacı, Türkiye'nin orta bölgesinde yaşayan çocukların D vitamini durumunu belirlemektir. Ayrıca, çalışma yaş, cinsiyet ve mevsimsel değişiklikleri değerlendirdi.
Gereç ve Yöntem: Bu çalışmaya Konya'da ikinci basamak bir Kadın Doğum ve Çocuk Hastanesi'ne başvuran 1-17 yaş arası çocuklar dahil edildi. Katılımcıların tıbbi kayıtları Temmuz 2016 ve Aralık 2021 tarihleri arasında geriye dönük olarak hastane bilgi sisteminden incelendi. Tüm hastalar yaş, cinsiyet ve kanlarının alındığı mevsime göre kategorize edildi.
Bulgular: Toplam 3547 çocuk çalışmaya dahil edildi. Çalışma popülasyonundaki ortalama serum 25-hidroksivitamin D düzeyi 16.45±9.39 ng/ml idi. Kış aylarında elde edilen örnek sayısı sırasıyla 1063 (%30) ve yaz aylarında 756 (%21,3) olmuştur. Katılımcıların sadece %7.4'ü (n=262) çalışma popülasyonunda yeterli D vitamini düzeyine (>30 ng/ml) sahipti. Ayrıca şiddetli serum 25-hidroksivitamin D düzeyi eksikliği en çok kış mevsiminde ölçüldü (378 hasta, %45). Şiddetli eksiklik (352 hasta, %41.9) en yaygın olarak 12-17 yaş arası çocuklarda görüldü. Tüm hastalar arasında sadece %7.4'ünde yeterli serum 25-hidroksivitamin D seviyeleri vardı. Ayrıca, kızların %5,2'si (103 hasta) ve erkeklerin %3,7'si (59 hasta) yeterli 25-hidroksivitamin D düzeyine sahipti. Diğer taraftan, serum 25-hidroksivitamin D düzeylerinin ciddi eksikliği, kızlardan (137 hasta, %6.9) daha çok erkek çocuklarda (521 hasta, %33.1) yaygındı.
Sonuç: D vitamini eksikliği/yetersizliği dünyada ve Türkiye'de çocuklar arasında yaygın olarak görülmektedir. Çalışmamız mevsimsel farklılıklar, yaş ve cinsiyetin çocuklarda 25-hidroksivitamin D serum düzeylerini etkilediğini ortaya koydu. Bu bağlamda D vitamini yönünden zengin besinlerin veya D vitamini takviyesinin önemi giderek artmaktadır.

Anahtar Kelimeler: Vitamin D, çocuk, adölosan, yaş, mevsimsel farklılık, tedavi.

Introduction

Vitamin D is a fat-soluble vitamin that acts as a steroid hormone. Most of vitamin D is synthesized endogenously whereas a small amount of vitamin D is taken from foods. During exposure to sunlight, 7-dehydrocholesterol is synthesized in the skin. 7-dehydrocholesterol is hydroxylated in the liver to 25-hydroxyvitamin D. It is then hydroxylated in the kidney to 1.25-hydroxyvitamin D (1).

Vitamin D together with parathyroid hormone plays an important role in the regulation of calcium and phosphate homeostasis in the body. 1.25 dihydroxyvitamin D3, active form of vitamin D, enhances calcium absorption in the duodenum and phosphate absorption in the ileum and reduces calcium excretion by the kidney (1,2).

Many organs have 25(OH)D receptors which bind 25-hydroxyvitamin D (2). Instead of relying on the renal production of 1.25-dihydroxyvitamin D from 25-hydroxyvitamin D, these organs form 1.25-dihydroxyvitamin D locally in a paracrine fashion. Therefore, these organs depend on the availability of vitamin D and its transformation to 25-hydroxyvitamin D by the liver to provide circulating 25-hydroxyvitamin D (1,2). In the early 21st century, there were reports of vitamin D's potential role in disease processes not related to calcium homeostasis and bone health. These disease processes in adults found to have an association with vitamin D status include cancer, specifically breast, colon, and prostate; heart disease; autoimmune disease, specifically diabetes, rheumatoid arthritis, and systemic lupus erythematosus; infectious disease, specifically influenza and tuberculosis; and allergic disease (3).

Vitamin D deficiency is a highly prevalent condition among infants, children, and adolescents around the world. In addition to rickets, growing evidence suggests that vitamin D deficiency may be a risk factor for the development of many chronic diseases throughout the life span, including autoimmune conditions, cardiovascular diseases, and cancer (4). Identification, treatment and prevention of vitamin D deficiency in childhood may, therefore, have profound future health effects.

Hypovitaminosis D may be a result of inadequate effective sun exposure, poor dietary intake of vitamin D, malabsorption syndromes, conditions or drugs that impair vitamin D metabolism, life style habits, age, low maternal levels of vitamin D, and/or genetic predisposition (5).

The aim of this retrospective single centre study was to determinate the prevalence of vitamin D deficiency in a population of children and adolescents. Secondary aims were to determine the risk factors for hypovitaminosis D including age, gender and seasonal variations if current guidelines are applicable to this population.

Materials and Methods

This study was conducted in a pediatric clinic of a secondary hospital in Turkey. The medical records of the participants were retrieved from the hospital information system, retrospectively. Patients who had health problems requiring regular treatment and/or a special diet, with either or both lasting for 3 months or longer, were excluded from the study. The exclusionary health problems included asthma, diabetes mellitus, epilepsy, malabsorption syndromes and toxic levels of vitamin D (vitamin D level >100 ng/ml). Additional exclusion criteria were the presence of growth retardation–defined as having a weight and height under the 3rd percentile and according to the growth charts based on age and sex for Turkish children (6) and suffering from obesity–defined as having a body mass index (weight in kilograms divided by height in meters squared) at or above the 95th percentile, according to the growth curves based on age and sex for Turkish children (7).

A total of 3547 healthy children aged 1 to 17 years who were referred to pediatric outpatient clinics at our hospital from July 2016 to December 2021, were included in this study. Their weights were measured with a calibrated digital scale and their heights with a stadiometer, before the physical examination. Venous blood samples were obtained from all the patients after a physical examination that took place in the morning hours, 8.30 a.m. -12.00 noon. Serum 25-hydroxyvitamin D levels (normal values: 20-100 ng/ ml) were measured by electrochemiluminescence method using Adivia Centeur XP (Siemens, Erlangen, Germany). Vitamin D levels were analyzed immediately after the blood samples were taken. For the evaluation of the results the participants were divided into 4 age groups: <1 year, 1 to 5 years, 6 to 11 years, and 12 to 17 years. They were also classified according to their vitamin D status, as: severely deficiency, <10 ng/ml; moderately insufficiency, 10–20 ng/ml; mildly deficiency 21-30 ng/ml; and sufficiency >30 ng/ml (8,9). Also, vitamin D levels were classified according to seasons to determine the seasonal variations.

Statistical analysis

Statistical analyses were done using SPSS for Windows Version 17.0 software (Chicago, IL, USA). Data distributions and test of normality were evaluated with Shapiro–Wilk test. Categorical data were presented as frequencies (%) and median (data range) or mean±SD depending on whether the distribution was homogeneous using Chi-square test. Mann–Whitney U test was used for nonparametric data analysis. The Chi-square or Fisher's exact tests were used to compare the categorical variables. All p values were two-tailed and values below 0.05 were considered statistically significant.

Results

In this study, the vitamin D status of 3547 healthy children categorized according to age, gender, and the season in which their blood had been sampled was presented (Table 1). Of these children 44.4% (1574 patients) were boys and 55.6% (1973 patients) were girls. The mean age of the population was 6.99±5.05 years (1–17 years) and no statistical significance was found between the girls and boys for age (p=0.532). Also, 1626 (45.8%) children were in the age group of 1-5 years, while only 53 (1.6%) children were <1 year old age. On the other hand, there was a significant statistical difference between the groups in terms of the number of cases included by age groups (p<0.001, for all).

The mean serum level of 25-hydroxyvitamin D in the study population was 16.45±9.39 ng/ml (4-97.8 ng/ml). In addition, the mean serum concentrations of 25-hydroxyvitamin D were 16.3±9.71 ng/ml in the

boys and 15.19±10.13 ng/ml in the girls, respectively (p<0.001).

The number of samples obtained in winter was 1063 (30%), in spring 656 (18.5%), in summer 756 (21.3%) and in autumn 1072 (30.2%), respectively. Only 7.4% (n=262) of the participants had sufficient vitamin D levels (>30 ng/ml) in the study population, whereas majority of children (51.4%, 1823 patients) had moderately insufficient serum levels of 25-hydroxyvitamin D (Table 1). Additionally, severely deficiency of serum 25-hydroxyvitamin D level was mostly measured in winter season (378 patients, 45%), while sufficiency of serum 25-hydroxyvitamin D level was usually measured in autumn (8 patients, 32.2%) and summer (77 patients, 29.5%) (Table 2).

Table 1: Demographic and laboratory characteristics of study population.

Variable	N	%
Age		
Female	1973	55.6
Male	1574	44.4
Gender		
<1 year	53	1.6
1-5 years	1626	45.8
6-11 years	1058	29.8
12-17 years	810	22.8
Seasons		
Spring	656	18.5
Summer	756	21.3
Autumn	1072	30.2
Winter	1063	30
Serum 25-hydroxyvitamin D status (ng/ml)		
severely deficiency (<10 ng/ml)	840	23.6
moderately insufficiency (10–20 ng/ml)	1823	51.4
mildly deficiency (21-30 ng/ml)	623	17.6
sufficiency (>30 ng/ml)	261	7.4

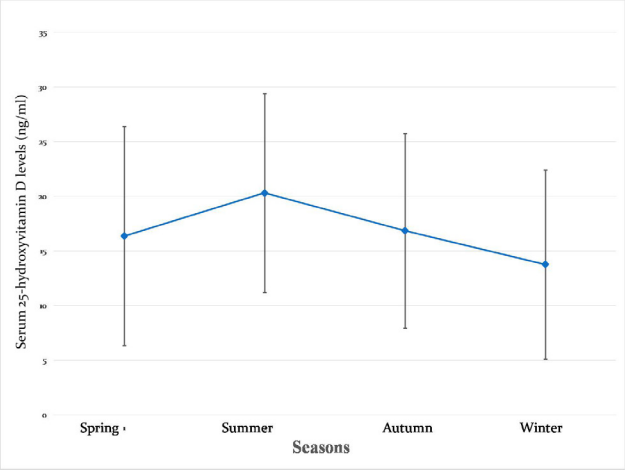

Figure 1: Variations of serum 25-hydroxyvitamin D levels in different seasons.

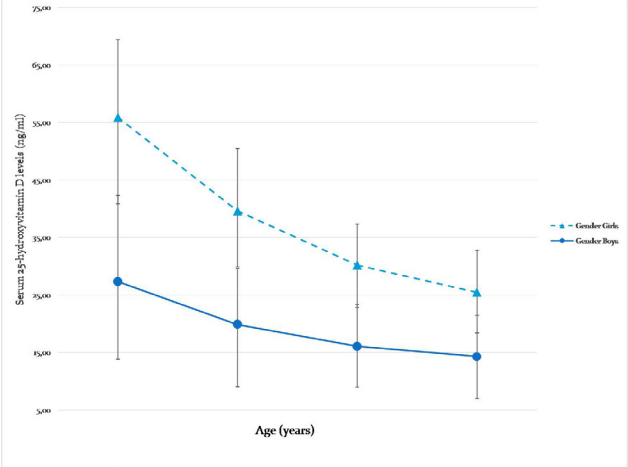

Figure 2: Variations of serum 25-hydroxyvitamin D levels according to age and gender.

Table 2: Seasonal variations and serum 25-hydroxyvitamin D status in the study population.

Serum 25-hydroxyvitamin D status (N, %)	Seasons (N)				Total
	Spring	Summer	Autumn	Winter	
Severely deficiency (<10 ng/ml)	192 (22.8)	67 (8.0)	203 (24.2)	378 (45.0)	840
Moderately insufficiency (10–20 ng/ml)	315 (17.3)	388 (21.3)	578 (31.7)	542 (29.7)	1823
Mildly deficiency (21-30 ng/ml)	93 (14.9)	224 (36)	207 (33.2)	99 (15.9)	623
Sufficiency (>30 ng/ml)	56 (21.5)	77 (29.5)	84 (32.2)	44 (16.8)	261
Total	656	756	1072	1063	3547

Table 3: Serum 25-hydroxyvitamin D status and age groups in the study population.

Serum 25-hydroxyvitamin D status (N, %)	Age groups (N)				Total
	<1 year	1-5 years	6-11 years	12-17 years	
Severely deficiency (<10 ng/ml)	7 (0.8)	213 (25.4)	268 (31.9)	352 (41.9)	840
Moderately insufficiency (10–20 ng/ml)	12 (0.7)	813 (44.6)	612 (33.6)	386 (21.2)	1823
Mildly deficiency (21-30 ng/ml)	9 (1.4)	402 (64.5)	150 (24.1)	62 (10.0)	624
Sufficiency (>30 ng/ml)	25 (9.6)	198 (75.9)	28 (10.7)	10 (3.8)	261
Total	53	1626	1058	810	3547

On the other hand the mean serum 25-hydroxyvitamin D levels were evaluated considering the season in which blood samples were taken. In winter and spring, the mean serum concentrations were 13.76±8.66 ng/ml and 16.36±10.01 ng/ml, respectively. The levels were significantly higher in summer and autumn with the values of 20.30±9.10 ng/ml and 16.85±8.89 ng/ml,

respectively (Figure 1). In addition, among the mean values of serum 25-hydroxyvitamin D level according to the seasons; significant statistical differences were found between spring and summer (p<0.001), spring and winter (p<0.001), summer and autumn (p<0.001), summer and winter (p<0.001), autumn and winter seasons (p<0.001).

The age group, 1-5 years was the largest group of the study, with 1626 participants and most of them (813 patients, 44.6%) had moderately insufficiency of serum 25-hydroxyvitamin D levels (Table 3). Similarly, mildly deficiency (402 patients, 62.5%) and sufficiency (198 patients, 75.9%) were most common in children aged 1-5 years. However, severely deficiency (352 patients, 41.9%) was most common in children aged 12-17 years. Among all patients, only 7.4% had sufficient serum 25-hydroxyvitamin D levels. Moreover, 5.2% (103 patients) of the girls and 3.7% (59 patients) of the boys had sufficient 25-hydroxyvitamin D levels. Also, severely deficiency of serum 25-hydroxyvitamin D levels were most common in boys (521 patients, 33.1%) than in girls (137 patients, 6.9%) (Figure 2).

Discussion

In our study, a high prevalence of poor vitamin D status was found in a sample of children aged 1to 17 years old. These results show that low vitamin D status is an important and common public health problem in children in the central Anatolia region and is related to age, gender and season (worsening in those with less sunlight). In our study, the highest frequency of severe insufficiency was commonly detected in boys and in children aged 12-17 years.

Vitamin D, a prohormone, is converted in the liver to 25-hydroxyvitamin D, and then in the kidney to 1,25-dihydroxyvitamin D, the active metabolite involved in calcium and phosphorus homeostasis (10). Vitamin D deficiency appears to be a widespread global problem prevalent in all age groups. Estimates suggest that up to 1 billion people around the world may have vitamin D deficiency or insufficiency, if insufficiency is defined as a 25-hydroxyvitamin D level ≤30 ng/mL (11).

Increasing evidence suggests that optimal vitamin D status throughout the lifespan—even in utero—may be important not only in maintaining bone health, but also in protecting against many chronic conditions, including autoimmune diseases, diabetes, cardiovascular diseases, and cancer (12). Many bodily tissues express the nuclear receptor for 1,25-dihydroxyvitamin D, including the stomach, pancreas, brain, skin, gonads, activated T and B lymphocytes, and activated macrophages (5,13). Several of these tissues are also capable of producing the 1-alpha hydroxylase enzyme, allowing for the local production of 1.25-dihydroxyvitamin D 1.25-dihydroxyvitamin D (13). 1.25-dihydroxyvitamin D is involved in the regulation of genes controlling cell proliferation and differentiation, apoptosis, and angiogenesis (13).

In Turkiye, there were reports from the Eastern and Western regions that evaluated the serum vitamin D levels. From Western regions o Turkey: Doğan et al. and Kocaman reported the mean serum vitamin D levels as 28.00±15.55 ng/mL and 30.3±16.2 ng/mL, respectively (14,15). On the other hand, studies from Eastern region of Turkey revealed the mean serum vitamin D levels as 17.1 ng/mL in the study of Fettah et al. and 21.3 ng/mL in girls with 22.5 ng/mL in boys in the study of Topal et al. (16,17).

Reports from the Northern region of Turkey revealed lower serum levels of 25-hydroxyvitamin D. Durmaz et al. reported the mean serum level of 25-hydroxyvitamin D as 16.3 ng/mL in children aged 0-18 years (18). Similarly, the study of Güven et al. revealed that the mean serum levels of 25-hydroxyvitamin D were 23.3±8.88 ng/mL in winter and 27.9±8.27 ng/mL in autumn in children, respectively (19). Additionally, Karagüzel et al. reported the mean serum level of 25-hydroxyvitamin D as 34.3±18.3 nmol/L in their series (20).

The studies reported from the Southern region of Turkey revealed higher serum levels of 25-hydroxyvitamin D. Bucak et al. reported the mean serum level of 25-hydroxyvitamin D as 32.9±13.9 ng/mL in girls and 34.4±14.6 ng/mL in boys, respectively (21). Similarly, Matyar et al. reported higher levels of serum 25-hydroxyvitamin D as 48.42±0.54 nmol/L in girls and 52.95±0.92 nmol/L in boys, respectively (22). Reversely, the study of Savaş et al. revealed the serum levels of 25-hydroxyvitamin D as 15.44 ng/mL in girls and 17.73 ng/mL in boys, respectively (23).

In the central Anatolia region, in a study of Solak et al., among 35667 patients they found the serum vitamin D level as 14.5±8.8 ng/ml in women and 18.1±8.4 ng/ml in men, respectively (24). Also, Öğüş et al. reported the mean vitamin D levels as 22.49±13.88 ng/mL in female patients and 23.75±10.57 ng/mL in male patients (25).

In our study, the mean serum level of 25-hydroxyvitamin D was determined as 16.45±9.39 ng/ml and this finding is similar to the reports from Eastern and Northern regions of Turkiye. Also, our findings revealed that seasonal variations affect the serum levels of 25-hydroxyvitamin D in children whose lowest levels were measured in winter and spring. Additionally, severely deficiency (352 patients, 41.9%) was the most common in children aged 12-17 years. These findings were similar to previous reports from our country.

In 2008, in response to the growing evidence of vitamin D deficiency in children, the American Academy o Pediatrics recommended at least 10 µg/day vitamin D for all children (26). In children, the ideal 25-hydroxyvitamin D serum level to prevent short and long-term health complications is unknown, but limited existing data suggest a similar threshold of ≥30 ng/mL (75 nmol/L) (10,11). Supplementation trials in preterm

and term infants, and children have shown that 25-hydroxyvitamin D levels reach a plateau around 30 ng/mL (75 nmol/L) (1,2). To achieve this serum level, infants need vitamin D supplements of 400–1,000 IU per day depending on their vitamin D stores at birth (1). Daily doses as high as 3,000 IU of vitamin D2 in premature infants, and 4,000 IU in older children, have been used to achieve 25-hydroxyvitamin D levels of 30 to 33 ng/mL (75 to 83.5 nmol/L) without adverse effects (1,2).

Finally, vitamin D deficiency/insufficiency is wide spread among children in the world and in Turkiye. It is known that sunlight is not utilized enough due to various reasons today. In this context, the importance of vitamin D rich foods or vitamin D supplementation is increasing. Our study was a large children based study which showed a high prevalence of poor vitamin D status. Furhermore, the study revealed that seasonal variations, age and gender affect the serum levels of 25-hydroxyvitamin D in children.

Conflicts of Interest: None.

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Ethical Standards: This is a retrospective study. The authors assert that all procedures contributing to this study comply with the ethical standards of the Turkish Council of Medical Research and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by Republic of Turkey, Ministry of Health, Konya Provincial Health Directorate on 14.03.2022 with the number of E-86737044-806.01.03-1498.

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