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Original Article

The Status of Vitamin D Among Children Aged 0 to 18 Years

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ABSTRACT

Aim: This study aimed to examine the status of vitamin D in children, to compare vitamin D levels according to the seasons, and to estimate vitamin D testing trends during the years of the study.

Materials and Methods: Blood 25-hydroxyvitamin D [25(OH)D] levels of 51,560 children aged between 0-18 years who had been admitted to nine hospitals between 2015 and 2017 were evaluated. Comparisons of 25(OH)D levels with age groups, gender, and seasons were made. Additionally, vitamin D testing was compared year by year in terms of frequency.

Results: Of the patients, 20% (n=10,611) had vitamin D deficiency and 34% (n=17,385) had vitamin D insufficiency. Serum 25(OH)D levels were significantly higher in boys than in girls ($p<0.01$). There was a significant difference between serum 25(OH)D levels and the age groups. The highest mean 25(OH)D levels were detected in infants (33.95 ng/mL) and the lowest in adolescents (18.3 ng/mL). Significant seasonal variability of 25(OH)D levels was detected ($p<0.01$). Vitamin D deficiency was determined most frequently in winter with a frequency of 30.7%. A three-fold increase in 25(OH)D testing was determined over the 3-year period.

Conclusion: Female gender, adolescence, and the winter season were found to be important risk factors for vitamin D deficiency or insufficiency. Further evidence is needed to clarify whom to test in order to avoid over-testing.

Keywords: Children, 25-hydroxyvitamin D, seasonality, vitamin D deficiency

Introduction

The main source (about 90%) of vitamin D is synthesized in the skin from provitamin D3 (7-dehydrocholesterol) upon ultraviolet B exposure and 10% comes from animal-derived foods with oily fish being the most important (1). Vitamin D plays a key role in regulating calcium and phosphorus homeostasis and bone health. Vitamin D also exerts extra-skeletal actions. A growing number of studies have demonstrated that low vitamin D status plays a possible role in the pathogenesis of several pathological conditions, including infectious, allergic, neuropsychiatric, and autoimmune diseases (2).

It is widely acknowledged that 25-hydroxyvitamin D [25(OH)D] serum concentration is the best indicator to evaluate vitamin D status. In the literature, several cut-off points have been proposed for vitamin D levels (2). A global consensus statement of 11 international scientific societies defined 25(OH)D levels as follows; >50 nmol/L

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(>20 ng/mL) indicates sufficiency, 30-50 nmol/L (12-20 ng/mL) indicates insufficiency and <30 nmol/L (<12 ng/mL) indicates deficiency (3). Vitamin D insufficiency and deficiency are common worldwide among children of all age groups (4-6).

The winter season, non-white ethnicity, the amount of time spent outdoors during summer, female gender, higher age, higher Tanner stage, and lower household income have all been observed to be associated with vitamin D deficiency in childhood (7). The dietary vitamin D intake is often insufficient to cope with the seasonal deficits of sunlight exposures during winter. Vitamin D deficiency is an important problem in countries with relatively low sun exposure (1). Seasonal variability of 25(OH)D concentrations in children has been reported in studies from different countries (4-6).

Most patients with vitamin D deficiency are asymptomatic, so whom to test is becoming a major question. Also, increasing awareness of vitamin D deficiency among physicians, the media, and the public causes vitamin D to be more or over investigated in comparison with previous years (8). Reports demonstrate that there is over-screening, overdiagnosis, and overtreatment for vitamin D deficiency in healthy individuals (9). Large increases in vitamin D testing have been reported from Australia, the UK, and the USA in recent years (9-11). A similar increase has been observed in our country, Turkey, but there has been no study on this subject to date. This study aimed to examine vitamin D status in children aged between 0 and 18 years, to compare vitamin D levels according to the seasons, and to evaluate vitamin D testing trends during the years of our study.

Materials and Methods

In this study, the data of 51,560 children aged between 0 and 18 years who had been admitted to nine hospitals in Ankara between the years 2015 and 2017 were evaluated. The hospitals participating in the study were Ankara Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Ankara Children's Hematology-Oncology Training and Research Hospital, Ankara Numune Training and Research Hospital, Ankara Yüksek İhtisas Training and Research Hospital, Dr. Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara Physical Medicine and Rehabilitation Training and Research Hospital, Haymana State Hospital, Şereflikoçhisar State Hospital, and Ankara Gölbaşı Şehit Ahmet Özsoy State Hospital. The present study was approved by the Ethics Committee of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital (15.05.2019/297). Informed consent was not obtained because this was a retrospective study.

The data regarding blood 25(OH)D levels were obtained from hospital registration systems and recorded on a chart. The children were categorized into age groups as follows; infancy group (0-2 years), preschool age group (3-5 years), school-age group (6-9 years), and adolescents (10-18 years). 25(OH)D level determination had been made by tandem mass spectrometry (LC-MS/MS) using API 3200 (Applied Biosystem Sciex, Concord, Canada, L4K4V8) from blood samples where 25(OH)D levels were determined in units of "ng/mL". Vitamin D levels were classified into three groups as follows; <12 ng/mL indicating deficiency, 12-20 ng/mL indicating insufficiency, and >20 ng/mL indicating normal (3). The seasonal variation of serum 25(OH)D levels was also evaluated. The seasons were categorized as "Spring" (March-April-May), "Summer" (June-July-August), "Autumn" (September-October-November), and "Winter" (December-January-February). Comparisons of 25(OH)D levels with age, gender, and the seasons were made. Vitamin D testing was compared year by year in terms of frequency.

Statistical Analysis

Statistical analysis of the data was performed using the SPSS 20.0 software system for Windows (IBM Corp., Armonk, NY). Frequency and percentage values were given for nominal variables and mean and standard deviation values for continuous variables. Student's t-test was used to investigate the difference in vitamin D levels between males and females. One-way ANOVA was used to investigate the difference in vitamin D levels according to the seasons and age groups. Differences between each season and age group were compared with Tukey's honestly significant difference test. Nominal variables were compared using Pearson chi-square or Fisher's exact test. $P<0.05$ was considered statistically significant.

Results

The mean serum 25(OH)D level of 51,560 children was 22.86±16 (interquartile range: 15) ng/mL. Of the patients in this study, 28,309 (45%) were girls and 23,251 (55%) were boys. The mean serum 25(OH)D level was 25.1±16.6 ng/mL in boys, and 21.0±15.5 ng/mL in girls. Serum 25(OH)D levels were significantly higher in boys than in girls ($p<0.01$, Student's t-test). Of the patients, 20% (n=10,611) had vitamin D deficiency and 34% (n=17,385) had vitamin D insufficiency. It was determined that 61.4% (n=37,331) of girls and 45.6% (n=10,603) of boys suffered from vitamin D deficiency or insufficiency. Vitamin D deficiency was 26.1% (n=7,424) in girls and 13.7% (n=3,187) in boys. Vitamin D insufficiency was 35.2% (n=9,969) in girls and 31.9% (n=7,416) in boys (p<0.01). There was a significant difference between serum 25(OH)D levels in terms of the age groups (p<0.01, ANOVA). The highest mean 25(OH)D levels were detected in infants (33.95 ng/mL) and the lowest in adolescents (18.3 ng/mL) compared with preschool and school-age groups. The mean serum 25(OH)D levels according to gender and age groups are shown in Table I.

Significant seasonal variability of 25(OH)D levels was detected (p<0.01, ANOVA). Summer and autumn had higher mean levels of 25(OH)D than winter and spring. Vitamin D deficiency was determined most frequently in winter with 30.7% followed by 28.4% in spring, 12.7% in summer, and 12.2% in autumn. In autumn, the prevalence of vitamin D deficiency (12.2%) or insufficiency (32.6%) was 44.8% in total giving the lowest seasonal percentage. In winter, 64.8% of children had vitamin D deficiency or insufficiency, and this was the highest percentage among the four seasons. The seasonal variation of 25(OH)D levels is shown in Table II. The frequency of vitamin D testing was observed to increase gradually. Vitamin D levels were examined in 8,834 children in 2015 and 27,282 in 2017 (Figure 1). A three-fold increase in 25(OH)D testing was determined over a 3-year period.

Multivariate regression analysis showed that being of adolescent age [odds ratio (OR): 6.98], being in the spring season (OR: 2.64) and being a girl (OR: 1.78) were significantly associated with vitamin D insufficiency (95% confidence interval) (Table III).

Discussion

Vitamin D deficiency is a serious public health problem worldwide. Vitamin D status has been intensively determined in different populations, including various ethnic and age groups in recent decades (12). In our study, vitamin D deficiency was determined at a frequency of 20% in our full study population. 26.3% of girls and 13.8% of boys had vitamin D deficiency consistent with the literature which reports higher vitamin D deficiency in the female gender (7). In this study, there was a gradual decrease in vitamin D levels with age after infancy. We found vitamin D deficiency at frequencies of 7.9%, 12.1%, 14.6%, and 29.8%, respectively in infancy, preschool, school, and adolescent age groups. In our study, the mean levels of 25(OH)D

Table I. Vitamin D level classification in children

Characteristics of children	Sufficiency >20 ng/mL		Insufficiency 12-20 ng/mL		Deficiency <12 ng/mL		p-value
	n	%	n	%	n	%	
Age groups							
Infant (0-2 years)	7,828	75.1	1,770	17.0	824	7.9	<0.01
Preschool (3-5 years)	3,478	53.4	2,235	34.4	789	12.1	
School (6-9 years)	4,185	47.5	3,331	37.8	1,290	14.6	
Adolescent (10-18 years)	8,073	31.3	10,049	38.9	7,708	29.8	
Gender							
Boy (n=23,251)	12,473	54.1	7,416	31.9	3,187	13.7	<0.01
Girl (n=28,309)	10,754	38.2	9,969	35.2	7,424	26.2	

Table II. Seasonal variation of serum 25(OH)D levels

25(OH)D levels	Sufficiency >20 ng/mL		Insufficiency 12-20 ng/mL		Deficiency <12 ng/mL		p-value
	n	%	n	%	n	%	
Spring (n=12,476)	4,555	36.5	4,378	35.1	3,543	28.4	<0.01
Summer (n=13,001)	6,998	53.8	4,355	33.5	1,648	12.7	
Autumn (n=13,969)	7,715	55.2	4,554	32.6	1,700	12.2	
Winter (n=12,114)	4,296	35.5	4,098	33.8	3,720	30.7	
Total (n=51,560)	23,598	45.7	17,385	33.7	10,611	20.6	

25(OH)D: 25-hydroxyvitamin D

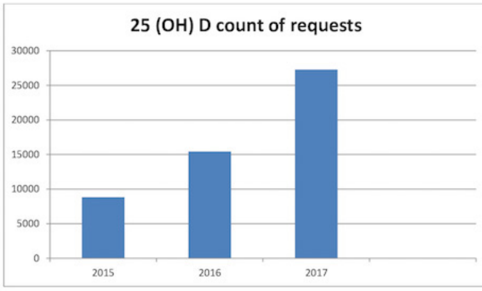

Figure 1. 25(OH)D count of requests according to years
25(OH)D: 25-hydroxyvitamin D

Table III: The effect of gender, age, and season in determining vitamin D insufficiency

	Adjusted OR (95% CI)	p-value
Gender		
Male (reference)		<0.01
Female	1.78 (1.72-1.85)	
Age group (years)		
0-2 (reference)		
3-5	2.82 (2.63-3.02)	<0.01
6-9	3.55 (3.33-3.78)	
10-18	6.98 (6.61-7.36)	
Seasons		
Autumn (reference)		
Winter	2.51 (2.38-2.64)	<0.01
Spring	2.64 (2.50-2.78)	
Summer	1.11 (1.05-1.16)	

OR: Odds ratio, CI: Confidence interval

were the highest in infants and the lowest in adolescents. Nearly 70% of adolescents and 25% of infants were found to have vitamin D deficiency or insufficiency. A daily 400 IU vitamin D supplement is provided to all infants during their first year in Turkey. This supplement may explain why we determined the lowest frequency in the infant group. As age increases, exposure to sunshine decreases due to spending more time indoors in front of a TV or computer. Insufficient playgrounds, the use of sunscreens with high sun protection factors, and covered clothing in adolescent girls have an influence on vitamin D levels (8,13). Vitamin D levels in adolescents may also have been found to be lowest for these reasons in our study. Preschool and school-age children have more chance to spend time outdoors than adolescents in our country because adolescents have to spend more time indoors preparing for exams in order to enter the college or university of their choice among the 2 million individuals they have to compete with.

In the HELENA study, vitamin D levels were determined to be below 30 ng/mL in approximately 80% of European adolescents and sufficient 25(OH)D levels were slightly higher in girls than in boys (22% versus 15%) (14). Bener et al. (15) reported vitamin D levels below 20 ng/mL in 61.6% of adolescents aged 11-16 years, 28.9% of schoolchildren aged 5-10 years, and 9.5% of preschool children under the age of 5 years in Qatar, which has ample sunshine. In a study from Afghanistan, vitamin D levels were reported to be <20 ng/mL in 61% of adolescents of whom 65% were girls. This result was speculated to be related to less sunlight exposure because of the wearing of traditional clothes and inadequate intake of vitamin D rich foods and supplements (13). The prevalence of 25(OH)D insufficiency among preschool children in Canada was found to be 51.7% in summer and 72.8% in winter (6). In another study from Canada, 14% of children aged 6-11 years had a plasma 25(OH)D concentration of <20 ng/mL (16). Pekkinen et al. (17) determined that 71% of Finnish children aged 7-11 years had vitamin D levels <20 ng/mL, despite having met or exceeded the recommended daily intake of vitamin D. Akman et al. (18) reported that vitamin D levels were below 20 ng/mL in 14.5% of children aged 1-7 years.

Vitamin D deficiency has been attracting more attention due to an increase scientific studies and frequent mentions in the media (19). The frequency of testing for vitamin D increased dramatically over an 11-year period in Australia (20). A six-fold increase in 25(OH)D testing was reported between 2007 and 2010 in the UK (8). We determined that there was increased vitamin D testing in Turkey during our study years. This may be because of increased awareness of vitamin D deficiency and its related diseases in recent years. Further evidence is needed to clarify whom to test in order to avoid over-testing and overdiagnosis.

In the literature, vitamin D deficiency has generally been found to be highest in winter or spring (5,21-23). The main factors suggested to be responsible for the seasonal variations of vitamin D are latitude and inadequate sunlight exposure during winter. Between November and February, above a latitude of 37°, there are evident decreases in the number of UVB photons reaching the earth. Furthermore, below a latitude of 37° and closer to the equator, more vitamin D3 synthesizes in the skin throughout the year (24).

Corrêa et al. (25) reported that vitamin D synthesis may reduce by 39% in high latitudes in their study regarding effective UV doses for vitamin D synthesis in low (10.5°N-16.5°S), mid (23.6°S-34.6°S) and high latitudes (54.8°S-62.1°S). In Poland, at 50.3°N-53.4°N latitudes at the end of March, a serum concentration of 25(OH)D below 20 ng/mL was determined in 84.2% of children aged between 9 and 13 years (22). Vitamin D deficiency or insufficiency was reported to be 60.2% in one study involving Norwegian adolescents (Latitude 69°N) (26). In our study, Vitamin D deficiency (30.7%) or insufficiency (33.8%) were determined in 64.5% of the study group in winter in Ankara, which is the capital city of Turkey, at 39°N latitude.

Study Limitations

Our study has some limitations. The data was obtained from both healthy and sick children together and it was gathered retrospectively. Some patients may have diseases which affect vitamin D absorption and metabolism. Moreover, we do not know how much exposure to sunlight children got on a daily basis, their eating habits, their body mass index, or whether or not they took vitamin D supplements. Nevertheless, our study is valuable in being the largest epidemiological study to evaluate vitamin D status in children in Turkey.

Conclusion

Vitamin D deficiency or insufficiency was determined in more than half of all children in our study. Female gender, adolescence, and also the winter and spring seasons were found to be important risk factors for vitamin D deficiency or insufficiency. The frequency of vitamin D testing has increased dramatically over the years. Further evidence is needed to clarify whom to test. We propose that the Health Ministry pay attention to our study in order to develop a strategy or plan for vitamin D supplementation in adolescents, especially during the winter months.

Ethics

Ethics Committee Approval: The present study was approved by the Ethics Committee of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital (15.05.2019/297).

Informed Consent: Informed consent was not obtained because this was a retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.S., Data Collection or Processing: G.Ç., Analysis or Interpretation: F.Z.Ö.Ç., Literature Search: E.A.A., Writing: E.S., E.A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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