SELÇUK TIP DERGİSİ
SELCUK MEDICAL JOURNAL

Araştırma Makalesi / Research Article

Selcuk Med J 2021;37(4): 365-370
DOI: 10.30733/std.2021.01528

Evaluation of the Effects of Age Group, Gender and Seasonal Factors on Vitamin D Levels in 9496 Children

Yaş Grubu, Cinsiyet ve Mevsimsel Faktörlerin D Vitamini Düzeylerine Etkisinin 9496 Çocukta Değerlendirilmesi

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Geliş Tarihi/Received: *11 August 2021*
Kabul Tarihi/Accepted: *30 November 2021*

Öz

Amaç: Bu çalışmada, Orta Anadolu'daki bir eğitim ve araştırma hastanesi'nin çocuk kliniğinde bir yıl boyunca belirlenen D Vitamini düzeylerinin yaş gruplarına, cinsiyete ve mevsim özelliklerine göre değerlendirilmesi amaçlanmıştır.
Hastalar ve Yöntem: Bu retrospektif çalışma, bir hastanenin çocuk polikliniğine Ocak 2019-Aralık 2019 tarihleri arasında başvuran ve D vitamini düzeyi belirlenen 0-18 yaş arası çocukların verileri kullanılarak yapılmıştır. Çocuklar, Standart 6 önerilerine göre 28 gün-12 ay, 13 ay-2 yaş, 2-5 yaş, 6-11 yaş ve 12-18 yaş olmak üzere beş farklı yaş grubuna ayrıldı. D vitamini düzeyleri yaş grubu, cinsiyet ve başvuru mevsimi açısından değerlendirildi.
Bulgular: Çalışmaya 5360 (56.4%)'i kız, 4136 (43.6%)'sı erkek olmak üzere toplam 9496 çocuk dahil edildi. Katılımcıların 6472 (%68.2)'sinin 25(OH)D düzeyi 20 ng/mL'nin altında (eksikliği temsil eder), 2085 (%21.9)'inin 21-29 ng/mL arasında (yetersizliği temsil eder), 939 (%9.9)'unun ise 30 ng/mL'nin üzerinde (yeterliliği temsil eder) idi. Kızlarda D vitamini düzeylerinin erkeklere göre daha düşük olduğu, D vitamini düzeylerinin yaşla ters orantılı olduğu, D vitamini düzeylerinin en düşük değerlerine kışın, en yüksek değerlerine ise yazın ulaştığı belirlendi. Yaş grubu, cinsiyet ve başvuru mevsiminin D vitamini düzeyleri üzerindeki etkileri istatistiksel olarak anlamlıydı ($P < 0,001$).
Sonuç: Tüm yaş grupları için ortalama D vitamini düzeyleri ya yetersiz ya da eksikti. 0-18 yaş arası çocuklarda D vitamini seviyeleri yaş, cinsiyet ve mevsim ile ilişkilidir. Özellikle risk altındaki gruplarda D vitamini eksikliğini veya yetersizliğini önlemek için gerekli önlemler alınmalıdır.

Anahtar Kelimeler: D vitamini düzeyleri, çocuk, yaş grubu, mevsim

Abstract

Aim: This study aimed to evaluate vitamin D levels, which were determined over a year in the pediatric clinic of a training and research hospital in Central Anatolia, according to age groups, gender, and seasonal characteristics.
Patients and Methods: This retrospective study was conducted using the data of children aged 0–18 years who applied to the children's clinic of a hospital between January 2019 and December 2019 and whose vitamin D levels were determined. Children were divided into five different age groups, 28 days–12 months, 13 months–2 years, 2–5 years, 6–11 years, and 12–18 years, in accordance with Standard 6 recommendations. Vitamin D levels were evaluated in terms of age group, gender, and admission season.
Results: A total of 9496 children, 5360 (56.4%) females and 4136 (43.6%) males, were included in the study. A 25(OH)D level below 20 ng/mL (representing a deficiency) was found in 6472 (68.2%) of the participants, while 2085 (21.9%) participants had a 25(OH)D level between 21–29 ng/mL (representing an insufficiency) and 939 (9.9%) participants had a 25(OH)D level over 30 ng/mL (representing sufficiency). It was determined that vitamin D levels are lower in girls than in boys, vitamin D levels are inversely proportional to age, and vitamin D levels reach their lowest values in winter and highest values in summer. The effects of age group, gender, and season of admission on vitamin D levels were statistically significant ($P < 0.001$).
Conclusion: The mean vitamin D levels for all age groups were either insufficient or deficient. Vitamin D levels in children aged 0–18 is related to age, gender, and season. Necessary measures should be taken, especially for at-risk groups, to prevent vitamin D deficiency or insufficiency.

Key words: Vitamin D levels, child, age group, season

Cite this article as: Bagci Z. Evaluation of the Effects of Age Group, Gender and Seasonal Factors on Vitamin D Levels in 9496 Children. Selcuk Med J 2021;37(4): 365-370

Disclosure: *Author has not a financial interest in any of the products, devices, or drugs mentioned in this article. The research was not sponsored by an outside organization. Author has agreed to allow full access to the primary data and to allow the journal to review the data if requested.*

INTRODUCTION

Vitamin D, a fat-soluble vitamin, is a steroid that is essential for a healthy life. Its main function is to ensure the growth and development of the skeletal structure by regulating the calcium and phosphorus metabolism. There are two major form of vitamin D. Ergocalciferol (vitamin D2) is found in plants and can be taken with food, and Cholecalciferol (vitamin D3) is an endogenously synthesized form (1). More than 90% of the vitamin D in the human body is synthesized in the skin by the effect of sunlight. During exposure to sunlight, 7-dehydrocholesterol in the skin is converted to previtamin D3, which is thermally converted to vitamin D3. Vitamin D (D represents D2 or D3) hydroxylated first to 25(OH)D in the liver and then to 1,25(OH)2D in the kidneys. 25(OH)D is the main circulating form of vitamin D and has a half-life of 2–3 weeks. It is the preferred indicator for measuring serum vitamin D levels due to its long half-life. 1,25(OH)2D is the active form and its half-life is between 4–6 hours (2).

Sunlight is required for the endogenous production of vitamin D, though living indoors, the use of high factor skin protection, dark skin color, and seasonal and geographical conditions may reduce exposure to sunlight. In addition, vitamin D deficiency or insufficiency may develop due to inadequate dietary intake or malabsorption (3). In children with a vitamin D deficiency, the mineralization of bone tissue is impaired and rickets may develop. Vitamin D deficiency or insufficiency is also a risk factor for many acute and chronic diseases (4). According to different prevalence studies, vitamin D deficiency varies between 30%–80% worldwide (5). Although some regional studies conducted in Turkey have reported the prevalence of vitamin D deficiency/insufficiency in children, there is no prevalence study covering the whole country yet. The aim of this study is to determine the prevalence of vitamin D levels in children aged 0–18 to reveal the distribution of vitamin D levels by age group, gender, and seasons.

PATIENTS AND METHODS

Children between the ages of 0–18 who applied to a training and research hospital pediatric clinic between January 01, 2019 and December 31, 2019 and whose serum 25-hydroxyvitamin D levels were measured were included in this study. For this retrospective study, 01.07.2021 date and 01-25 number of the permission of the local ethic committee was obtained. Information about the patients was obtained from the electronic record archive of the hospital. Patients were grouped by age into five groups: 28 days–12 months (infancy), 13 months–2 years (toddler), 2–5 years (early childhood), 6–11 y (middle childhood), and 12–18y (early adolescence) in accordance with Standard 6 recommendations (6, 7). A 25(OH)D level lower than 20 ng/mL was defined as a “deficiency,” with a level between 20–30 ng/mL being defined as an “insufficiency,” and a level over 30 ng/mL being defined as a “sufficiency” (8, 9). 25(OH) D levels were determined using a chemiluminescent immunoassay (Siemens ADVIA Centaur XP, Siemens Healthcare Diagnostics, Erlangen, Germany).

Statistical Analysis: Statistical analysis was performed using the IBM SPSS Statistics program (Version 19.0 for Windows, NY: IBM Corp.). For the categorical variables, including age group, gender and season, descriptive statistics are presented as numbers and percentages. Numerical variables that are normally distributed are presented as means and standard deviations, and those that are not normally distributed are presented as medians, minima, and maxima. The normal distribution of vitamin D levels was evaluated with the Kolmogorov-Smirnov test. The chi-square test was used to compare the categorical groups. Gender, age group, and admission season were determined as the main effects on vitamin D levels. These factors and their interactions were evaluated with a univariate three-way analysis of variance. Sidak test adjustment was used for multiple comparisons. All statistical analyzes were performed formulating a two-way hypothesis with a 5% significance.

RESULTS

A total of 9496 children, 5360 (56.4%) girls and 4136 (43.6%) boys, were included in this study. Thirteen children with 25(OH)D3 levels between 100–150 ng/ml (excess) and 16 children with intoxication above 150 ng/mL were not included in the study. A 25(OH)D level below 20 ng/mL (representing a deficiency) was found in 6472 (68.2%) of the participants, while 2085 (21.9%) participants had a 25(OH)D level between 21–29 ng/mL (representing an insufficiency) and 939 (9.9%) participants had a 25(OH)D level over 30 ng/mL (representing sufficiency). The distribution of the participants included in the study according to “gender,” "age group,” “application season,” and “Vit D status” is given in Table 1.

When the age groups were evaluated in terms of gender, the difference was statistically significant (P <

Table 1. Distribution of patients by gender, age group, admission season and vitamin D status

	n	%
Gender		
Female	5360	56.4
Male	4136	43.6
Age Groups		
28 d-12 m	525	5.5
13 m-2 y	957	10.1
2-5 y	2074	21.8
6-11 y	2640	27.8
12-18 y	3300	34.8
Season		
Winter	2963	31.2
Spring	2054	21.6
Summer	2041	21.5
Autumn	2438	25.7
Vit-D Status		
Deficiency	6472	68.2
Insufficiency	2085	21.9
Sufficiency	939	9.9

0.001). The male gender was dominant under the age of 5 years, and the female gender was dominant over the age of 6 years (P < 0.001). When the participants were evaluated in terms of gender according to the seasons of application, no statistically significant difference was found (P = 0.327). The prevalence of vitamin D deficiency was significantly higher in girls (3998 participants, 61.8%) than boys, (2474 participants, 38.2%) with P < 0.001. Comparison of age groups, admission seasons, and vitamin D statuses in terms of gender are given in Table 2.

According to the results of a univariate three-way analysis of variance, it was determined that the main effects of age group, gender, and application season on vitamin D levels, as well as the interaction of these three factors, were statistically significant with P = 0.047 (Table 3). The seasonal variation of 25(OH) D levels by age group and gender is presented in Figure 1. When vitamin D levels were evaluated in terms of gender, the vitamin D levels of boys were found to be higher than those of girls, yielding values of 19.4 ± 10.3 ng/mL for boys and 15.8 ± 10.1 ng/mL for girls, with P < 0.001. The vitamin D levels were highest in the infancy group and lowest in the early adolescence group, yielding values of 27.3 ± 16.6 ng/mL for the infancy group and 13.6 ± 7.9 ng/mL for the early adolescence group, with P < 0.001. According to the results of the multiple comparisons test, it was determined that values of vitamin D levels across all age groups were statistically different (P < 0.001) as

Table 2. Comparison of age group, admission season and vitamin D status in terms of gender

		Female n (%)	Male n (%)	P*
Age groups	28 d-12 m	241 (45.9)	284 (54.1)	
	13 m-2 y	460 (48.1)	497 (51.9)	
	2-5 y	1002 (48.3)	1072 (51.7)	<0.001
	6-11 y	1391 (52.7)	1249 (47.3)	
	12-18 y	2266 (68.7)	1034 (31.3)	
Season	Winter	1692 (57.1)	1271 (42.9)	
	Spring	1124 (54.7	930 (45.3)	
	Summer	1167 (57.2)	874 (42.8)	0.327
	Autumn	1377 (56.5)	1061 (43.5)	
Vitamin D Status	Deficiency	3998 (61.8)	2474 (38.2)	
	Insufficiency	935 (44.8)	1150 (55.2)	<0.001
	Sufficiency	427 (45.5)	512 (54.5)	

*Chi-Square test

Table 3. Evaluation of the effects of gender, age group and season on vitamin D levels

	df	F	P*	Partial Eta Squared
Gender	1	37.052	<0.001	0,004
Age group	4	304.352	<0.001	0,114
Season	3	240.630	<0.001	0,071
Gender * Age group	4	33.826	<0.001	0.014
Gender * Season	3	2.412	0.065	0.001
Age group * Season	12	6.621	<0,001	0.008
Gender * Age group * Season	12	1.771	0.047	0,002

*General linear model-Univariate analysis, R2 = 0.250

Table 4. Comparison of vitamin D levels by gender, age group, admission season and vitamin D status.

		Vitamin D Levels (Mean ± SD)	P*
Gender	Female	15.8 ± 10.1	<0.001
	Male	19.4 ± 10.3	
Age group	28 d-12 m	27.3 ± 16.6	
	13 m-2 y	22.5 ± 13.4	
	2-5 y	18.9 ± 9.3	<0.001
	6-11 y	17.2 ± 8.3	
	12-18 y	13.6 ± 7.9	
Season	Winter	13.1 ± 8.9	
	Spring	18 ± 11	<0.001
	Summer	21 ± 10.4	
	Autumn	19.1 ± 9.4	

*Sidak adjusted multiple comparisons, SD: Standard deviation

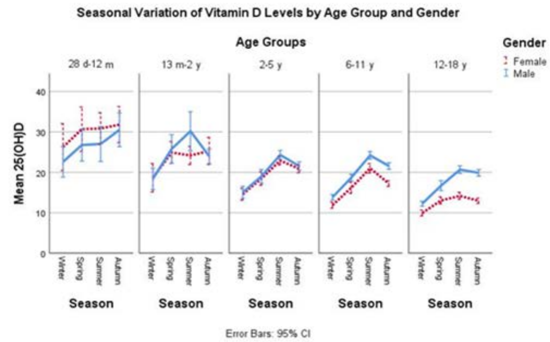

Figure 1. Seasonal variation of vitamin D levels by age group and gender.

shown in Table 4.

The vitamin D levels in the winter season were the lowest, and those in the summer season were the highest, yielding values of 13.1 ± 8.9 ng/mL in the winter and 21 ± 10.4 ng/mL in the summer ($P < 0.001$). According to the multiple comparisons tests, the differences in vitamin D levels between seasons were statistically significant ($P < 0.001$) (Table 4). The vitamin D level of the patients in the deficiency group were 12 ± 4.4 ng/mL, while a value of 24.1 ± 2.7 ng/mL was determined in the insufficiency group and a value of 39.7 ± 11.3 ng/mL was determined in the sufficiency group. Vitamin D levels by gender, age group, and season of admission are presented in Table 5.

DISCUSSION

This study is the first study in which the Vitamin D levels of children aged 0-18 in the central Anatolian region were evaluated according to age groups, gender, and seasons. It differs from similar studies in the literature in terms of a large number of cases and the comparison of mean vitamin D levels according to vitamin D status (deficiency, deficiency, adequacy). In this regional study, we found that vitamin D levels were lower than expected values and that these levels were significantly affected by age group, gender, and the season of admission.

Vitamin D is a vitamin that has important functions in the human body and has been associated with many systems. Its functions are not limited to calcium and phosphate metabolism. Apart from its effects on the skeletal system, vitamin D deficiency has been associated with obesity, asthma, Type 2 diabetes mellitus, cardiovascular diseases, neurological problems, and cancer (2, 4, 10). It has been reported that vitamin D is effective in the development and maintenance of the immune system, and the tendency to some infectious diseases increases in cases of vitamin D deficiency (11). Today, vitamin D deficiency/insufficiency is accepted as global and important public health problems (3, 12). In fact, some recent studies consider vitamin D deficiency as a worldwide pandemic (10). The Middle East, India, China, and Mongolia are regions where vitamin D deficiency is widespread and most severe. The main risk groups are

Table 5. Vitamin D levels by gender, age group and admission season.

		Age group (Mean ± SD)				
		28 d-12 m	13 m-2 y	2-5 y	6-11 y	12-18 y
Winter	Male	21.6 ± 15.2	17.7 ± 13.3	14.1 ± 7.6	13.8 ± 7.1	12.2 ± 5.7
	Female	24.2 ± 17.6	16.6 ± 11.4	14.1 ± 10.1	11.6 ± 5.3	9.6 ± 6.8
Spring	Male	26.8 ± 17.5	24.7 ± 15.1	18.1 ± 8.2	18.7 ± 7.5	16.7 ± 9
	Female	28.8 ± 15.7	24.9 ± 15.1	17.9 ± 9.3	15.4 ± 8	13.1 ± 9.1
Summer	Male	27 ± 16	25.6 ± 15.1	24.3 ± 8.5	24.2 ± 7.3	20.7 ± 7.3
	Female	30.9 ± 15.8	24.2 ± 11.6	22.9 ± 8.4	21.0 ± 9.5	13.7 ± 7
Autumn	Male	30.5 ± 17.3	24 ± 10.3	21.3 ± 7.7	21.6 ± 7.5	19.9 ± 6.7
	Female	31.8 ± 15	23.4 ± 10.9	20.9 ± 8.3	17.2 ± 6.7	12.8 ± 6.5

SD: Standard deviation

children, adolescents, pregnant women, the elderly, and immigrants. It is estimated that more than 50% of the world population do not have sufficient vitamin D levels, especially in winter (13). There is not yet a prevalence study regarding vitamin D deficiency or insufficiency in children that covers the whole country of Turkey. However, there are studies conducted on a regional or provincial basis. The data obtained as a result of regional studies involving children over the last 10 years show that the western and southern regions of Turkey have higher vitamin D levels than the eastern and northern regions. Doğan et al. (14) reported that the mean vitamin D levels of the cases aged 1 month to 18 years in Izmir in 2015 were 28 ng/mL, and in 2016, Fettah et al. (15) demonstrated that the vitamin D levels of the cases aged 0–18 years in Erzurum were 17.1 ng/mL. Durmaz et al. (16) reported a mean vitamin D level of 16.3 ng/mL in children aged 0–18 in Amasya in 2015, and Bucak et al. (17) reported a mean vitamin D level of 32.9 ng/mL in children aged 1 month to 10 years in Adıyaman in 2016.

There are some factors that affect the regional variation of vitamin D levels in Turkey. The main influencing factor is the degree of exposure to sunlight. Seasonal and climatic conditions, altitude above sea level, geographical location, and social lifestyle (for example, the way of dressing) affect the exposure time of the skin to the sun. In terms of the geographical location of Turkey, the most suitable period of the year for vitamin D synthesis is between May and November and between the hours of 10:00 to 15:00 during the day (18). Vitamin D levels in the Central Anatolia region reflect the average of Turkey in terms of geographical location (18-22). Studies on the vitamin D levels of children in the last 10 years in the Central Anatolia region included different age groups. Demiral et al. (19) reported the mean vitamin D level as 11.9 ng/mL for cases aged 3–18 years in Ankara in 2016, and Solak et al. (18) found the mean vitamin D levels to be 15.2 ± 8.8 ng/mL (14.5 ± 8.8 ng/mL in females, 18.1 ± 8.4 in males) for participants aged 0–18 years in their study that included adults in 2018. In this study, the mean vitamin D levels were found to be 15.8 ± 10.1 ng/mL in girls and 19.4 ± 10.3 ng/mL in boys, and these results are consistent with the literature.

Studies on Vitamin D levels in children in Turkey are not homogeneous in terms of demographic characteristics and study methodologies. Although the units of measurement for vitamin D (ng/mL) are the same in the studies, the reference intervals for the diagnosis of vitamin D deficiency or insufficiency are different. In addition, many of the studies include different and partial age ranges between the ages of 0–18 or included adults. Methodologically, the closest study to our study is the study by Topal et al. (7) in 2016, in which the vitamin D levels of children aged 0–18 in Erzincan were evaluated according to age, gender, and seasonal characteristics. The mean vitamin D levels obtained by Topal et al. (7) were 21.3 ± 14.9 ng/mL in girls and 22.5 ± 13.9 ng/mL in boys. These results are higher than the values we obtained, and the gender difference is less than found in our study. In both studies, the highest vitamin D levels belonged to children aged 0–12 months, vitamin D levels decreased with age, and the lowest vitamin D levels belonged to children aged 12–18 years. In both this study and the study conducted by Topal et al. (7), the lowest vitamin D levels were observed in the winter months, and the highest values are observed in the summer months. Although Topal et al. (7) reported that there was no difference between winter and spring in terms of mean vitamin D levels, in our study, vitamin D levels determined in spring were significantly higher than those determined in winter. The probable reason for this is that the number of sunny days in spring is higher in the Central Anatolia region than in the Eastern Anatolia region.

In our study, in addition to previous studies, we also evaluated mean vitamin D levels according to vitamin D status (deficiency, insufficiency, sufficiency). We think that this is important in terms of revealing the severity of vitamin D deficiency and insufficiency. According to our results, the mean vitamin D levels were 12 ± 4.4 ng/mL in the deficiency group, 24.1 ± 2.7 ng/mL in the insufficiency group, and 39.7 ± 11.3 ng/mL in the sufficiency group. We think that these results will serve as a reference for studies with similar methodologies. Topal et al. (7) reported that apart from the main effects of age, gender, and season, only the interaction between age and season affected vitamin D levels. According to the general linear model procedure we used in our study, it was determined that the main effects of age group, gender and application season, as well as, the interactions of these three factors were significantly effective on vitamin D levels.

When all age groups are taken into account, vitamin D levels are at the level of deficiency in children under the age of two and deficiency was detected in children between the ages of 2-18. The key limitation of this study is that it is a retrospective archive study. This study includes children who applied to the hospital and whose vitamin D levels were determined after the evaluation. It does not include the symptoms, physical examination findings and related laboratory findings suggesting vitamin D deficiency in the participants. Despite the large number of participants, the fact that vitamin D deficiency/insufficiency is so evident raises the questions about the vitamin D levels in healthy children. Prevalence studies on vitamin D deficiency/ insufficiency in asymptomatic and healthy children may provide reference ranges determined according to age groups.

As in the whole world, vitamin D levels in children were found to be lower than expected in this regional study. Vitamin D levels in children aged 0–18 have significant variability according to gender, age group, and seasons. In order to prevent health problems that may develop due to vitamin D deficiency or insufficiency, public awareness should be raised about a balanced diet, benefiting from sunlight in a healthy way. Further, public health practices that support nutrition in terms of vitamin D should be planned, and these interventions should all be developed according to age, gender, and seasonal conditions. We think that future studies should follow a similar methodology to the one used in this study in order to reveal the prevalence of vitamin D deficiency/ insufficiency in children and to make temporal and regional comparisons across different age groups.

Conflict of interest: *Authors declare that there is no conflict of interest between the authors of the article.*

Financial conflict of interest: *Authors declare that they did not receive any financial support in this study.*

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