



# Frequency of Vitamin D Deficiency in Children: A Single-Center Cross-Sectional Study in Istanbul

## Çocuklarda D Vitamini Eksikliğinin Sıklığı: İstanbul'da Tek Merkezli Kesitsel Bir Çalışma

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### Abstract

**Aim:** Vitamin D deficiency is highly prevalent among children worldwide. This study aims to assess the frequency of vitamin D deficiency in children and how it varies according to gender, age, and season in Istanbul.

**Material and Method:** The study included 3096 children aged 0-18 admitted to the pediatric outpatient clinic in Istanbul. The serum 25 hydroxyvitamin D concentration was analyzed by the High-Performance Liquid Chromatography method using HPLC systems analyzers, and the results were categorized into four groups: deficiency (<20 ng/mL), insufficiency (20–30 ng/mL), sufficiency (30-100 ng/mL), and toxicity (>100 ng/mL). Descriptive methods, Chi-square, Independent Samples T-Test, ANOVA, and correlation test were used in the statistical analysis of the data.

**Results:** Of children, 52% were girls and 48% boys. The mean serum 25 hydroxyvitamin D concentration was 21.8±15.8 ng/mL, and the frequency of vitamin D deficiency was 53.1%. There was a different distribution of vitamin D status between age groups. Vitamin D deficiency was more common in older children. The frequency of vitamin D deficiency was significantly higher in girls than boys (57.6% versus 48.3%). The mean serum 25 hydroxyvitamin D concentration was significantly lower in winter and spring. A moderate negative correlation was found between age and serum 25 hydroxyvitamin D concentration (correlation coefficient:-0.36).

**Conclusion:** This study showed that female sex, older children, and the winter/spring seasons were significantly associated with a higher frequency of vitamin D deficiency and a lower mean serum 25 hydroxyvitamin D concentration.

**Keywords:** Vitamin D deficiency, children, outpatient clinic, frequency

### Öz

**Amaç:** D vitamini eksikliği dünya çapında çocuklar arasında oldukça yaygındır. Bu çalışmada, İstanbul Tıp Fakültesi çocuk polikliniğine başvuranlarda D vitamini eksikliği sıklığının cinsiyet, yaş ve mevsime göre nasıl değiştiğinin değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntem:** Araştırmaya İstanbul'da çocuk polikliniğine başvuran 0-18 yaş arası kronik hastalığı olmayan 3096 çocuk dahil edildi. HPLC sistem analizörleri kullanılarak Yüksek Performanslı Sıvı Kromatografi yöntemiyle analiz edilen Serum 25 hidroksivitamin D konsantrasyonu dört grupta değerlendirildi; eksiklik (<20 ng/mL), yetersizlik (20-30 ng/mL), yeterlilik (30-100 ng/mL) ve toksisite (>100 ng/mL). Verilerin istatistiksel analizinde tanımlayıcı yöntemler, Ki-kare, Bağımsız Örneklem T-Testi, ANOVA ve korelasyon testi kullanıldı.

**Bulgular:** Çocukların %52'si kız, %48'i erkekti. Ortalama serum 25 hidroksivitamin D konsantrasyonu 21,8±15,8 ng/mL ve D vitamini eksikliği sıklığı %53,1 idi. Yaş grupları arasında D vitamini eksikliği anlamlı olarak farklıydı. Yaş ilerledikçe eksikliğin arttığı görüldü. D vitamini eksikliğinin sıklığı kızlarda erkeklere göre anlamlı olarak daha yüksekti (%57,6'ya %48,3). Ortalama serum 25 hidroksivitamin D konsantrasyonu kış ve ilkbaharda önemli ölçüde daha düşüktü. Yaş ile serum 25 hidroksivitamin D konsantrasyonu arasında orta derecede negatif korelasyon bulundu (korelasyon katsayısı: -0,36).

**Sonuç:** Bu çalışma, kadın cinsiyetin, yaşı büyük çocukların ve kış/ilkbahar mevsimlerinin, daha yüksek D vitamini eksikliği sıklığı ve daha düşük bir ortalama serum 25 hidroksivitamin D konsantrasyonu ile önemli ölçüde ilişkili olduğunu gösterdi.

**Anahtar Kelimeler:** D vitamini eksikliği, çocuk, poliklinik, sıklık



## INTRODUCTION

Vitamin D is a steroid hormone that plays a vital role in human physiology and is mainly synthesized in the skin by sunlight. Humans also obtain vitamin D from foods and supplements.<sup>[1]</sup> Vitamin D is necessary for calcium homeostasis, bone mineralization, and providing the intestinal absorption of calcium and phosphorus.<sup>[1]</sup> Vitamin D also has extra-musculoskeletal roles. Evidence shows that vitamin D deficiency is related to autoimmune disorders, cardiovascular disease, diabetes, and immune deficiency, in addition to rickets and other musculoskeletal disorders.<sup>[2-5]</sup>

Vitamin D deficiency is highly prevalent among children worldwide.<sup>[2]</sup> Similarly, vitamin D deficiency was commonly reported in studies conducted in different regions of Turkey.<sup>[6-10]</sup> In most studies, vitamin D deficiency prevalence estimates vary due to deficiency definitions, assessed areas, and considered risk factors. Primary causes of vitamin D deficiency are inadequate vitamin D intake by nutrition and insufficient sunlight exposure.<sup>[4]</sup> However, vitamin D metabolism is affected by many factors. Wearing sun-protective clothes, living at a northern latitude, winter season, dark skin or race, female gender, and sunscreen creams reduce vitamin D synthesis in the skin.<sup>[4]</sup> In addition, obesity, fat malabsorption syndromes, hyperparathyroidism, some medications such as anticonvulsants and anti-HIV drugs are associated with vitamin D deficiency.<sup>[2]</sup>

The present study objective was to investigate the rate of vitamin D deficiency and investigate the effects of age, gender, and season in children with similar living conditions by using data available on vitamin D in a large sample in Istanbul.

## MATERIAL AND METHOD

**Study design:** The study was designed as a single-center and cross-sectional observational study. The study period is between February 2020 and February 2021.

**Participant and data collection:** A total of 3096 children aged 0 to 18 years admitted to the pediatric outpatient clinic in Istanbul Medical Faculty were enrolled. Subjects who had any chronic diseases such as skeletal diseases, genetic syndromes, or malabsorptive disorders were excluded from the study.

Data were obtained from the hospital database. Demographic features and serum vitamin D levels of participants were enrolled. Age was divided into four groups: infantile period (0 days–1 year), toddler period and preschool age (2–7 years), puberty period (8–13 years), and adolescence (14–18 years).

**Laboratory assessment:** The serum 25 hydroxyvitamin D concentration was analyzed by the High-Performance Liquid Chromatography method using HPLC systems analyzers. Vitamin D status was categorized into four groups: deficiency (<20 ng/mL), insufficiency (20–30 ng/mL), sufficiency (30–100 ng/mL), and toxicity (>100 ng/mL)(2).

**Statistical analyses:** Data were evaluated using IBM SPSS 21 for Windows. Equality of variances was checked with Levene's Test for Equality of Variances, and normality of distribution was examined with the Kolmogorov-Smirnov test. Descriptive statistical analyses were used to obtain the means and standard deviations of continuous variables. Independent Sample T-Test and One-way ANOVA were used to compare variables between the separate groups. In addition, the Chi-square test was used to compare frequencies. P values <0.05 were accepted as significant.

**Ethical approval:** The study was carried out with the permission of İstanbul University Faculty of Medicine Department of Child Health and Diseases Ethics Committee (Date: 10.09.2021, Decision No: 2021/1482-16).

## RESULTS

Of a total of 3096 children, 52% were girls and 48% boys. The mean serum 25(OH) D concentration was 21.8±15.8 ng/mL, and the frequency of vitamin D deficiency was 53.1%. There was a different distribution of vitamin D status between age groups. The frequency of vitamin D deficiency in the infantile age group was found at 9%. However, the frequency in the adolescent group was 70.1%. Demographic properties and serum vitamin D status according to sex and age group are summarized in **Table 1**.

A significant difference in serum 25(OH)D concentration was found between girls (20.6±15.5 ng/mL and boys (23.1±16.0 ng/mL). There was also a significant difference between girls and boys in the frequency of vitamin D deficiency (57.6% versus 48.3%) (**Table 2**).

**Table 1.** Demographic properties and serum vitamin D status according to sex and age group

	n, %	Age, year	Serum Vitamin D (ng/mL)	Deficiency %	Insufficiency %	Sufficiency %	Toxicity %
Sex							
Girl	1599.52	8.8±5.4	20.6±15.5	57.6	23.1	18.9	0.3
Boy	1497.48	7.9±5.1	23.1±16.0	48.3	26.9	24.6	0.3
Age group							
0-1 y	199.6	0.6±0.2	44.0±30.3	9.0	14.1	75.4	1.5
2-7 y	1160.37	3.7±1.8	24.5±13.2	41.3	28.6	29.9	0.2
8-13 y	975.31	10.0±1.8	18.2±11.2	62.9	26.1	11.0	0.1
14-18 y	762.25	15.5±1.5	16.5±12.8	70.1	20.7	8.8	0.4
Total	3096	8.4±5.3	21.8±15.8	53.1	24.9	21.7	0.3

y: year, Age and serum vitamin D parameters presented as mean±standard deviation, Serum vitamin D values <20 ng/mL were accepted as a deficiency, 20-30 ng/mL as insufficiency, 30-100 ng/mL as sufficiency and >100 ng/mL as toxicity.

**Table 2.** Serum vitamin D status by sex

	All cases n=3096	Girl n=1599	Boy n=1497	P
Serum vitamin D	21.8±15.8	20.6±15.5	23.1±16.0	<0.05
Vitamin D status, n (%)				
Deficiency	1644 (53.1)	921 (57.6)	723 (48.3)	<0.05
Insufficiency	772 (24.9)	370 (23.1)	404 (26.9)	<0.05
Sufficiency	671 (21.7)	303 (18.9)	368 (24.6)	<0.05
Toxicity	9 (0.3)	5 (0.3)	4 (0.3)	>0.05

Serum vitamin D parameters presented as mean±standard deviation, Serum vitamin D values <20 ng/mL were accepted as a deficiency, 20-30 ng/mL as insufficiency, 30-100 ng/mL as sufficiency and >100 ng/mL as toxicity.

There were also significant differences in mean serum 25(OH)D levels between seasons. Mean serum 25(OH) D concentration was the lowest in winter and the highest in summer. The mean serum 25(OH) D concentration was significantly lower in winter and spring (**Table 3**).

**Table 3.** Serum vitamin D status by season

	Allcases n=3096	Winter n=1201	Spring n=268	Summer n=843	Fall n=784
Serum vitamin D	21.8±15.8	17.6±15.4	19.8±12.7	26.3±17.1	24.2±14.0
Vitamin D status, n (%)					
Deficiency	1644 (53.1)	842 (70.1)	163 (60.8)	303 (35.9)	336 (42.9)
Insufficiency	772 (24.9)	204 (17.0)	65 (24.3)	266 (31.6)	237 (30.2)
Sufficiency	671 (21.7)	152 (12.7)	40 (14.9)	270 (32.0)	209 (26.7)
Toxicity	9 (0.3)	3 (0.2)	0 (0.0)	4 (0.5)	2 (0.3)

Serum vitamin D parameters presented as mean±standard deviation, Serum vitamin D values <20 ng/mL were accepted as a deficiency, 20-30 ng/mL as insufficiency, 30-100 ng/mL as sufficiency and >100 ng/mL as toxicity.

Chi-square test results showed significant differences in the frequency of vitamin D deficiency, insufficiency, and sufficiency in different sex, ages, and seasons. In addition, One-way ANOVA with post hoc analysis showed significant differences in the mean serum 25(OH) D concentration in different age groups and seasons. Among children, female sex, older children, and the winter/spring seasons were significantly associated with a higher frequency of vitamin D deficiency and a lower mean serum 25(OH) D concentration.

A moderate negative correlation was found between age and serum 25(OH) D concentration (correlation coefficient:-0.36).

## DISCUSSION

We conducted a cross-sectional observational study with a large sample to investigate the rate of vitamin D deficiency and insufficiency in the pediatric outpatient clinic and evaluated demographic features and laboratory data of 3096 children aged 0-18. The results showed that Vitamin D deficiency (53.1%) and insufficiency (24.9%) were highly prevalent in children living in Istanbul. In particular, the rate of vitamin D deficiency was significantly higher in girls and adolescents. Besides, vitamin D deficiency was most common in winter.

Vitamin D deficiency is a global problem, varying in frequency in different populations.<sup>[1]</sup> In recent studies conducted in Turkey, the prevalence of vitamin D deficiency has been reported from 16.5% to 89.6% (**Table 4**).<sup>[6-17]</sup> Among these studies, the highest rate of vitamin D deficiency was found in the study included pubertal children and adolescents.<sup>[11]</sup> The lowest deficiency rate was shown in a study conducted on children younger than 10 years old.<sup>[15]</sup> However, the studies with all pediatric age groups reported that vitamin D deficiency was in the range of 35.1% to 65.0%.<sup>[7,8,13,14,16,17]</sup> In a study with more than ninety thousand participants, Sahin et al.<sup>[6]</sup> found that vitamin D deficiency was 45-50% in children younger than 10 and 80-90% older than 10. The results of this study were significant due to the high number of participants. In another study conducted by Yetim et al.<sup>[10]</sup>, the rate of vitamin D deficiency in children older than 10 was reported as 56%. Many studies also showed this relationship, as in the present study (**Table 5**).<sup>[9,13,16,18-20]</sup> In contrast, some studies found a lower frequency of vitamin D deficiency in adolescents.<sup>[8,21]</sup>

A cohort study of neonates performed by Kanike et al.<sup>[22]</sup> reported a high prevalence of vitamin D deficiency (31%) and insufficiency (49%) at birth. Similarly, a multicenter study in China conducted by Yang et al.<sup>[19]</sup> reported that vitamin D deficiency was seen most commonly in neonates. These two studies pointed to maternal vitamin D deficiency as the cause of vitamin D deficiency in infants. Similar studies also showed this relationship.<sup>[23-25]</sup> However, this study was unable to analyze this due to the small number of neonates.

Some studies found that the frequency of vitamin D deficiency was higher in girls as in the present study.<sup>[9,16]</sup> However, some studies reported no difference.<sup>[18,26]</sup> Cultural factors also have an essential role in vitamin D levels. In particular, traditional dress-style limits sun exposure and decreases vitamin D production. Therefore, vitamin D deficiency prevalence was reported higher among girls in Muslim countries.<sup>[20,27-29]</sup>

Many studies reported that vitamin D levels were at the lowest in spring and winter.<sup>[16,19]</sup> Sunlight exposure is the main factor in vitamin D synthesis. High latitudes are associated with inadequate levels of vitamin D. However; vitamin D insufficiency is not explained only by season and latitude. Recently, vitamin D insufficiency and deficiency are reported commonly in sunny countries.<sup>[30-33]</sup>

The present study assessed the role of age, sex, and season on vitamin D deficiency. A large sample of participants was the strong aspect of our research. However, there were a few significant limitations to this study. First of all, it was a cross-sectional design study and could not reflect the cause-effect relationship. Secondly, some important factors affecting vitamin D concentration, such as body composition and physical activity, skin pigmentation and sun exposure time, vitamin D intake, and socioeconomic status, could not be evaluated.<sup>[1]</sup> Many studies have established the relationship between obesity and lower serum vitamin D concentrations.<sup>[18,27,34-36]</sup> Vitamin D deficiency related to obesity is likely due

to the deposition of vitamin D in body fat tissues and the decreased bioavailability.<sup>[36]</sup> It has long been known that ethnicity and darker skin can greatly reduce vitamin D synthesis.<sup>[37]</sup>

Low vitamin D intake and breastfeeding were other important causes of vitamin D deficiency.<sup>[1,23]</sup> In addition, many study results showed that vitamin D deficiency was more prevalent among populations with lower socioeconomic status.<sup>[18,27,38,39]</sup>

**Table 4.** Studies on the prevalence of vitamin D deficiency in Turkey

Study	Year	n	Age	Mean Serum Vitamin D (ng/mL)	Deficiency %	Insufficiency %
Dogan et al. <sup>[13]</sup>	2015	2909	0-18 y	28.0±15.5	35.1	61.2
Ozhan et al. <sup>[14]</sup>	2016	556	0-18 y	27.2±15.9	39.3	24.1
Demiral et al. <sup>[9]</sup>	2016	171	3-18 y	-	86.6	-
Bucak et al. <sup>[15]</sup>		775	0-10 y		16.5	25.3
Girl	2016	335	-	32.9±13.9	-	-
Boy		440	-	34.4±14.6	-	-
Yetim et al. <sup>[10]</sup>		187	10-20 y	-	56	36
Girl	2017	103	-	18.7±8.9	-	-
Boy		84	-	19.2±9.3	-	-
Topal et al. <sup>[16]</sup>		2346	0-18 y	-	42.3	27.3
Girl	2018		-	21.3±15.0	-	-
Boy			-	22.5±13.9	-	-
Acik et al. <sup>[17]</sup>		417	0-17 y	-	51.7	16.7
Case-ICU	2018	327	-	-	55	16
Control		90	-	25.9±14.4	40	20
Sahin et al. <sup>[6]</sup>		90042	0-18 y	-	-	-
Girl		47928		22.3±14.0	-	-
Boy	2018	42114		25.3±13.4	-	-
<10 y		-		-	45-50	-
>10 y		-		-	80-90	-
Coskun et al. <sup>[7]</sup>	2018	346	0-18 y	-	49.1	27.5
Atasoy et al. <sup>[11]</sup>	2019	77	6-18 y	-	89.6	10.4
Naiboglu et al. <sup>[12]</sup>	2019	103	0-14 y	23.9±13.7	49	-
Ture et al. <sup>[8]</sup>	2020	4153	0-17 y	18.1±11.2	65.0	23.1
Varkal MA*	2021	3096	0-18 y	21.8±15.8	53.1	24.9

y: year, Serum vitamin D parameters presented as mean±standard deviation, Serum vitamin D values <20 ng/mL were accepted as a deficiency and 20-30 ng/mL as insufficiency.  
\* The present study

**Table 5.** Studies on the prevalence of vitamin D deficiency

Study	Year	n	Age	Mean/Median Serum Vitamin D (ng/mL)	Deficiency %	Insufficiency %
Turer et al. <sup>[35]</sup>	2013	12292	6-18 y			
Healthy-Weight		7728		-	21	-
Overweight		2086		-	29	-
Obese		1897		-	34	-
Severely obese		581		-	49	-
Zhang et al. <sup>[34]</sup>	2014	1488	7-11 y	18.4 (6.7-33.1)	56.4	23.3
Moore et al. <sup>[18]</sup>	2015	2492	6-18 y	-	26.8	46.7
Al-Sadat et al. <sup>[27]</sup>	2016	1361	13-15 y	-	92.6	-
Beer et al. <sup>[21]*</sup>	2020	2104	1-2 y	23.0±16	42.5	-
		6813	2-5 y	26.1±19	27.7	-
		16454	5-13 y	26.4±23	21.8	-
		6470	13-18 y	26.9±19	20.4	-
Kanike et al. <sup>[22] †</sup>	2020	1517	newborn	19.0 (3-223)	31	49
Yang et al. <sup>[19]</sup>	2020	460537	0-18 y	28.9±12.0	22.6	-
Chen et al. <sup>[26]</sup>	2021	1510	2-6 y	28.0±7.3	11.4	52.6
Varkal MA‡	2021	3096	0-18 y	21.8±15.8	53.1	24.9

y: year, Serum vitamin D parameters presented as mean±standard deviation or median (minimum-maximum), Serum vitamin D values <20 ng/mL were accepted as a deficiency and 20-30 ng/mL as insufficiency.  
\* In the study, standard errors were converted to standard deviation, and serum vitamin D values <20 ng/mL were shown in the deficiency column. †In the study, serum vitamin D values <15 ng/mL were accepted as a deficiency and 15-30 ng/mL as insufficiency. ‡The present study



## CONCLUSION

This study showed that female sex, older children, and the winter/spring seasons were significantly associated with a higher frequency of vitamin D deficiency and a lower mean serum 25 hydroxyvitamin D concentration. The study findings suggest the need for caution in vitamin D supplementation of girls and older children. These children may require additional vitamin D supplementation to prevent vitamin D deficiency.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of İstanbul University Faculty of Medicine Department of Child Health and Diseases Ethics Committee (Date: 10.09.2021, Decision No: 2021/1482-16).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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