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ORIGINAL ARTICLE

Vitamin D Deficiency in Children Admitted to a Tertiary Care Hospital

Üçüncü Basamak Bir Hastaneye Başvuran Çocuklarda D Vitamini Eksikliği

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ABSTRACT

Introduction: This study aims to determine the prevalence of vitamin D deficiency/insufficiency according to age, gender, and seasonal variables in children admitted to a tertiary hospital.
Methods: A cross-sectional study was conducted in the pediatric clinic of a tertiary care hospital in Ankara. Healthy children whose 25-hydroxyvitamin D levels were measured for any reason from January 2015 to January 2020 were included in the study. The vitamin D levels of the participants were analyzed according to age, gender, and measuring season. Children were divided into 4 subgroups according to their age: infancy (0-1 years), preschool (2-5 years), school (6-11 years), and adolescence (12-18 years). 25-hydroxyvitamin D less than 12ng/ml was defined as a deficiency, 12-19 ng/ml were insufficiency, 20-50 ng/ml sufficiency and more than 50ng/ml were defined as the risk of potential adverse effects
Results: A total of 16321 children were included in the study. The participants detected Vitamin D deficiency in 5243 (32.1%). The deficiency was mostly detected during adolescence (n:3313, 63.2%). This was followed by the school period (23.5%), preschool period (10.5%), and infancy (2.7%), respectively. The deficiency was mostly detected during the winter months. While vitamin D deficiency was more common in females over the age of six, no difference was found between the sexes under the age of six.
Conclusions: In this study, a high frequency of vitamin D deficiency/insufficiency was found in children. We believe that screening programs to be determined according to age groups can be beneficial to realize this deficiency without delay.

Keywords: Vitamin D deficiency, children, age, gender

ÖZ

Giriş: Bu çalışmanın amacı üçüncü basamak bir hastaneye başvuran çocuklarda yaş, cinsiyet ve mevsimsel değişkenlere göre D vitamini eksikliği/yetmezliği sıklıklarını belirlemektir.
Metot: Ocak 2015- Ocak 2020 yılları arasında üçüncü basamak bir hastanenin çocuk kliniğinde, herhangi bir nedenle 25-hidroksivitamin D düzeyi ölçülen sağlıklı çocukların D vitamini düzeylerinin yaş, cinsiyet ve mevsim özellikleri ile ilişkisinin analiz edildiği kesitsel bir çalışmadır. Çocuklar yaşlarına göre infant (0-1 yaş), okul öncesi (2-5 yaş), okul dönemi (6-11 yaş) ve adolesan (12-18 yaş) olmak üzere 4 alt gruba ayrılmıştır. 25-hidroksi vitamin D düzeyleri <12 ng/ml ise eksiklik, 12-19 ng/ml yetmezlik, 20-50 ng/ml normal, > 50ng/ml potansiyel yan etki açısından riskli düzey olarak kabul edilmiştir.
Bulgular: Çalışmaya toplam 16321 çocuk dahil edildi. Katılımcıların 5243(%32.1)'ünde D vitamini eksikliği tespit edildi. Eksiklik en sık ergenlik döneminde saptandı (n: 3313, %63.2). Bunu sırasıyla okul dönemi (%23.5), okul öncesi dönem (%10.5) ve infant dönemi (%2.7) izledi. Eksiklik çoğunlukla kış aylarında tespit edildi. D vitamini eksikliği altı yaş üstünde kızlarda sık görülürken, altı yaş altında cinsiyetler arasında fark yoktu.
Sonuç: Bu çalışmada çocuklarda D vitamini eksikliği/ yetmezliği yüksek sıklıkta saptanmıştır. Bu eksikliğin gecikmeden fark edilmesi için yaş gruplarına göre belirlenecek olan tarama programlarının faydalı olabileceğine inanıyoruz

Anahtar kelimeler: D vitamini eksikliği, çocuk, yaş, cinsiyet

Introduction

Vitamin D deficiency and insufficiency have impacts on the skeleton as well as non-skeletal organs While the effects of vitamin D deficiency on skeletal health have been known since the 17th century, its extraskeletal effects have been demonstrated in the last few decades (1). The extraskeletal effects of vitamin D have been increasingly understood since the 1980s, with the demonstration of vitamin D receptors (VDRs) and biological effects in various cells. At least 37 cell types are expressed to have VDR. Vitamin D shows its effect on target cells by binding to VDR. One of its effects on target cells is to regulate the transcription of about 2000 genes (2).

Approximately 90% of the vitamin D in the human body is synthesized from the skin after UVB exposure, while 10% enters the body through the diet (2). Therefore generally thought that populations in regions with plentiful sunshine during the year would have sufficient vitamin D status. However, the prevalence of vitamin D deficiency may be high even in areas with abundant sunlight. It is thought that genetic factors play an essential role in this deficiency, apart from diet and environmental circumstances (2, 3). Recent studies show that genetic tendency plays an important role in sensitivity to vitamin D deficiency and that both vitamin D intake via diet and supplements and cutaneous generation after sun exposure are strongly linked to individual genetic variations (4).

Vitamin D deficiency has been associated with many diseases such as asthma (5), type 1 diabetes mellitus (6), and inflammatory bowel disease (7, 8). Although the importance of vitamin D on human health is understood more and more every day, vitamin D deficiency is widespread all over the world, regardless of climate and economy (1, 9).

In the present study, we primarily aimed to test the hypothesis that vitamin D deficiency and insufficiency are prevalent in children. Secondly, we aimed to determine the relationship between vitamin D deficiency/insufficiency with gender, age, and seasonal variations.

Methods

A retrospective, single-center, cross-sectional study was conducted on patients admitted to the pediatric outpatient clinic of a tertiary hospital over five years. The results of the children younger than 18 years whose vitamin D levels were measured during the visits were determined from the hospital database. Exclusion criteria were defined as chronic kidney or liver disease and the use of drugs that affect bone metabolism. Eventually, 16321 children were included study. Subjects were divided into four groups according to their ages; infancy (0-1years), preschool (2-5 years), school-age (6-11years), and adolescence (12-18 years). Participants' 25 (OH) D level, age, gender, and seasonal information were recorded. Vitamin D status was categorized by using the Institute of Medicine's definition of a serum 25(OH)D. 25-hydroxyvitamin D less than 12ng/ml was defined as a deficiency, 12-19 ng/ml insufficiency, 20-50 ng/ml sufficient, and more than 50ng/ml were defined as the risk of potential adverse effects (10)

25 (OH) D levels were measured by competitive electrochemiluminescence protein binding assay using Cobas e601 Immunoassay analyzer (Roche Diagnostics, Kaiseraugst, Switzerland).

This study was approved by the Ministry of Health Ankara Training and Research Hospital Clinical Research Ethics Committee in terms of compliance with the Declaration of Helsinki(no: 318/2020, 10 July 2020).

Statistical Analysis

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation and as median and minimum-maximum where appropriate. The Chi-square test was used to compare categorical variables between the groups. To evaluate the correlations between measurements, Pearson Correlation Coefficient was used. All analyses were performed using IBM SPSS Statistics Version 20.0 statistical software package. The statistical level of significance for all tests was considered to be 0.05.

Results

A total of 16,321 children, 9174(56.2%) female, and 7147(43.8%) male were included in this research. The mean age of patients was 9.5 ± 5.3 years (median 10 years). Vitamin D deficiency was detected in 10777 (66%) of participants. The participants were separated into four age groups. The first group was 0-1 years (n= 1308), the second group was 2-5years (n=3312), the third group was 6-11 years (n=4983) and the fourth group was 12-18 years (n=6718). The frequency of vitamin D deficiency increased with increasing age and it was most common in adolescents ($p<0.001$) (Table 1, Figure 1). In other words, 25(OH)D levels of children decrease with increasing age($r=-0.413$, $p<0.001$). Descriptive statistics for gender and season characteristics based on vitamin D levels for each age group are given in Table 2. While there was no significant difference between vitamin D levels according to gender in groups 1 and 2 ($p=0.307$ and $p=0.997$ respectively), it was shown that low vitamin D levels were more prevalent in females in groups 3 and 4 (both $p<0.001$). Besides, in all age groups, the concentration of vitamin D changed according to the seasons ($p<0.001$ for all) (Table 2). In each age group, vitamin D deficiency (≤20) was most prevalent in winter (33.1% in group 1, 42.7% in group 2, 44.7% in group 3, and 39.1% in group 4)(Figure 2)

Table 1. Vitamin D levels distribution for each age group

	Vitamin D Levels				
	Deficiency (n=5243)	Insufficiency (n=5534)	Sufficiency (n=5222)	Potential side effects (n=322)	p
Age Groups, n(%)					
0-1 years	144(11.0)	149(11.4)	848(64.8)	167(12.8)	<0.001
2-5 years	552(16.7)	1072(32.4)	1621(48.9)	67(2.0)	
6-11 years	1234(24.8)	2128(42.7)	1589(31.9)	32(0.6)	
12-18 years	3313(49.3)	2185(32.5)	1164(17.3)	56(0.8)	

Table 2. Gender and season characteristics based on vitamin D levels for each age group

		Vitamin D Levels				
Age Groups		**Deficiency (n=5243)**	**Insufficiency (n=5534)**	**Sufficiency (n=5222)**	**Potential side effects (n=322)**	**p**
	n	144	149	848	167	
	Gender					
	Female	67(46.5)	78(52.3)	382(45.0)	86(51.5)	0.224
	Male	77(53.5)	71(47.7)	466(55.0)	81(48.5)	
0-1 years	Season					
(Group 1)	Spring	42(29.2)^{a}	35(23.5)^{a,b}	156(18.3)^{b,c}	19(11.4)^{c}	
	Summer	21(14.6)^{a}	25(16.8)^{a,b}	243(28.7)^{c}	49(29.3) ^{b,c}	<0.001
	Autumn	32(22.2)^{a}	41(27.5)^{a}	232(27.4)^{a}	48(28.8)^{a}	
	Winter	49(34.0)^{a}	48(32.2)^{a}	217(25.6)^{a}	51(30.5)^{a}	
	n	552	1072	1621	67	
	Gender					
	Female	269(48.7)	495(46.2)	763(47.1)	31(46.3)	0.808
2-5 years	Male	283(51.3)	577(53.8)	858(52.9)	36(53.7)	
(Group 2)	Season					
	Spring	166(30.1)^{a}	252(23.5)^{b}	233(14.4)^{c}	9(13.4)^{b,c}	
	Summer	41(7.4)^{a}	176(16.4)^{b}	482(29.7)^{c}	16(23.9)^{b,c}	<0.001
	Autumn	57(10.3)^{a}	239(22.3)^{b}	485(29.9)^{c}	12(17.9)^{a,b,c}	
	Winter	288(52.2)^{a}	405(37.8)^{b}	421(26.0)^{c}	30(44.8)^{a,b}	
	n	1234	2128	1589	32	
	Gender					
	Female	727(58.9)	1118(52.5)	681(42.9)	13(40.6)	<0.001
6-11 years	Male	507(41.1)	1010(47.5)	908(57.1)	19(59.4)	
(Group 3)	Season					
	Spring	354(28.7)^{a}	374(17.6)^{b}	116(7.3)^{c}	3(9.4)^{a,b,c}	
	Summer	92(7.5)^{a}	448(21.0)^{b}	558(35.1)^{c}	9(28.1)^{b,c}	<0.001
	Autumn	141(11.4)^{a}	449(21.1)^{b}	567(35.7)^{c}	13(40.6)^{c}	
	Winter	647(52.4)^{a}	857(40.3)^{b}	348(21.9)^{c}	7(21.9)^{b,c}	
	n	3313	2185	1164	56	
	Gender					
	Female	2642(79.7)	1278(58.5)	509(43.7)	35(62.5)	<0.001
	Male	671(20.3)	907(41.5)	655(56.3)	21(37.5)	
12-18 years	Season					
(Group 4)	Spring	722(21.8)	302(13.8)	84(7.2)	4(7.1)	
	Summer	537(16.2)	621(28.5)	409(35.2)	21(37.5)	<0.001
	Autumn	574(17.3)	593(27.1)	417(35.8)	10(17.9)	
	Winter	1480(44.7)	669(30.6)	254(21.8)	21(37.5)	

Data were expressed as n(%).

Percentages with different subscript letters ($^{a, b, c}$) within columns are significantly different at the 0.05 level.

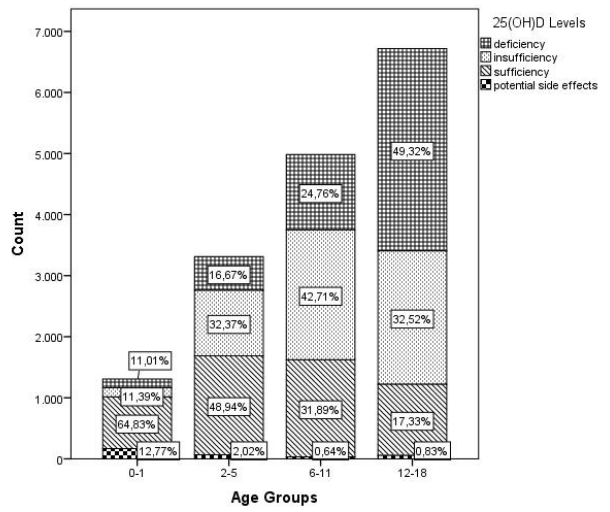

Fig 1. Vitamin D levels distribution according to age groups

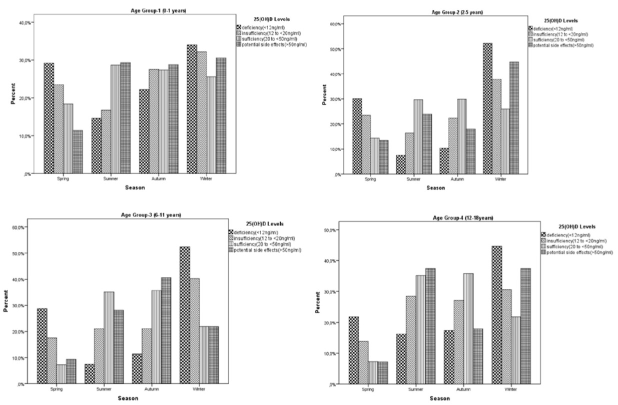

Fig 2. Vitamin D levels distribution according to seasons in four age groups

Discussion

The present study demonstrated that vitamin D deficiency is extremely prevalent (n= 10777, 66%) in children admitted to our pediatric clinics. Deficiency was detected most frequently in winter(n= 4443, 41.2%). While this deficiency is more common in females over the age of six, no gender difference was found under the age of six. Our data demonstrated that vitamin D deficiency increases with increasing age. So the prevalence was highest in adolescents and lowest in participants younger than one-year-old. We believe that the reason why there is less vitamin D deficiency under the age of one is the campaign carried out by the Ministry of Health since 2005. In this campaign, 400 IU/day of free vitamin D support is started for each newborn and continues until the age of one year. A study conducted in our country before this campaign found that the incidence of rickets due to vitamin D deficiency in children aged 0-3years was 6.09%, while the other study conducted in the second year of the campaign with the same team in the same region, this frequency was found to be 0.099% (11).

Vitamin D supplements are routinely used in children only to prevent rickets. However, childhood and adolescence are also critical periods for skeletal development. 90% of adult bone mineralization is completed by the end of adolescence, and 40% of this rate occurs during adolescence. Therefore, vitamin D supplementation is important for bone health during these periods. Although it has been reported that vitamin D supplementation may be beneficial for bone health in children and adolescents, there is still uncertainty about vitamin D supplementation after infancy in the guidelines (12). The Institute of Medicine recommends a daily allowance of at least 15 mcg of vitamin D for children older than one year (10). The American Academy of Pediatrics recommends 10 mcg/day (400 IU) for breastfed and partially breastfed infants until they are fed at least 1 L/day of vitamin D–fortified formula or whole milk. In addition, the APA recommends taking 400 IU/day of vitamin D supplements for adolescents who do not obtain 400 IU of vitamin D daily through vitamin D fortified foods (13). European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) reported that children younger than one year old should take 10 mcg/day of vitamin D. For children older than 1 year, they suggested that vitamin D supplementation should only be considered for the risk group (dark skin, lack of adequate sun exposure, use of sunscreen with high SPF, staying indoors for much of the day, wearing clothes covering most of the skin, living in northern latitudes during wintertime, and obesity) (14).

The reports demonstrated there is no need and no sufficient evidence to support universal screening for vitamin D status. Despite this, it is reported that the cost of vitamin D analysis is increasing rapidly in the National Health Systems of many countries. To reduce these unnecessary costs, it is recommended to use questionnaires for those outside the risk group who need supplements (sunlight exposure, daily supplement intake, etc.). Thus, it will be easier to identify patients with vitamin D deficiency. It is recommended that these be supplemented first and then a serum 25(OH)D test be ordered to confirm that proficiency has been achieved (9).

Different study results have been reported on the prevalence of vitamin D deficiency in children in different parts of the world. A study in Poland reported that 46.7% of children aged 3-18 had vitamin D deficiency (15). In a study conducted in Colombia, a tropical region, this rate was found to be 23.7% in children under the age of 18 (16). In southern China, a sunny region 22.6% of children aged 0 to 18 years had a vitamin D deficiency(17). In a study conducted between 11-16 years of age in Kuwait, another sunny region, vitamin D deficiency was found to be 81.2%(18). In a study examining vitamin D deficiency in Turkey, this frequency was found to be 63% in the general population, 86.6% in infants, and 39.8% in children(19). Although different results are expected due to reasons such as age group differences, different geographical features, genetic structure, and nutritional differences between studies, a high rate of vitamin D deficiency was found in our study. We found that this deficiency increased with increasing age, so it was most common in adolescents, and it was detected least in infants. This result is in agreement with those of previously investigated studies that demonstrated an association between lower levels of vitamin D and increasing age(15, 17). We think that the sufficiency of vitamin D levels in the first years of life is due to the inclusion of these periods by the national support campaign. In addition, assuming that young children spend more time outside to play than older children, the decrease in their contact with sunlight over the years may be another reason for vitamin D deficiency, which increases with age. In addition, decreased consumption of dairy products may be another reason for low vitamin D, as parental control is reduced in the feeding of older children.

In our study, no gender difference was found in the first 6 years of life in terms of vitamin D deficiency. From 6 years of age, this deficiency was more common in females. Similar results have been reported in different studies(15-17, 20, 21).

In these studies, some ideas have been put forward to explain the tendency of vitamin D deficiency to be higher in females than in males. The first is that females have less physical activity than males. The other is that females spend less time outdoors and, according to the beliefs and cultures of some societies, wearing completely closed clothing reduces sun exposure and prevents the synthesis of vitamin D. However, we think that the lifestyles of males and females in very different cultures cannot be parallel enough to affect vitamin levels similarly. We assume that hormonal mechanisms may also be effective in the relative increase in vitamin D levels in males with increasing age. For example, we think that it will be useful to examine whether the androgen hormone has a positive effect on vitamin D synthesis, similar to its effect on erythropoietin and its contribution to erythrocyte production.

The present study evaluated the prevalence of vitamin D deficiency according to seasonal variability. In all age groups, vitamin D deficiency was detected most frequently in winter. Similar results have been reported in previous studies (15, 22, 23). We believe that the high prevalence of vitamin D deficiency during the winter is a result of insufficient sun exposure.

We have some limitations in this study. Our study is retrospective and single-center. Therefore, the results may not reflect the entire pediatric population in Ankara. In addition, since our study was retrospective, we could not obtain sufficient data to determine the prevalence of rickets in those with vitamin D deficiency. Although it is considered a limitation that we did not evaluate the factors that may be associated with vitamin D levels (sunlight exposure, vitamin supplementation, exercise, body mass index, etc.), our aim in this study was to determine the prevalence of the vitamin. D deficiency.

We have some limitations in this study. Our study is retrospective and single-center. Therefore, the results may not reflect the entire pediatric population in Ankara. In addition, since our study was retrospective, we could not obtain sufficient data to determine the prevalence of rickets in those with vitamin D deficiency. Although it is considered a limitation that we did not evaluate the factors associated with vitamin D level (sunlight exposure, vitamin supplementation, exercise, body mass index, etc.), we aimed to determine the prevalence of vitamin D deficiency.

In conclusion, vitamin D deficiency was common in our study. Vitamin D deficiency causes nonspecific complaints in children and does not always present symptoms on physical examination. The lack of routine screening programs to determine the vitamin D status of children in clinical practice suggests that many deficiencies may not be noticed. However, in childhood, when there is a high bone growth rate, bone mineralization deficiency that can be caused by vitamin D deficiency is very important. To prevent this, it is crucial to take anamnesis in terms of daily vitamin D intake in children. Children with insufficient daily intake should be supported. After that, it is essential to measure serum 25(OH)D levels for determining whether vitamin D levels reach optimal levels.

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