

Vitamin D Status in Turkey

Türkiye’de D Vitamini Düzeyleri

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Abstract

Background/ Aim: Vitamin D deficiency is highly prevalent condition. The aim of the present study was to assess vitamin D status in people living in Turkey.

Methods: This was a single center, retrospective study on subjects who attended to Acıbadem Hospitals and outpatient clinics for the measurement of 25(OH)D. Data on 25(OH)D was available for 179464 subjects.

Results: Mean 25(OH)D was 19, 56 ± 0,04 ng/mL and mean age of the subjects was 39, 28 ± 0, 05 years. Mean 25(OH)D of women were lower than men; (18, 79 ± 0, 05 vs 22, 07 ± 0, 09 ng/mL; p<0.001). 25(OH)D of 111510 subjects (62, 1%) was <20 ng/mL. 42592 (23, 7%) were between 20-32 ng/mL. 24276 (13, 5%) of the subjects demonstrated normal 25(OH)D levels. 25(OH)D level was excess in 776 (0, 4%) of the subjects. Three hundred and ten (0, 2%) had toxic 25(OH)D levels. Totally 85, 9% of the subjects had low 25(OH)D levels. Adolescents, adults and elderly had lower 25(OH)D levels than newborns and children (p<0.001). Vitamin D deficiency and insufficiency were more common in adolescents, adults and elderly than in new born and children (p<0.001).

Conclusions: A considerable number of subjects in our study had 25(OH)D below the normal ranges for all age groups except neonates, demonstrating that vitamin D deficiency and insufficiency in western part of the country is a major healthcare concern in Turkey.

Keywords: Vitamin D status, Vitamin D deficiency, 25(OH)D, Turkey.

Özet

Amaç: D vitamini eksikliği oldukça yaygın bir durumdur. Bu çalışmanın amacı Türkiye’de yaşayan kişilerde D vitamini durumunu değerlendirmektir.

Yöntem: Acıbadem Hastaneleri ve polikliniklere 25(OH)D ölçümü için başvuran kişiler üzerinde yapılan tek merkezli, retrospektif bir çalışmaydı. 25(OH)D’ye ilişkin veriler 179464 denek için mevcuttu.

Bulgular: Ortalama 25(OH)D 19, 56 ± 0,04 ng/mL ve olguların yaş ortalaması 39, 28 ± 0,05 yıldı. Kadınların ortalama 25(OH)D’si erkeklerden daha düşüktü; (18, 79 ± 0, 05’e karşı 22, 07 ± 0, 09 ng/mL; p<0,001). 111510 denegin 25(OH)D’si (62, %1) <20 ng/mL idi. 42592 (%23, %7) 20-32 ng/mL arasındaydı. Deneklerin 24276’sı (13, %5) normal 25(OH)D düzeyleri gösterdi. Olguların 776’sında (%0,4) 25(OH)D düzeyi fazlaydı. Üç yüz on tanesinde (%0,2) toksik 25(OH)D seviyeleri vardı. Toplamda deneklerin %85,9’unda 25(OH)D düzeyi düşüktü. Ergenler, yetişkinler ve yaşlılarda 25(OH)D düzeyleri yenidoğan ve çocuklara göre daha düşüktü (p<0,001). D vitamini eksikliği ve yetersizliği adölesan, erişkin ve yaşlılarda yeni doğan ve çocuklara göre daha sık görüldü (p<0,001).

Sonuç: Çalışmamızda önemli sayıda olguda yenidoğanlar hariç tüm yaş gruplarında 25(OH)D normal aralığın altındaydı; bu durum ülkenin batı kesimindeki D vitamini eksikliği ve yetersizliğinin Türkiye’de önemli bir sağlık sorunu olduğunu ortaya koymaktadır.

Anahtar Kelimeler: D vitamini durumu, D vitamini eksikliği, 25(OH)D, Türkiye.

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INTRODUCTION

Vitamin D plays an essential role in the regulation of metabolism, calcium and phosphorus absorption of bone health. However, the effects of vitamin D are not limited to mineral homeostasis and skeletal health maintenance. The presence of vitamin D receptors in other tissue and organs suggest that vitamin D physiology extends well above and beyond bone homeostasis (1). Vitamin D also plays a critical role in many cellular and immunological processes, and low levels have been associated with osteoporosis, osteomalacia, rickets, muscle weakness, metabolic syndrome, diabetes, cardiovascular disease, cancer, autoimmune diseases, schizophrenia, depression, asthma, low antimüllerian hormone levels, and microbial infections (2-3).

Vitamin D deficiency is a major public health problem worldwide in all age groups, even in those residing in countries with low latitude, where it was generally assumed that UV radiation was adequate enough to prevent this deficiency, and in industrialized countries, where vitamin D fortification has been implemented now for years. However, most countries, including Turkey, are still lacking data, particularly population representative data, with very limited information in infants, children, adolescents and pregnant women. Vitamin D status can be influenced by multiple variables, including race, geographic latitude, environment, lifestyle, and genetics. It is now recognized across many scientific disciplines that vitamin D deficiency is pandemic (1, 4, 5).

The clinical advantages of choosing 25(OH)D instead of calcitriol as a marker for vitamin D status has been listed by Holick MF (6). The vitamin D level needed to optimize intestinal calcium absorption (34 ng/mL) is lower than the level needed for neuromuscular performance (38 ng/mL). Experts however believe that the lower limit of adequate 25(OH)D levels should be 30 ng/mL. Still others recommend a lower limit of 40 ng/mL, since impaired calcium metabolism due to low serum 25(OH)D levels may trigger secondary hyperparathyroidism, increased bone turnover and progressive bone loss. The proposed 25(OH)D cut-off for optimum skeletal health is the level that reduces parathormon (PTH) to a minimum and increases calcium absorption to its maximum. Several studies have shown that PTH levels plateau at a minimum steady-state level as serum 25(OH)D levels approach and rise above approximately 30 ng/mL. The established consensus of several vitamin D cut-offs is as; 25(OH)D < 20 ng/mL is deficiency, 20-32 ng/mL is insufficiency, > 100 ng/mL is excess, and > 150 ng/mL is toxic (6-15). The mean vitamin D levels in Turkey varied widely between 4 ng/mL and 63 ng/mL, and vitamin D deficiency is highly prevalent condition, present in approximately up to 78% of the general population (16, 17). Therefore, the aim of the present study was to assess vitamin D status in people living in Turkey.

METHODS

This was a single center, retrospective study on subjects who attended to Acibadem Acibadem Hospitals and outpatient clinics for the measurement of 25 (OH)D. Acibadem University Ethics Committee for Human Studies approved the study protocol. Data on 25(OH)D was available for 179464 subjects (137810 women and 41654 men). First measurements were chosen in duplicated measurements for the same subjects. A triple quadruple mass spectrometric method (in Agilent 6460) with ESI+ mode used for 25(OH)D analysis which was developed with calibration traceable to The National Institute of Standards and Technology (NIST), Standard Reference Material (SRM) 972 . Serum samples first mixed with protein denaturing solution containing internal standard, 25-OH Vitamin D3 (D6) and after centrifugation, the clear

supernatant was transferred to liquid chromatography vials. Fragments of 25-OH vitamin D3, 25-OH vitamin D2 and IS were detected by MRM using the following mass-to-charge (m/z) transitions: 401.3→383,3 for 25-OH vitamin D3, 413.3→395,3 for 25-OH vitamin D2, and 407.3→389,3 for the labelled IS.

NIST SRM 972 was also used as a quality assurance tool. SRM 972, Vitamin D in Human Serum, consists of four blood serum sample pools (Level 1 – Level 4) with varying levels of 25(OH)D. SRM 972 has certified values for 25(OH)D2, 25(OH)D3, and 3-epi-25(OH)D3.

The presented method was found to be linear between 4, 4-191 ng/ml. The limit of detection and quantitation were 1, 3 ng/ml and 4, 4 ng/ml respectively. The interassay and intraassay precision values represented as %CV and were both found to be ≤5%.

Descriptive statistics were presented as mean ± standard error mean (SEM) for normally distributed data, and as counts and percentages for categorical data. The relationship between the categorical variables was examined using the Pearson Chi-square test. The t-test or one-way Anova test was used to compare independent variables and Levene's test for homogeneity of variances. To determine the correlation between 2 variables, Pearson correlation analysis was performed. Results were evaluated with a confidence interval of 95%, and $p < 0.05$ was considered statistically significant.

RESULTS

Mean 25(OH)D was 19, 56 ± 0,04 ng/mL and mean age of the subjects was 39, 28 ± 0, 05 years. Mean 25(OH)D of women were lower than men; (18, 79 ± 0, 05 vs 22, 07 ± 0, 09 ng/mL; $p < 0.001$) and they were older than men (42, 17 ± 0, 06 vs 29, 71 ± 0, 12 years; $p < 0.001$). 25(OH)D of 111510 subjects (62, 1%) was <20 ng/mL (vitamin D deficiency).

Table 1. Adolescents, Adults And Elderly Had Lower 25(OH)D Levels Than New Born And Children

Age [years]	New born	1-8	9-16	17-40	41-60	>60
25 [OH]D [ng/mL]	34,32±0,39	25,16±0,15	17,82±0,11	17,27±0,07	18,69±0,07	19,71±0,10

$P < 0.001$

Forty two thousand five hundred ninety two (23, 7%) were between 20-32 ng/mL (insufficiency). Twenty four thousand two hundred seventy six (13, 5%) of the subjects demonstrated normal 25(OH)D (between 32-100 ng/mL) levels. 25(OH)D level was excess in 776 (0, 4%) of the subjects (25(OH)D > 100 ng/mL).

Three hundred and ten (0, 2%) had toxic 25(OH)D (>150 ng/mL) levels. Totally 85, 9% of the subjects had low 25 (OH)D levels (25(OH)D < 32 ng/mL). There was a considerable variation among the subgroups.

Adolescents, adults and elderly had lower 25 (OH)D levels than newborns and children as given in Table 1 ($p < 0.001$). Vitamin D deficiency and insufficiency were more common in adolescents, adults and elderly than in new born and children as given in Table 2 ($p < 0.001$).

Table 2. Vitamin D Deficiency And Insufficiency Were More Common In Adolescents, Adults And Elderly Than In New Born And Children

Age [years]		25 [OH]D [ng/mL]				
		<20	20-32	33-100	101-150	>150
New born	Count	1507	1277	2756	49	35
	% within age	26,8%	22,7%	49,0%	,9%	,6%
	% within 25(OH)D	1,4%	3,0%	11,4%	6,3%	11,3%
	% of Total	,8%	,7%	1,5%	,0%	0,0%
1-8	Count	7474	6746	3980	78	69
	% within age	40,7%	36,8%	21,7%	,4%	,4%
	% within 25(OH)D	6,7%	15,8%	16,4%	10,1%	22,3%
	% of Total	4,2%	3,8%	2,2%	,0%	,0%
9-16	Count	8410	3306	1008	24	5
	% within age	65,9%	25,9%	7,9%	,2%	,0%
	% within 25(OH)D	7,5%	7,8%	4,2%	3,1%	1,6%
	% of Total	4,7%	1,8%	,6%	,0%	,0%
17-40	Count	36146	10804	4907	169	70
	% within age	69,4%	20,7%	9,4%	,3%	0,1%
	% within 25(OH)D	32,4%	25,4%	20,2%	21,8%	22,6%
	% of Total	20,1%	6,0%	2,7%	,1%	,0%
41-60	Count	37254	12888	6886	262	73
	% within age	64,9%	22,5%	12,0%	,5%	,1%
	% within 25(OH)D	33,4%	30,3%	28,4%	33,8%	23,5%
	% of Total	20,8%	7,2%	3,8%	,1%	,0%
>61	Count	20719	7571	4739	194	58
	% within age	62,3%	22,7%	14,2%	,6%	,2%
	% within 25(OH)D	18,6%	17,8%	19,5%	25,0%	18,7%
	% of Total	11,5%	4,2%	2,6%	,1%	,0%

DISCUSSION

To our knowledge, this is the first study in which serum 25(OH)D concentrations were analyzed in one laboratory with this number of subjects in Turkey. The use of 32 ng/mL as cut-off value for low 25(OH)D concentrations in our study agrees with the finding that 25(OH)D levels below 32 ng/mL are associated with secondary hyperparathyroidism, increased bone turnover, and decreased bone-mass density at the hip (6-15).

This retrospective study showed that 25(OH)D concentrations below 32 ng/mL are widespread among people in Turkey. Low 25(OH)D concentrations could generally be explained by reduced sunlight exposure; avoidance of sunlight, clothing habits, performance of outdoor leisure time activities; and by problems with performing activities of daily living.

A small part of the serum 25(OH)D comes from dietary intake, especially fatty fish. The dietary intake is more important when sunshine exposure is less. Vitamin D status in Europe varies according to latitude, season and skin pigmentation (17-32). Serum 25(OH)D is higher in Northern Europe than in Southern Europe and higher in Western than in Eastern Europe. The higher levels in Northern Europe were also observed in some multicenter studies in which one laboratory facility was used (10, 33-35). The high serum 25(OH)D levels in Scandisk countries are probably due to a high intake of fatty fish and cod liver oil, and vitamin D supplementation. The low serum 25(OH)D in Spain, Italy, and Greece may be due to more skin pigmentation and sunshine avoiding behavior. Previous studies in Turkey and Jordan in women showed a strong relationship with clothing (17, 36-39). Serum 25(OH)D decreased from women with western clothing going to traditional women with hijab and completely veiled women with hijab. In concordant to our study, men in these countries have higher levels than women.

Turkey's vitamin D prophylaxis augmentation program started in 2005 and has resulted in a marked decrease in vitamin D deficiency in healthy children less than 1 year of age. In the present study, mean 25(OH)D level of new born is higher than the others, and percentage of subjects with vitamin D deficiency and insufficiency was the lowest in the group. In contrast to our finding, previous studies in Turkey found higher percentage of vitamin deficiency in neonates (40, 41). In our study, 25(OH)D levels were significantly lower in children and adolescents compared with new born group. Recent studies from Turkey and other countries have also demonstrated that vitamin D deficiency is common in children and adolescents (42-45).

CONCLUSION

A considerable number of subjects in our study had 25(OH)D below the normal ranges for all age groups except neonates, demonstrating that vitamin D deficiency and insufficiency is a major healthcare concern in Turkey. The results emphasize the need for continuous monitoring in all regions, even in a country which gets lots of sunlight.

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Author Contributions

Working Concept / Design	: AG, LÖ, KÇ
Data collecting	: AG, LÖ, KÇ
Data Analysis / Interpretation	: AG, LÖ, KÇ
Writing Draft	: AG, LÖ, KÇ
Technical Support / Material Support	: AG, LÖ, KÇ
Critical review of content	: AG, LÖ, KÇ
Literature Review	: AG, LÖ, KÇ

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