Prevalence of vitamin D deficiency and hypervitaminosis D among adult patients admitted to the tertiary care hospitals in Turkey

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Abstract

Purpose: Vitamin D deficiency is a common health problem around the world. This study aimed to evaluate the nationwide prevalence of vitamin D status in tertiary care hospitals in Turkey. Methods: Retrospectively, the data of vitamin D levels from 33 tertiary care hospitals' clinical biochemistry laboratories around Turkey between 2 January 2016 and 31 December 2016 were conducted. Results: In total 706434 serum samples from adult subjects (F/M: 469028/ 237406; 66.4%/ 33.6%) were included. While vitamin D levels were sufficient in 20.3% (n=14222), they were insufficient in 21.9% (n=154360) and deficient in 57.8% (n=408882). Of the deficient group, 25.0% (176608) had levels <10 ng/mL consistent with profound deficiency. We observed the highest rates of deficiency in those aged between 18-29 years 62.9% (n=70235) and lowest rates in 60-69 years (52.3%, n=61121) and in 70-79 years (52.3%, n=32397). Hypervitaminosis D were consisting of 5.5% of adult subjects. highest rates of hypervitaminosis D were observed in over 80 years (6.6%) and 70-79 years (6.5%), and the lowest in 18-29 years (2.8%). Deficiency rates were 55.4% (n=131468) in men and 59.2% (n=277384) in women. Higher deficiency rates were observed in January (67.9%), February (71.6%), and March (66.7%). Conclusion: In this cohort, over half of the subjects admitted to the tertiary care hospitals in Turkey had vitamin D deficiency, required vitamin D supplementation. The elderly population had the lowest prevalence of vitamin D insufficiency and the highest prevalence of hypervitaminosis D. That may indicate overtreatment of vitamin D supplementation in the elderly group.

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Keywords: 25-hydroxyvitamin D; vitamin D deficiency; vitamin D insufficiency, vitamin D toxicity, seasonal variation

Abstract

Purpose: Vitamin D deficiency is a common health problem around the world. This study aimed to evaluate the nationwide prevalence of vitamin D status in tertiary care hospitals in Turkey.

Methods: Retrospectively, the data of vitamin D levels from 33 tertiary care hospitals' clinical biochemistry laboratories around Turkey between 2 January 2016 and 31 December 2016 were conducted.

Results: In total 706434 serum samples from adult subjects (F/M: 469028/ 237406; 66.4%/ 33.6%) were included. While vitamin D levels were sufficient in 20.3% (n=14222), they were insufficient in 21.9% (n=154360) and deficient in 57.8% (n=408882). Of the deficient group, 25.0% (176608) had levels <10 ng/mL consistent with profound deficiency.

We observed the highest rates of deficiency in those aged between 18-29 years 62.9% (n=70235) and lowest rates in 60-69 years (52.3%, n=61121) and in 70-79 years (52.3%, n=32397). Hypervitaminosis D were consisting of 5.5% of adult subjects. highest rates of hypervitaminosis D were observed in over 80 years (6.6%) and 70-79 years (6.5%), and the lowest in 18-29 years (2.8%). Deficiency rates were 55.4% (n=131468) in men and 59.2% (n=277384) in women. Higher deficiency rates were observed in January (67.9%), February (71.6%), and March (66.7%).

Conclusion: In this cohort, over half of the subjects admitted to the tertiary care hospitals in Turkey had vitamin D deficiency, required vitamin D supplementation. The elderly population had the lowest prevalence of vitamin D insufficiency and the highest prevalence of hypervitaminosis D. That may indicate overtreatment of vitamin D supplementation in the elderly group.

What's known?

The highest rates of deficiency are seen in spring and winter

Over half of the subjects have vitamin D deficiency

What's new?

The overall prevalence of vitamin D deficiency in hospital admitted subjects is similar to those in hospital-derived studies

The elderly population has the lowest prevalence of vitamin D insufficiency

The elderly population has the highest prevalence of hypervitaminosis D that may indicate overtreatment vitamin D supplementation in the tertiary care hospitals

Introduction

Vitamin D deficiency is a major public health problem worldwide in all age groups. Low serum vitamin D levels have been associated with adverse clinical outcomes; identifying and treating deficiency may improve outcomes. The estimated prevalence of vitamin D levels below 20 ng/mL was previously reported as 37% in world overview [1], 72% in China [2], 26% in US [3], 40% in Europe [4], 37% in Canada [5], and 24% in US [6, 7]. In a meta-analysis from Turkey vitamin D, deficiency/insufficiency rates were 63.5% among adults [8]. Vitamin D deficiency was found to be higher in specific groups, such as subjects from nursing homes [9], long-term indoor healthcare workers [10], and patients with obesity and diabetes [11, 12].

Vitamin D deficiency is related to chronic diseases, the tendency of some infections, and worsening of infections [13]. Treating vitamin D deficiency is cheap, and treating deficiency may improve some clinical outcomes of chronic diseases and infections. Diagnosis and treatment of vitamin D deficiency and toxicity depend on laboratory measurements of 25(OH) D levels [14]. Vitamin D deficiency is relatively more common in hospital admitted patients, and an inverse relationship between the frequency of vitamin D deficiency and hospital admission had been reported [15]. In Rai et al. study [16] and Amrein, et al. study [17], vitamin D deficiency was detected in 73.6% and 60.2% of tertiary care center admitted patients, it was 71.23% among 6957 patients from secondary care hospital laboratory [8], and it was found as 65.4% in a general hospital from India [18].

Vitamin D levels vary seasonally, usually increase from spring to summer and decrease afterward. Aging, female gender, increased skin pigmentation, higher latitude, winter season, less sunlight exposure, topical application of sunscreen, dietary habits, obesity are found to be associated with lower 25(OH) D levels [14, 19, 20]. Also, the hospital admitted patients affected from seasons, in Sezgin et al. study vitamin D levels were higher in summer compared to winter [21]. In line with previous reports, in Amrein et al study [17] vitamin D deficiency was higher in winter compared to summer and autumn.

We hypothesize that the frequency of vitamin D deficiency in subjects who are admitted to hospitals is higher than the general population, and vitamin D intoxication is also higher than reported. This study aimed to evaluate the nationwide prevalence of vitamin D status in tertiary care hospitals in Turkey. We determined age and gender-related rates of vitamin D insufficiency, deficiency, and hypervitaminosis D in adult subjects admitted to tertiary care hospitals.

Materials and methods

Study population and study locations

This nationwide study included 33 reference hospital laboratories, where vitamin D measurement is available in Turkey. In total, 21 biggest cities from south to north of country between 36° N -42° N lattitudes with third-level reference hospitals were selected; [Adana (37° N), Ankara (39° N), Antalya (36° N), Aydın (37° N), Diyarbakir (37° N), Eskisehir (39° N), Erzurum (39° N), Giresun (40° N), Istanbul (41° N), Izmir (38° N), Kahramanmaras (37° N), Kayseri (38° N), Kocaeli (40° N), Konya (37° N), Malatya (38° N), Mersin (36° N), Samsun (41° N), Tekirdag (40° N), Trabzon (41° N), Yozgat (39° N), Zonguldak (41° N)].

Data were collected retrospectively for the date of sample, age of the participant on the date the sample was taken, sex, and vitamin D levels. Consecutive measurement of vitamin D levels in the tertiary care hospitals' clinical biochemistry laboratories around Turkey between 2 January 2016 and 31 December 2016 was recorded.

Data of age over 18 yrs with no additional exclusion criteria were included in the final analysis.

Thirty labs were used chemiluminescence immunoassays (CLIA), and 3 labs were used high-performance liquid chromatography (HPLC) for the measurement of serum 25(OH)D levels. The measurement range was 2-167 ng/ml for the CLIA method, and 1.2-160 ng/ml for HPLC.

The study protocol was approved by the Marmara University Medical School Ethics Committee (09.2017.519) and conducted following the International Conference on Harmonization Guidelines for Good Clinical Practice and the Declaration of Helsinki.

Study design

Vitamin D deficiency was defined as a circulating 25(OH)D levels of less than 20 ng/mL (50 nmol/L), insufficiency as 20–29 ng/mL, sufficiency as [?]30 ng/mL (75nmol/L) according to the Endocrine Society Clinical Practice Guideline [14]. Severe vitamin D deficiency is defined as 25(OH)D levels less than 10 ng/mL [22]. Hypervitaminosis D defined serum level of 25(OH)D >50 ng/mL (125 nmol/L) and toxicosis as >100 ng/mL (250 nml/L) [23, 24]. Subjects were evaluated into subgroups according to age, sex, the season for vitamin D levels. The data were classified according to age (18–29 years, 30–39 years, 40–49 years, 50–59 years, 60-69 years, 70–79 years, and [?]80 years). Season classifications were: winter (December, January, and February), spring (March, April, and May), summer (June, July, and August), and autumn (September, October, and November).

Statistical analyses

Continuous variables were summarized using descriptive statistics presented as mean and standard deviation (SD). Categorical variables were summarized using counts and percentages. Categorical data were analyzed using the Chi-square ($\chi2$) test or Fisher exact test appropriately. Mann Whitney U and Kruskal Wallis ANOVA were used for comparing groups.

The results were evaluated at a 95% confidence interval, and $p < 0.05$ was considered statistically significant. All statistical analyses were performed using software (Prism; GraphPad Software, Inc., San Diego, CA, USA).

Results

706434 subjects' data were included in the study. Of the total, 66.4% (n=469028) were women. The distribution of 25(OH)D levels according to age groups, sex and seasons is shown in Table 1.

25(OH)D levels in the whole group

The median 25(OH)D level was 17.4 ng/mL (min-max: 0.1-945 ng/mL) in the whole group. The median 25(OH)D level was 16.6 ng/mL (min-max: 0.3-945 ng/mL) in women, 18.3 ng/mL (min-max: 0.1-905 ng/mL) in men. There was no statistically significant difference in terms of vitamin D levels between men and women in the whole group (p=0.300) (Table 1).

Vitamin D deficiency was present in 57.8% (n=408852) of the whole subjects' blood samples measured for a year. Severe vitamin D deficiency (<10 ng/mL) was detected in 25% (n=176608) of the samples. 25(OH)D levels were over 50ng/mL in 5.5%, of the samples and 0.8% (n=5455) was over 100 ng/ml accepted as a toxic range (Table 1).

Vitamin D levels according to age

The lowest median 25(OH)D level was 14.6 ng/mL (min-max: 0.8-945 ng/mL) in subjects aged between 18 and 29 years. The highest median 25(OH)D level was 19.5 ng/mL (min-max: 0.3-623 ng/mL) in subjects in sixth decade 19.5 ng/mL (min-max: 0.3-623 ng/mL), and seventh decade 19.4 ng/mL (min-max: 0.3-647 ng/mL). The lowest median vitamin D levels were observed in the twenties and thirties, which was statistically significant compared with the 60-69 and 70-79 years group (p=0.001) (Table 1).

Although the highest vitamin D deficiency rates observed in 18-29 years and 30-39 years, the prevalence of vitamin D deficiency (p=0.240), and insufficiency (p=0.970) were not statistically significant among the age groups (Table 2).

Vitamin D levels in men and women

Median vitamin D levels were similar in men and women in the whole group (Table 1). the frequency of vitamin D deficiency was not different in women (59.2%) and men (55.4%) groups (p=0.660).

Male subjects within an age group 18-29 years, 39-39 years, and over 80 years have higher vitamin D levels compared to the women group at the same age (p <0.001, p <0.001, p=0.010 respectively) (Table 3).

The frequencies of vitamin D deficiency and insufficiency according to gender are shown in Table 4. The frequency of deficiency was higher both in the female and male groups than in the insufficiency (p<0.001) and sufficient groups (p=<0.001).

Vitamin D levels and deficiency according to seasons

Mean vitamin D levels were 23.6±17.3 ng/mL for autumn, 23.3±18.0ng/ml for summer, 19.6±18.5 ng/ml for winter and 20.0±18.6 ng/ml for spring.

Median vitamin D levels were higher in autumn and summer serum samples compared to winter and spring serum samples (p<0.001) (Table 1). The frequency of vitamin D deficiency was higher in January, February, March, and April compared to in June, July, August, September, and October (p=0.005) (Figure 1). While the frequency of vitamin D deficiency was the highest in February (71.6%) it was the lowest in September with a 44.2% ratio.

Discussion

Our study confirms previous reports that vitamin D insufficiency and deficiency are common in the tertiary care hospital admitted subjects, which affected 57.8% of our cohort. Severe vitamin D deficiency was observed in 25% and toxic levels in 0.8% of the cohort. While the highest vitamin D levels were detected in subjects aged between 60 and 79 years, the frequency of vitamin D deficiency was similar between the age groups. Median 25(OH)levels and vitamin D deficiency frequencies were similar between women and men in the whole group. Median 25(OH)D levels in summer and autumn were higher than spring and winter in the whole cohort. To date, this is the largest study of vitamin D status among hospital admitted patients in Turkey.

The levels of vitamin D below 30 ng/mL have been reported in a wide range of distribution; ranged between 26.4% to 77.7 % in the literature [14, 25-28]. While in Korea National Health and Nutrition Examination Survey (KNHANES) 65.7% of males and 76.7% of females had deficient vitamin D levels [29], it was detected in 55.4% and 59.2% of males and females, respectively, in our study. Delos Reyes et al. study which included 15708 subjects admitted to tertiary care hospitals reported that the vitamin D deficiency rate was 11.2%, insufficiency was 32.4% and sufficiency was 56.4% [28]. Vitamin D deficiency was detected in 73.6% and 60.2% of tertiary care center hospitalized patients [16, 17]. While severe deficiency was reported as 26.9%

[30], 20.8% [31], 11.2% [28] in previous reports, it was 25 % in our study. In our study sufficient vitamin D levels were detected in 20.3% of patients, while it was ranged between 2.7 to 56.4% in the literature [28, 31].

Similar to previous reports [28, 29, 31], in our study, 25(OH)D levels were higher in older subjects compared to subjects aged below 30 years. Vitamin D deficiency in the young adult group is related to decreased outdoor activities and aggressive sun protection [14]. We attribute the higher levels of 25(OH)D in the elderly population to the representation of the elderly population in this cohort is low, and to the supplementation of vitamin D in this group.

In Forrest et al. study, which evaluated data from 2005 to 2006 of NHANES, the subjects aged between 55 to 59 and 60 to 64 had the highest prevalence rate of vitamin D deficiency [19]. On the other side, in Basile et al. study, subjects aged [?]45years or 46-64 years had higher vitamin D levels compared to those older than 65 years [26].

There controversial results about the effect of gender on vitamin D deficiency. Similar to Forrest et al. study [19], we found that vitamin D levels were similar both in men and women. In Yu et al. [31] and Muscogiuri et al. [12] studies, women had lower vitamin D levels than men. In Hilger et al. study, 25(OH)D levels in women tended to be lower, especially in the Asia/Pacific and Middle East/Africa regions [1]. Contrary to this, in Basile [26] and Delos Reyes [28] et al. studies, vitamin D levels were significantly higher in women than in men [26, 28].

In line with previous reports the median 25(OH)D levels varied significantly according to the seasons, deficiency was found to be most prevalent in spring and winter compared to other seasons [5, 14, 30-33].

Limitations

The 25(OH)D results of the hospital admitted patients may not completely compatible with the healthy population. Due to the retrospective design, dietary habits of patients, food fortifications, taking vitamin D supplements, or duration of sun exposure are not known. Lastly, two different methodologies for 25(OH)D measurement was used, CLIA and HPLC. The most valid method has been reported as HPLC, and measurements with CLIA could result in lower values [34].

Conclusion:

The overall prevalence of vitamin D deficiency in hospital admitted subjects is similar to those in hospital-derived studies from national Turkish and European populations. In this cohort, over half of the subjects admitted to the general hospitals in Turkey had vitamin D deficiency requiring vitamin D supplementation. Although this retrospective study was not able to exclude vitamin D-related diseases and vitamin D-treated patients, the highest prevalence of hypervitaminosis D is observed in the elderly population that may indicate overtreatment vitamin D supplementation in the tertiary care hospitals in Turkey. Further prospective studies are needed to guide appropriate vitamin D supplementation for subgroups and to prevent overtreatment.

Abbreviations:

CLIA, chemiluminescence immunoassays

HPLC, high-performance liquid chromatography

F, female

M, male

25(OH)D, 25 hydroxyvitamin D levels

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Author contribution statement

All authors made substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and gave final approval of the version to be submitted.

Ethical Approval: All procedures performed in studies involving human participants were following the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Figure legends

Figure 1 The frequency of Vitamin D deficiency in the whole group according to months

Table 1 Median 25(OH)D levels according to gender, age groups, and seasons measured in tertiary hospital laboratories from Turkey

	n (%)	25(OH)D vitamin levels, ng/mL, median (min-max)	p
Whole group	706434	17.4 (0.1-945)	
Sex			0.300
Female	469028 (66.4)	16.6 (0.3-945)	
Male	237406 (33.6)	18.3 (0.1-905)	
25(OH)D vitamin levels			
<10 ng/mL	176608 (25.0)		
10-19 ng/mL	232274 (32.8)		
20-29 ng/mL	154360 (21.9)		
30-49 ng/mL	104573 (14.8)		
50-100 ng/mL	33194 (4.7)		
100-149 ng/mL	4627 (0.7)		?¿?
150 ng/mL	828 (0.1)		
Age			**0.001**
18-29 yrs	104188 (14.7)	14.6 (0.8-945)	
30-39 yrs	114936 (16.3)	15.8 (0.1-636)	
40-49 yrs	134637 (19.1)	17.2 (0.1-606)	
50-59 yrs	146583 (20.7)	18.4 (0.3-905)	
60-69 yrs	118476 (16.8)	19.5 (0.3-623)	
70-79 yrs	62754 (8.9)	19.4 (0.3-647)	?¿?
80 yrs	24860 (3.5)	17.9 (0.3-288)	
Season			**<0.001**
Winter (Dec, Jan, Feb)	166420 (23.5)	15.0 (0.1-945)	
Spring (Mar, Apr, May)	194120 (27.6)	15.2 (0.1-647)	
Summer (Jun, Jul, Aug)	160336 (22.6)	19.3 (0.1-905)	
Autumn (Sep, Oct, Nov)	185558 (26.3)	20.3 (0.1-623)	

Apr, April; Aug, august; Dec, December; Feb, February; Jan, January; Jul, Jully; Jun, June; Mar, March; Nov, November; Oct, October; Sep, September

25(OH)D levels	18-29 yrs n=103491	30-39 yrs n=114025	40-49 yrs n=133453	40-49 yrs n=133453	50-59 yrs n=145000	60-69 yrs n=116955	70-79 yrs n=61927	[?]80 yrs n=24424	p
<20 ng/mL, n (%)	70235 (67.9)	72375 (63.5)	72375 (63.5)	79211 (59.3)	79942 (55.1)	61121 (52.3)	32397 (52.3)	13571 (55.5)	0.2
20-29 ng/mL, n (%)	19675 (19.0)	23461 (20.6)	23461 (20.6)	31045 (23.3)	33785 (23.3)	27816 (23.8)	13851 (22.4)	4727 (19.4)	0.9
30-49 ng/mL, n (%)	10667 (10.3)	14078 (12.3)	14078 (12.3)	18641 (14.0)	23801 (16.4)	21245 (18.1)	11634 (18.8)	4507 (18.5)	0.4
[?]50 ng/mL, n (%)	3611 2.8	5022 3.6	5022 3.6	5740 3.4	9055 5.2	8294 5.8	4872 6.5	2055 6.6	0.6

Table 2 25(OH)D levels according to age groups

p values were given for each line.

Table 3 Mean 25(OH)D levels according to age groups and gender

Age	Women n= 469028	Men n= 237406	25(OH)D levels	25(OH)D levels	p
			Women	**Men**	
18-29	69863 (14.9)	34325 (14.5)	17.2±16.3	20.3±15.6	**<0.001**
30-39	78137 (16.6)	36799 (15.5)	19.5±17.2	21.5 ±15.2	**<0.001**
40-49	91717 (19.5)	42920 (18.1)	21.3±18.6	21.6±17.5	0.430
50-59	98365 (20.9)	48218 (20.3)	23.3±19.0	22.3±16.7	0.070
60-69	76084 (16.2)	42392 (17.8)	23.6±21.0	23.4±17.1	0.260
70-79	39212 (8.6)	23542 (9.9)	24.5±21.2	23.1±18.0	0.320
[?]80	15650 (3.3)	9210 (3.9)	21.1±22.2	22.5 ± 20.2	**0.010**

Values reported as n (%) and mean±standard deviation. The numbers in bold is the statistical significance ($p < 0.05$)

Table 4 Vitamin D status according to gender and seasons

	Deficiency ([?]20 ng/mL)	Insufficiency (20-30 ng/mL)	Sufficiency ([?]30 ng/mL)	p
Total	408852 (57.9)	162363 (23.0)	135219 (19.1)	**<0.001**
Female	277384 (59.2)	101542 (21.6)	90102 (19.2)	**<0.001***
Male	131468 (55.4)	60821 (25.6)	45117 (19.0)	**<0.001***
Age				
Female	47.03±16.7	50.21±16.8	52.9±16.3	0.730
Male	49.14±17.2	50.05±16.6	52.4±16.1	
Frequency according to seasons				
Winter	106974 (63.5)	32607 (19.4)	28843 (17.1)	**<0.001**
Spring	128163 (63.8)	36521 (18.2)	36178 (18.0)	**<0.001**
Summer	84603 (54.3)	42631 (27.3)	28701 (18.4)	**<0.001**
Autumn	89112 (49.2)	50604 (27.9)	41497 (22.9)	**<0.001**

Values reported as n (%) and mean±standard deviation.

** p values were given for each line. The numbers in bold is the statistical significance ($p < 0.05$)*

ns; not significant

Figure 1 The frequency of Vitamin D deficiency in the whole group according to months