

## SEASONAL VARIATION OF VITAMIN-D LEVELS IN THE ADULT POPULATION IN ISTANBUL/TURKEY: A POPULATION-BASED STUDY

### İSTANBUL / TÜRKİYE'DE YETİŞKİN POPÜLASYONDA D VİTAMİNİ DÜZEYLERİNİN MEVSİMSEL DEĞİŞİMİ: POPÜLASYONA DAYALI BİR ÇALIŞMA

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#### ABSTRACT

**Objective:** The current research examined if there is a variance in the frequency of vitamin D deficiency or insufficiency among adults visiting the hospital for medical problems in winter and summer, and whether comorbidities have an impact on this.

**Material and Method:** A total of 1155 patients (771 women, 384 men, mean age:48±15 years) who were admitted to the outpatient clinics of Istanbul Medeniyet University Goztepe Training and Research Hospital in August and February were tested for 25(OH)D levels for any reason were included. A 25(OH)D level of <20 ng/ml was stated as inadequate, and 20–29 ng/ml was defined as insufficient. The two groups were examined in contrast in terms of vitamin D deficiency and insufficiency and the frequency of comorbidities.

**Results:** 25(OH)D levels were inferior in the winter compared to the summer (16.1±12.5 ng/ml versus 22.2±15.8 ng/ml, p<0.001). Vitamin D deficiency was detected in 769 (66.6%) patients, and vitamin D insufficiency was detected in 226 (19.6%). Furthermore, 51.9% and 78.6% of patients had vitamin D deficiency (p< 0.001) and 27.3% and 13.1% had vitamin D insufficiency (p<0.001) during summer and winter, respectively. Prevalence rates of diabetes (60.1% and 39.9%, respectively, p=0.04) and hypertension (62.7% and 37.3%, accordingly, p<0.01) were more common in the winter compared to the summer.

**Conclusion:** The findings of this research show that vitamin D insufficiency and deficiency are well-known health issues in Turkey, and although there has been some improvement, the problem persists even during the sunny seasons.

**Keywords:** Seasonal variation, vitamin D level, vitamin D insufficiency

#### Öz

**Amaç:** Vitamin D [25(OH)D] eksikliği veya yetersizliğinin mevsimsel değişiklik gösterdiği bildirilmektedir. Bu çalışmada hastaneye başvuran erişkinlerde vitamin D eksikliği veya yetersizliği sıklığının kış ve yaz aylarında farklılık gösterip göstermediği ve komorbid durumlardan etkilenip etkilenmediği araştırıldı.

**Gereç ve Yöntem:** Çalışmaya Ağustos 2014 (yaz grubu) ile Şubat 2015 (kış grubu) aylarında İstanbul Medeniyet Üniversitesi Göztepe Eğitim ve Araştırma Hastanesi polikliniklerine müracaat eden ve belirli bir sebeple 25(OH)D vitamini seviyelerine bakılan toplam 1155 olgu (771 kadın, 384 erkek, ortalama yaş: 48±15) dahil edildi. Vitamin D eksikliği<20 ng/ml, vitamin D yetersizliği 20-29 ng/ml olarak tanımlandı. Gruplar vitamin D ihtiyacı, yetersizliği ve komorbidite sıklıklarına göre karşılaştırıldı.

**Bulgular:** Tüm olgularda ortalama vitamin D düzeyi 18,9±14,4 ng/ml (kadınlarda 18,9±15,5 ng/ml, erkeklerde 18,9±12,1 ng/ml) idi. Vitamin D düzeyleri; kış grubunda yaz grubuna göre daha düşük (16,1±12,5 ng/ml'ye karşılık 22,2±15,8 ng/ml, p<0,001) bulundu. Vitamin D eksikliği 769 hastada (%66,6), vitamin D yetersizliği 226 hastada (%19,6) saptandı. Vitamin D eksikliği %51,9'u yaz aylarında, %78,6'sı kış aylarında (p<0,001), D vitamini yetersizliği % 27,3'ü yaz aylarında ve %13,1'i kış aylarında (p<0,001) idi. Kış grubunda yaz grubuna göre diyabet (sırasıyla %60,1 ve %39,9, p=0,04) ve hipertansiyon sıklığı (sırasıyla %62,7 ve %37,3, p<0,01) yüksekti.

**Sonuç:** Bu çalışmada güneşli yaz aylarında dahi popülasyonumuzun yaklaşık yarısında, kış aylarında ise yaklaşık her 4 kişiden 3'ünde vitamin D eksikliği olduğu görülmüştür. Bu bulgular ülkemizde D vitamini eksiklik ve yetersizliğinin yaygın bir sağlık problemi olduğunu, güneşli mevsimlerde bu problemin kısmen azalsa da devam ettiğini göstermiştir.

**Anahtar kelimeler:** Mevsimsel değişim, vitamin D düzeyleri, vitamin D yetersizliği

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## INTRODUCTION

Vitamin D deficiency is a well-known worldwide health issue that is linked with several health problems, including bone fractures, functional limitation, diabetes, cardiovascular disease, cancer, depression, and mortality (1, 2). The risk factors for inferior levels of 25(OH)D include dark skin pigmentation, decreased vitamin D uptake, low ultraviolet light exposure, and obesity, while advanced age, female gender, low physical activity, and education levels are also related to vitamin D deficiency (3). Measuring the serum 25(OH)D concentration is the best indicator of vitamin D levels although the ideal level is still debated (4). Numerous studies have shown that vitamin D deficiency is widespread around the world, particularly in the Middle East and Asia, regardless of risk factors (5,6). The seasonal variation in serum 25(OH)D concentration indicates that levels are at their highest in late summer and at lowest in late winter or early spring (7,8).

This study examined the prevalence of vitamin D deficiency in grown-ups visiting our outpatient clinics, evaluated whether there is an important variance in prevalence between the summer and winter, assessed the extent of cyclical variation, and investigated any links among the low vitamin D levels regarding sex, age, diabetes and hypertension.

## MATERIALS and METHOD

This study included 1,155 individuals (771 females, 384 males) aged  $48 \pm 15$  years who visited the outpatient clinics of Istanbul Medeniyet University Goztepe Training and Research Hospital in August 2014 (the summer group) and February 2015 (the winter group) and were tested for their 25(OH)D levels for any medical purpose. The patient records were obtained retrospectively from the hospital data system while following the ethical rules outlined in the Helsinki Declaration.

**Inclusion criteria:** Individuals who underwent testing to specify their 25(OH)D concentrations and fell between the age sphere of 18 to 75 years old were included in the study.

**Exclusion criteria:** This refers to individuals who received vitamin D replacement therapy, supplementation, or related medication within the previous month, individuals with chronic renal failure characterized by a GFR of less than 60 ml/min, and pregnant women.

### Study design

The study examined the age, sex, 25(OH)D levels, creatinine ranks, and GFR levels of individuals who met the criteria for inclusion. The GFR amount was found using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) recipe. Patient records were reviewed through the hospital information system and the Medula doctor, pharmacy, and electronic prescription system to identify comorbid diagnoses of diabetes or hypertension, and any use of vitamin D replacement therapy or related medications (9). The summer group consisted of patients who presented to the hospital in August 2014, while the winter

group consisted of patients who presented in February 2015. A comparison was made between the two groups regarding the occurrence of vitamin D deficiency and insufficiency, and also the mean seasonal serum concentrations of vitamin D.

### 25(OH)D Levels Analysis

The chemiluminescent microparticle immunological assay (CMIA) procedure was utilized to measure the 25(OH)D levels using the Abbott ARCHITECT system 25-OH vitamin D brand kits (Abbott, USA) with Abbott ARCHITECTi 2000SR immunoanalyzers. The results were quantitatively evaluated in ng/ml, with a reference range of 10–60 ng/ml for winter and 20-100 ng/ml for summer. The levels of 25(OH)D concentration in the serum were categorized as deficient in vitamin D for measurements less than 20 ng/ml, insufficient in vitamin D for measurements between 20 and 30 ng/ml, and normal for measurements are same or more than 30 ng/ml. (4).

### Statistical Analysis

The statistical analysis was conducted by utilizing IBM SPSS Statistics Version 20 software package (Copyright IBM Corporation and its Licensors 1989, 2011). The Kolmogorov-Smirnov test was utilized to assess the normality of variables. Numeric information was presented as mean and standard deviation, and categorical information was given in ratios and numbers. Qualitative data between independent groups were distinguished using the chi-square test, while Student's t-test was conducted for independent group comparisons. In cases where variables were not normally distributed or when comparing two independent groups, the Mann-Whitney U test was utilized. Statistical importance was determined as a p-value of less than 0.05 at a 95% confidence interval.

This study was approved by Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee (Date: 12.05.2015, No: 2015/0049).

## RESULTS

A number of 1.155 people were considered, consisting of 771 women and 384 men with an exact age of  $48 \pm 15$  years. Table 1 presents the comparison of patients' analytical specifics and comorbidities, and their vitamin D levels based on seasonal variations. The mean serum 25(OH)D concentration in all patients was  $18.9 \pm 14.4$  ng/ml, which was inferior in the winter compared to the summer ( $16.1 \pm 12.5$  ng/ml versus  $22.2 \pm 15.8$  ng/ml,  $p < 0.001$ ). Both sexes had lower serum 25(OH)D concentrations in the winter compared to the summer ( $p < 0.001$  for both). The frequency of diabetes and hypertension was greater during the winter season (with p-values of 0.04 and less than 0.001, respectively).

Following an adjustment for age differences among the groups, the average 25(OH)D concentration for all patients was  $18.36 \pm 14.25$  ng/ml, whereas the winter and summer concentrations were  $15.46 \pm 12.60$  ng/ml and  $21.60 \pm 15.28$  ng/ml, respectively (with a p-value of less than 0.001) (Table 2).

**Table 1:** Comparison of clinical characteristics and vitamin D levels between the studied groups according to the seasonal variation

		All population	Summer (August)	Winter	P value
Age (years)		48±15	45±14	50±15	<0.001 <sup>1</sup>
Sex (n, %)	Female	771 (100)	397 (51.5)	374 (48.5)	<0.001 <sup>2</sup>
	Male	384 (100)	125 (32.6)	259 (67.4)	
Diabetes frequency		276 (100)	110 (39.9)	166 (60.1)	0.04 <sup>2</sup>
Hypertension frequency		343 (100)	128 (37.3)	215 (62.7)	<0.001 <sup>2</sup>
Vitamin D (ng/mL) (Mean±SD)	All population	18.9±14.4	22.2±15.8	16.1±12.5	<0.001 <sup>3</sup>
	Male	18.9±15.5	21.3±16.6	16.4±13.8	<0.001 <sup>3</sup>
	Female	18.9±12.1	25.5±12.8	15.7±10.4	<0.001 <sup>3</sup>

<sup>1</sup>Student t test, <sup>2</sup>Pearson Chi-Square test, <sup>3</sup>Mann-Whitney U test

**Table 2:** Comparison of clinical characteristics and vitamin D levels between the studied groups according to the seasonal variation after adjusting for age

		All population (n=952)	Summer (August) (n=448)	Winter (n=504)	P value
Age (years)		45.53±14.11	45.71±13.84	45.36±14.37	0.707 <sup>1</sup>
Sex (n, %)	Female	678 (71.2)	332 (74.1)	346 (68.7)	0.063 <sup>2</sup>
	Male	274 (28.8)	116 (25.9)	158 (31.3)	
Diabetes frequency		209 (22)	95 (21.2)	114 (22.6)	0.599 <sup>2</sup>
Hypertension frequency		264 (27.7)	117 (26.1)	147 (29.2)	0.294 <sup>2</sup>
Vitamin D (ng/mL) (Mean±SD, median)	All population	18.36±14.25	21.60±15.28 (18.9)	15.46±12.60 (12.3)	<0.001 <sup>3</sup>
	Male	19.44±12.84 (16.5)	24.98±12.95 (22.85)	15.36±10.01 (13.15)	<0.001 <sup>3</sup>
	Female	17.92±14.96 (16.85)	20.42±15.86 (16.85)	15.51±13.64 (11.30)	<0.001 <sup>3</sup>

<sup>1</sup>Student t test, <sup>2</sup>Pearson Chi-Square test, <sup>3</sup>Mann-Whitney U test

**Table 3:** Comparison of the vitamin D deficiency (<20 ng/mL), insufficiency (20-30 ng/mL) and normal vitamin D levels (≥ 30 ng/mL) groups according to the seasonal variation.

25(OH)D levels	<20 ng/mL	20-30 ng/mL	≥30 ng/mL	P value <sup>1</sup>
Summer (August) (n, %)	271 (51.9)	143 (27.3)	108 (20.8)	<0.001
Winter (February) (n, %)	498 (78.6)	83 (13.1)	52 (8.5)	
p value <sup>1</sup>	<0.001	<0.001	<0.001	

<sup>1</sup>Pearson Chi-Square test

Table 3 shows that the prevalence of vitamin D deficiency was higher in the winter season in comparison to the summer season (78.6% versus 51.9%, with a p-value of less than 0.001).

Table 4 displays the vitamin D levels among the age groups, revealing that serum 25(OH)D concentrations were greater

in males aged 51-60 compared to females in the same age range (with a p-value of 0.03). Table 5 included a comparison of patients with deficient, insufficient, and normal vitamin D ranks due to season and sex, indicating that vitamin D inadequacy was more visible during the winter for both sexes (with a p-value of less than 0.001).

**Table 4:** Analysis of the vitamin D levels according to the age decades

	25(OH)D levels (ng/mL)			p value <sup>1</sup>
	Allpopulation (n=1155)	Male (n=384)	Female (n=771)	
18-30 years	17.3±13.2 (14)	16.8±9.3 (13.8)	17.5±14.9 (15)	0.43
31-40 yeares	19.6±15.8 (15.9)	16.8±17.1 (15.5)	20.7±17.6 (16)	0.85
41-50 years	19.8±16.7 (15.4)	19.6±13.4 (16.1)	19.9±18.1 (14.6)	0.13
51-60 yeasers	19.6±14.2 (15.2)	21.8±16.3 (16.6)	18.5±12.9 (14.2)	<b>0.03</b>
>60 years	17.9±12.4 (13.8)	18.2±10.1 (15.2)	17.8±13.6 (13.1)	0.06

<sup>1</sup>Mann-Whitney U test

**Table 5:** Comparison of the vitamin D deficiency, insufficiency and normal vitamin D levels groups according to the seasonal variation and sex

25(OH)D levels	<20 ng/mL	20-30 ng/mL	≥30 ng/mL	p value <sup>1</sup>
<b>Male</b>	254 (66.1)	82 (21.4)	48 (12.5)	0.42
<b>Female</b>	515 (66.8)	144 (18.7)	112 (14.5)	
<b>Summer</b>				<b>0.05</b>
<b>Male</b>	38 (30.4)	56 (44.8)	31 (24.8)	
<b>Female</b>	233 (58.7)	87 (21.9)	77 (19.4)	
<b>Winter</b>				<b>&lt;0.001</b>
<b>Male</b>	216 (83.4)	26 (10)	17 (6.6)	
<b>Female</b>	282 (75.4)	57 (15.2)	35 (9.4)	

<sup>1</sup>Pearson Chi-Square test

**Table 6:** Demographic characteristics and comorbidities of patients with and without vitamin D deficiency

25(OH)D vit	<20 ng/mL	≥20 ng/mL	p value
<b>Age</b>	47±15	48±14	0.41 <sup>1</sup>
<b>Sex (n, %)</b>			
Female	515 (66.8)	256 (33.2)	0.84 <sup>2</sup>
Male	254 (66.1)	130 (33.9)	
<b>Hypertansion (n, %)</b>	234 (68.2)	109 (31.8)	0.45 <sup>2</sup>
<b>Diabetes (n, %)</b>	191 (69.2)	85 (30.8)	0.30 <sup>2</sup>

<sup>1</sup>Student t test, <sup>2</sup>Pearson Chi Square test

Table 6 presents the demographic features and coexisting medical conditions of people with and without vitamin D deficiency. Age and sex characteristics and the prevalence of diabetes and hypertension did not change importantly among the people with and without vitamin D deficiency (with p-values greater than 0.05 for all). Furthermore, the levels of vitamin D were comparable throughout people with and without diabetes (17.4±11.9 ng/ml and 19.4±15.1 ng/ml, respectively, with a p-value of 0.12) as well as those with and without hypertension (18.1±13.1 ng/ml and 19.3±14.9 ng/ml, correspondingly, with a p-value of 0.189).

## DISCUSSION

According to the current research, our patients' average vitamin D level was less than anticipated, with 51.9% of the participants suffering from vitamin D deficiency in the summer and 75% during winter. Additionally, there was considerably less serum 25(OH)D concentration (37.8%) among the winter and summer, equating to a 6.1 ng/ml difference.

The current research examined vitamin D levels in different seasons among various populations. In a study of Japanese mu-

nicipal office workers, researchers found that vitamin D levels were higher in July than in November, and vitamin D deficiency was more visible in November than in July (7). In a study from Bilecik province, Çelik et al. found that 33.47% of the patients had vitamin D deficiency and reported that there were inadequate vitamin D levels in all participants. Inferior mean values were more noticeable in spring (10). Another study of office workers found that vitamin D levels were higher in summer compared to winter, and vitamin D deficiency was more visible in winter than in summer (11). In their study, Ucar et al. found that patients' vitamin D deficiency was 51.8% and vitamin D insufficiency 20.7% (12).

In this study, the predominance of vitamin D deficiency was extreme (66.6%) in both summer and winter among the general patient population admitted to the hospital. During winter, the predominance of vitamin D deficiency was more, at 78.6%, compared to 51.9% in summer, while vitamin D insufficiency was more common during summer at 27.3% compared to 13.1% in winter. The mean serum 25(OH)D concentration was  $18.9 \pm 14.4$  ng/ml, and an important growth of 37.8% was observed in vitamin D levels in the time of the summer relative to winter. The results were adjusted for both sex and age, and vitamin D levels remained less in the winter group. Thus, these findings are in accordance with prior research that have demonstrated the prevalence of vitamin D deficiency and insufficiency as widespread health issues that are more prevalent during winter.

Previous studies have indicated that gender may affect vitamin D levels. For example, Heidari et al. observed that females had lower vitamin D levels than males, but there was not any important variance in terms of vitamin D deficiency (13). Burnand et al. reported that there was no significant variation in vitamin D levels between males and females (14). However, in this research, we realized that vitamin D ranks and the pervasiveness of vitamin D deficiency were similar in both sexes.

Age is a widely recognized factor that can boost the risk of vitamin D deficiency (3). Although Atlı et al. identified a significant negative correlation between age and vitamin D levels in their study Çınar et al. found no remarkable correlation among the age and vitamin D levels (11, 15). Similarly, Uçar et al. did not see any important variances in vitamin D deficiency across different age groups (12). In our review, we did not observe any important correlation between vitamin D levels and age. Furthermore, we did not find any important decrease in serum vitamin D levels with increasing age when we analyzed vitamin D levels in age groups.

The relation among the vitamin D deficiency and type 2 diabetes has been well-documented (16). The NHANES III study showed a negative correlation between among D ranks and insulin resistance and diabetes (17). Our study found that people with diabetes had lower vitamin D levels than those without diabetes, although the variance was not remarkable. Moreover, individuals with diabetes had more prevalence of vitamin D deficiency (69.2%) compared to the overall population. However, there was no significant difference among those without vitamin D deficiency.

Several debates have established a link between vitamin D deficiency and hypertension (5). For example, Bhandari et al. reported an important link among the lower 25(OH)D levels and the incidence of hypertension. They found that the incidence of hypertension was 52.4%, 40.8%, 27.2%, and 19.4% for patients with 25(OH)D levels of <15 ng/ml, 15-29ng/ml, 30-39ng/ml, and  $\geq 40$  ng/ml, respectively (18). In our study, although the variance was not remarkable, we observed lower vitamin D ranks in people with hypertension. However, the prevalence of vitamin D deficiency was more (68.2%) in people with hypertension than in the general population.

#### Limitations of the study

Since this study was conducted in a hospital, the findings might not be applicable to the whole Turkish community. The limitations of the study include its retrospective design, inability to assess patient anthropometric and biochemical data except for creatinine, and not investigating patients' clothing and dietary habits. However, the exclusion of patients who had undergone therapies that could affect vitamin D levels through the screening of their medical records using Medula, hospital information system, and e-prescription system enhanced the credibility of the findings.

#### CONCLUSION

In summary, our study shows that vitamin D deficiency and insufficiency is still a common health problem in Turkey, even during the sunny seasons, although there has been some improvement. To get the reasons better behind low vitamin D levels in a country known for its sunny weather, future studies with different approaches are necessary. Additionally, it is important to explore the symptoms and consequences of this deficiency among people having low vitamin D levels in our population, as well as to investigate any comorbidities that require treatment.

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