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Prevalence of Vitamin D Deficiency in Healthy Adults

Sağlıklı Yetişkinlerde D Vitamini Eksikliği Prevalansı

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ABSTRACT

Objectives: Vitamin D is a well-known hormone and important for many metabolic pathways and different health outcomes. The physiology of vitamin D is very complex. Multiple factors like ethnicity, age, sex, diseases, and medication influence vitamin D concentrations. In this study, our aim was to determine the prevalence of vitamin D deficiency among adults in Turkey. **Material-methods:** The 25(OH) vitD_3 test results of 2007 patients admitted to Selçuk University Medicine Faculty hospital between the years of 2015 and 2016 were analyzed, retrospectively. Patients using any vitamin D consisting drug, having chronic disease and inflammatory disorders were excluded. Vitamin D levels were measured by a chromatographic method (LC/MS/MS) with API3200 which is the gold standard to measure 25(OH)D_3. **Results:** Our results show that the prevalence of vitamin D deficiency is about 67.9% in our society. The mean value of vitamin D was 16,87 ng/mL and females had significantly lower 25(OH)D_3 levels compared to males ($p<0.001$).The 25(OH)D_3 levels were higher in summer and in fall than in winter and spring. ($p<0.001$) **Conclusıons:** The results indicate that vitamin D deficiency is prevalent in this study population despite high levels of sunshine and UV radiation throughout the year. Preventive treatments should be planned.

Key words: Vitamin D deficiency, LC/MS/MS, prevalence

ÖZET

Amaç: D vitamini, birçok metabolik yolakta rol alan ve bazı hastalıklarla ilişkili olan bir hormondur. Vitamin D fizyolojisi çok karmaşıktır. Etnik köken, yaş, cinsiyet, hastalıklar ve ilaç kullanımı vitamin D konsantrasyonunu etkilemektedir. Bu çalışmada amacımız Türkiye'de sağlıklı erişkinlerde vitamin D eksikliği sıklığını belirlemekti. **Yöntem:** 2015-2016 yılları arasında Selçuk Üniversitesi Tıp Fakültesi Hastanesi'ne başvuran 2007 hastanın 25(OH)D_3 test sonuçları retrospektif olarak incelendi. Vitamin D içeren ilaç kullanan, kronik hastalık veya enflamatuar hastalıkları olan hastalar çalışma dışı bırakılmıştır. D vitamini seviyeleri, 25(OH)D_3 ölçmek için altın standart olan kromatografik yöntemle (LC / MS / MS) API3200 cihazı ile ölçülmüştür. **Sonuçlar:** Bulgularımız, çalışma popülasyonumuzda D vitamini eksikliği prevalansının yaklaşık %67,9 olduğunu göstermektedir. D vitamini ortalama değeri 16,87 ng/mL idi ve kadınlarda 25(OH)D3 seviyeleri, erkeklere göre anlamlı derecede düşüktü ($p <0,001$). Yaz ve sonbahar mevsiminde 25 (OH) D3 seviyeleri, kış ve ilkbahar mevsimine göre daha yüksekti.($p <0.001$) **Tartışma:** Sonuçlarımız yıl boyunca yüksek düzeyde güneş ve UV ışığına rağmen, D vitamini eksikliğinin popülasyonumuzda yaygın olduğunu göstermektedir. Önleyici tedaviler planlanmalıdır.

Anahtar kelimeler: D vitamini eksikliği, LC/MS/MS, prevalans

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INTRODUCTION

In the last few years, more attention has been given to Vitamin D deficiency and several studies demonstrated that Vitamin D deficiency is prevalent worldwide. Moreover, there is a strong relationship between low circulating concentrations of vitamin D and many common diseases including skeletal and non-skeletal diseases. They can be preventable with Vitamin D supplementation in order to reduce disease activity.

Vitamin D plays a major role in human biological functions, especially in the endocrine system. The pathway of vitamin D synthesis consists of many metabolites such as 25-hydroxyvitamin D (25(OH)D), and 1,25-dihydroxy vitamin D (1,25(OH)D). Synthesis of vitamin D_3 is induced by UV light in skin and Cholecalciferol converted to 25-hydroxyvitamin D [25-(OH)D] or calcidiol by 25α-hydroxylase in the liver and subsequently in the kidney into its' active metabolite 1,25 dihydroxy vitamin D by the 1α-hydroxylase, an enzyme which is stimulated by parathyroid hormone. The synthesis of the metabolites is under control of 25-hydroxylase in the liver and 1-hydroxylase in the kidney. Thereafter, the active metabolite can enter cells and bind to either the vitamin D-receptor or a responsive gene, such as that of calcium binding protein and help calcium absorption.[1] It has been estimated not more than 1% of the total solar UVB radiation reaches the earth's surface and especially in winters it is difficult to produce Vitamin D.[2-3] Clothing and glass absorbs all UVB radiation, so it prevents vitamin D production during sun exposure.[2] Dietary intake of vitamin D is generally limited to oily fish and eggs.[4] Multiple factors like ethnicity, age, sex, clothing, season, time of the day, diseases and medication influence vitamin D concentrations. Blood concentration of 25(OH)D is the biomarker usually used by clinicians to determine vitamin D status.[5]

Vitamin D deficiency is a major public health problem worldwide in all age groups, even in those residing 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 supplementation has been implemented for years.[6] It has been estimated that approximately 30% and 60% of children and adults worldwide are vitamin D deficient and insufficient, respectively.[7] There has been an association of vitamin D deficiency with many diseases including autoimmune disorders and endocrinological diseases such as osteomalacia. In spite of the fact that the exact mechanisms by which vitamin D may reduce the risk for autoimmune diseases are not fully understood, it was concluded that vitamin D plays an important role in cellular immunity.[8]

Up until 1998, vitamin D deficiency was defined as a blood level of 25 hydroxyvitamin D[25(OH)D]; which represents a total concentration of both 25-hydroxyvitamin D_2 and 25-hydroxyvitamin D_3] of less than 10 ng/mL (25 nmol/L).[3] This definition was mainly based on reports relating to blood levels of 25(OH)D and the development of rickets. [9] Recently, the following definitions are used to diagnose vitamin D status: for vitamin D deficiency 25(OH)D <20 ng/ml and for vitamin D insufficiency 25(OH)D ≥20 ng/ml and <30 ng/ml.[10]

The best method for determining a person's vitamin D status is to measure serum 25(OH)D concentration because of its' long half-life and easiness to measure. Most commercial assays are reliable enough to determine a person's vitamin D status.[9] These include various radioimmunoassays and what is recently considered to be the gold standard: liquid chromatography-tandem mass spectrometry.[11-12-13]

The purpose of this study was to examine the prevalence of vitamin D deficiency in people without chronic disease or a significant risk factor and its correlates to test the hypothesis that vitamin D deficiency was common in Turkish population.

MATERIALS and METHODS

Study Population

This was a single-ethnicity study of 2007 healthy subjects aged 18-65years admitted to hospital for routine check-ups between January 2015 and December 2016. We measured serum 25(OH) D_3 by a chromatographic method. The season of blood draw was classified as winter, spring, summer or fall.

The data archive of the laboratory information system was searched for a 2-year period between 2015 January and 2016 December and among 6736 subjects searched for vitamin D_3, 2007 remained (18–65 years old, 481 male and 1526 female) when we

excluded the outliers for estimation of the prevalence of vitamin D deficiency.

Subjects were excluded if they had a significant cardiac, hepatic, oncologic disease, or disorders known to affect bone mineral metabolism including hyperthyroidism, hyperparathyroidism, osteomalacia or Paget's disease. Pregnant women, patients with chronic renal failure or hospitalized patients were excluded from the study. Patients using any drugs containing vitamin D were also excluded. In the case of multiple test results for the same patient, only the first test result was included in the study. 4729 patients were excluded from the study because of having at least one of the above diseases and using Vitamin D containing drugs and 2007 patients remained.

Subjects were classified by sex and age. The season of blood draw was classified as winter (December through February), spring (March through May), summer (June through August) or fall (September through November).

We used the following definitions; vitamin D deficiency: 25(OH) D_3<20 ng/ml; insufficient vitamin D status: 25(OH)D_3 20–29 ng/ml and optimal vitamin D status: 25(OH)D_3 30–50 ng/ml .[10-14-15-16] The prevalence of vitamin D deficiency is defined by four different thresholds of 25(OH)D_3: ≤ 5, ≤ 10, ≤20, and ≤30 ng/mL in this study.

Method of Study

The analytical method used for serum 25(OH)D_3 was Liquid chromatography-tandem mass spectrometry (*LC-MS/MS*) performed by liquid chromatography (Shimadzu LC-20AD system (Japan)) tandem mass spectrometry (Applied Biosystems MDS SCIEX(USA) API 3200). The quality of analyses in this laboratory was ascertained through the Vitamin D External Quality Assessment Scheme external controls. The inter-assay coefficients of variation were lower than 5%. The limit of detection was 4 ng/mL Liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods quantify vitamin D metabolites based on the compound-specific precursor to production mass-to-charge (m/z) transitions.[17]

Statistical Analysis

Data analysis was performed using SPSS version 15(SPSS Inc, Chicago, IL, USA). Shapiro-Wilk analysis was used to test for gaussian or non-gaussian distribution. Our data were gaussian distributed variables. For gaussian distributed variables, data are expressed as arithmetic mean and ± standard deviation. Frequencies were presented as percentage (%). We assessed the significance of differences between two groups using independent samples t-test for gaussian-distributed data. P value ≤0.05 was considered statistically significant. The study was approved by Selçuk University Defense research ethics committee.

RESULTS

Using the definition of serum 25-OH-D_3 concentrations ≤20 ng/mL. It was found that over 60% of Turkish adults, both men, and women, would be categorized as vitamin D deficient. Table.1 clearly shows that the prevalence of vitamin D deficiency is about 67.9% and vitamin D insufficiency prevalence is 20%. Only 12.1% of our study population has an adequate vitamin D level.

Table 1. Prevalence of vitamin D deficiency and insufficiency

Serum 25(OH)D_3 level(ng/ml)	Number of patients	Percent rate (%)	Percent rate (%)
<5 ng/ml	177	8.8%	67.9%
5≤ and <10 ng/ml	488	24.3%	
10≤ and <20 ng/ml	699	34.8%	
≥20 and <30 ng/ml	403	20%	20%

The mean value of 25(OH)D_3 level for the cohort was 16.87 ng/mL (± 10.89 ng/mL). Females had significantly lower 25(OH)D levels compared with males (15.49 ±10.66ng/mL versus 21.25 ± 10.45 ng/mL, P<0.001). [Table.2]

The risk of a low vitamin D status was highest in March (mean: 11,93 ng/mL) and lowest in August (mean: 23,66ng/mL) during the year. [Figure.1] In our study, there were no significant differences between age groups. (p:0.18)

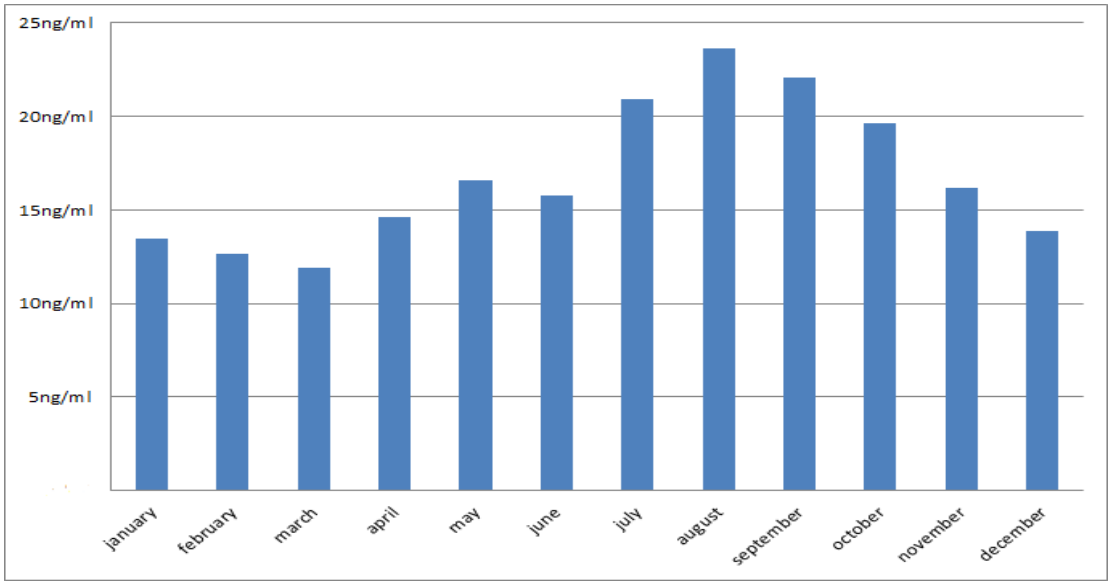

Figure 1. Vitamin D levels according to months

Table 2. Vitamin D status according to gender				
Gender	**N:2007**	**Mean (Ng/Ml)**	**Std.Deviation**	**P Value For Comparison**
Female	1526	15.49	10.66	P<0.001
male	481	21.25	10.45	

Table 3. Patients' Vitamin D status according to season					
SEASON	**N**	**Mean(ng/ml)**	**Std. Deviation**	**95% Confidence Interval for Mean**	
				Lower Bound	**Upper Bound**
Spring	398	14,30	9,67	13,34	15,25
Summer	462	20,41	11,77	19,33	21,49
Fall	569	19,57	10,61	18,70	20,44
Winter	578	13,14	9,53	12,36	13,92
Total	2007	16,87	10,89	16,39	17,34

The 25(OH)D levels were statistically higher in summer (20.41±9.6ng/mL) and in fall (19.5 ± 10.6 ng/mL) than in winter (13.14 □± 9.5 ng/mL), and spring (14.3□± 9.6 ng/mL)(p for comparison between summer - fall and winter-spring <0.001)[Table.3]

DISCUSSION

The aim of this study was to determine the prevalence of vitamin D deficiency specific to our region by using the archive of laboratory information system and find out whether deficiency of Vitamin D is similar to other populations.

The Institute of Medicine recently proposed that $25(OH)D_3$ level ≤20 ng/mL can be used to define vitamin D deficiency.[18] Using this definition, vitamin D deficiency was highly prevalent in Konya, Turkey despite high levels of sunshine and UV radiation throughout the most seasons. The risk of Vitamin D deficiency was particularly high during winter and spring and among females.

The prevalence of vitamin D deficiency was found to be 72% in a study conducted by Durmuş et al. in Kayseri, another city of the Central Anatolia region.[20] In addition, vitamin D deficiency was more frequent in women and there was no significant difference between age groups, similarly.

Hekimsoy et al. reported that Vitamin D deficiency was significantly more common among women (78.7%) than men (66.4%, $p < 0.01$). 25(OH)D levels were not significantly different in persons according to age as our study.[21]

Serum 25(OH) vitamin D levels vary depending on the seasons and reach its' highest levels during summer months.[22] Çidem et al. showed that the peak prevalence for vitamin D deficiency prevalence was in March during the year and the lowest level occurred in August in Turkey.[19] Vitamin D deficiency was higher among females than among males. These findings support our study.

According to studies conducted in Turkey, vitamin D deficiency is common[19-22] . An important reason why Vitamin D deficiency is common in Turkey may be that people's outdoor activities are limited because of living urban areas in flats and there is limited outdoor social activities.[19] Apartments are more common than houses with gardens. In our era, because of our era's working lifestyle, people must stay in closed areas for at least 8-10 hours in a day when there is sunshine. The use of sunscreen causes a reduction in the synthesis of vitamin D, while it protects the skin against the destructive effects of UVA and UVB[20]. Furthermore, because of wearing sun protection during sun exposure and increased incidence of obesity vitamin D deficiency increases all over the World.[9]

It is reported that vitamin D deficiency is higher in individuals who dressed in a style which blocks sunlight and reported that vitamin D deficiency is three times higher in individuals who dressed in a style which blocks sunlight in Turkey.[21] In a study conducted in Turkey, the serum vitamin D levels of women who prefer traditional clothing and covered clothes were shown to be at a lower level than in those whose clothing styles allowed exposure to sunlight.[22]

Regardless of latitude, lifestyle factors are crucial for vitamin D status and deficient. Insufficient vitamin D status and generally lower levels in females were observed in the Middle East with a strong relationship to the use of covering clothes [10] . According to the vitamin D test results of 60,979 people in the United Arab Emirates, Vitamin D deficiency was reported about 61.4% of women and 58.3% of males.[23] In the study done in Iraq, another neighboring country of Turkey, the deficiency of vitamin D was around 50%. [24] In a study in Iran, the prevalence of vitamin D deficiency was about 50.8%.[25] Surprisingly, Van der Wielen et al. reported that wintertime serum $25(OH)D_3$ concentrations of elder people from 11 European countries found 36% of men and 47% of women suffering from Vitamin D deficiency.[26] In subjects over 65 years of age, vitamin D deficiency prevalence (<20 ng /ml) was found to be 44.7% in males and 56.1% in females in Holland.[27]

As a result of our study, it can be said that vitamin D deficiency is highly prevalent in Konya. Our results indicate that the risk of vitamin D deficiency and insufficiency was particularly high during winter and among females.

The characteristic features of our study are that our study population do not use vitamin D containing drug and they do not have any significant diseases. Furthermore, our measurement method is a gold standard to evaluate vitamin D levels. In addition, there are only a few studies conducted in the healthy patient group who don't use Vitamin D containing drug in our country.

Limitations to our study need to be considered. The limitations were being a local study and our study includes female patients more than males.

In the literature, even in countries where is less sunshine, vitamin D levels are higher than us. We think that environmental factors such as clothing and lifestyle play a role in vitamin D deficiency in Konya region at such high level. Since vitamin D deficiency is common in our society, most people use vitamin D supplements. In order to prevent vitamin D deficiency, it should be told by family physicians to patients how it is secreted in human body and people should be directed to social activities. Preventive measures should be taken more in order to prevent Vitamin D deficiency.

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