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Evaluation of Vitamin D Levels in Kütahya Province: A Hospital-Based Retrospective Study

Kütahya İli D Vitamini Düzeylerinin Değerlendirilmesi: Hastane Bazlı Retrospektif Çalışma

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ABSTRACT

Objective: *The general health status and quality of life of individuals are negatively impacted by symptoms arising from vitamin D deficiency. Vitamin D, a steroid vitamin, is primarily synthesized in the skin (90-95%) under the influence of sunlight. This study aimed to determine the vitamin D status of outpatients admitted to Kütahya Health Sciences University Evliya Çelebi Training and Research (KHSU-ECTR) Hospital between 2017 and 2021, considering age, gender, and season.*

Material and Methods: *Retrospective analysis was conducted on patients whose 25-Hydroxy Vitamin D (25-OH VitD) levels were studied, using data from the hospital database. The study included a total of 121,727 patients. Logistic regression was utilized to determine factors influencing vitamin D deficiency, and risk assessments were conducted across different categories.*

Results: *The mean and standard deviation values of 25-OH VitD levels were 16.73±11.11 ng/ml. Using a cut-off value of 20 ng/ml, it was found that 71.5% of the patients exhibited vitamin D deficiency. Notably, vitamin D levels were particularly low among women and the elderly, especially during the winter season.*

Conclusion: *Vitamin D deficiency is prevalent among patients admitted to the hospital in Kütahya. We think that increasing sun exposure during the spring and summer seasons, as well as implementing dietary and lifestyle changes, will have a positive impact on vitamin D levels.*

Keywords:
Age
Gender
Season
Vitamin D

ÖZET

Amaç: *Güneş ışınlarının etkisiyle deride %90-95 oranında sentezlenen steroid bir vitamin olan D vitamini eksikliğine bağlı olarak ortaya çıkan semptomlardan insanların genel sağlık durumu ve yaşam kalitesi olumsuz etkilenmektedir. Bu çalışmanın amacı, 2017-2021 yılları arasında Kütahya Sağlık Bilimleri Üniversitesi Evliya Çelebi Eğitim ve Araştırma Hastanesi'ne ayakta tedavi edilen hastaların D vitamini durumlarının yaş, cinsiyet ve mevsime göre değerlendirilmesidir.*

Gereç ve Yöntemler: *25-Hidroksi Vitamin D (25-OH VitD) düzeyi çalışılan hastalar, hastane veri tabanından retrospektif olarak incelendi. 121727 hasta çalışmaya dahil edildi. D vitamini eksikliğini etkileyen faktörler lojistik regresyon yöntemi ile belirlendi ve kategoriler arasında risk değerlendirmeleri yapıldı.*

Bulgular: *25-OH VitD düzeylerinin ortalama ve standart sapma değerleri 16.73±11.11 ng/ml idi. Eşik değer olarak 20 ng/ml alındığında; hastaların %71.5'inde D vitamini eksikliği vardı. D vitamini düzeyleri özellikle kış mevsiminde, kadınlarda ve yaş ilerledikçe daha düşük bulundu.*

Sonuç: *Kütahya'da hastaneye başvuran hastalarda D vitamini eksikliğinin yaygın olduğu görülüyor. İlkbahar ve yaz aylarında güneş ışığından daha fazla yararlanmanın, beslenme ve yaşam tarzı değişikliklerinin D vitamini düzeyini olumlu yönde etkileyeceğini düşünüyoruz.*

Anahtar Kelimeler:
Yaş
Cinsiyet
Mevsim
D vitamini

INTRODUCTION

Vitamin D, most of which is obtained through sun exposure, has significant effects on human health, such as bone and calcium metabolism. However, due to certain personal characteristics and environmental factors, vitamin D synthesis in the skin may not occur with sunlight (1-6). The angle at which the sun's rays reach the Earth plays a crucial role in vitamin D synthesis. This angle, known as the Zenith angle, varies depending on the season and time of day. During the summer season, in areas with ample sunshine, the optimal period for vitamin D3 synthesis is between 10:00 and 15:00. As the Zenith angle increases in the late afternoon and early morning hours, as well as during winter, absorption increases while synthesis decreases. In Turkey, the Zenith angle is favorable between May and November. Exposing the skin to sunlight between 10:00 and 15:00, until it develops a slight pinkness, promotes the synthesis of vitamin D3. While the face is the body part most exposed to the sun, it is crucial to expose the arms, legs, and hands to ensure sufficient synthesis. Additionally, individuals with dark skin color have a lower rate of vitamin D synthesis

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compared to those with lighter skin color (7,8).
To assess the level of vitamin D in the body, serum 25-OH VitD is typically measured. Although the half-life of 1.25 Hydroxy vitamin D, the active form of vitamin D, is 4-6 hours, the half-life of 25-OH VitD is approximately 2-3 weeks (9-11). While there is no consensus on the optimal level of 25-OH VitD measurement, most experts consider levels lower than 20 ng/ml (50 nmol/L) as indicative of vitamin D deficiency (12). The elderly, individuals with dark skin, those using medications that accelerate vitamin D metabolism, and those with conditions such as obesity, osteoporosis, and absorption disorders are at risk of vitamin D deficiency. Treatment for vitamin D deficiency involves vitamin D supplementation based on the level of deficiency. For individuals with a 25-OH VitD level below 20 ng/ml, it is recommended to raise the level to 30 ng/ml or higher by taking 50,000 IU of vitamin D per week for 6-8 weeks (13).
Globally, it is estimated that approximately 1 billion people suffer from vitamin D deficiency (14). Vitamin D deficiency is prevalent in a large majority of both men and women across various age groups and geographical locations (15). Previous studies have reported vitamin D deficiency rates ranging from 40% to 100%, indicating a global epidemic (16-19). Some examples of vitamin D deficiency rates from different countries include 42% in Japan, 45% in China, 47% in Russia, 30%-48% in India, 67% in Iran, 84% in Lebanon, and 90% in Saudi Arabia (20,21). These studies have demonstrated the high prevalence of vitamin D deficiency worldwide, particularly during the winter season (10,19,22). In Turkey, the incidence of vitamin D deficiency among adults has been reported to range between 33% and 75% (21,23).
Since the general health status and quality of life of people can be adversely affected by vitamin D deficiency, maintaining sufficient vitamin D levels is crucial for promoting a long and high-quality life. It has been observed that 25-OH VitD levels are highest during summer and autumn, while they are lowest during winter and spring. International and national guidelines emphasize the importance of considering seasonal changes, as well as the effects of gender and age, in the measurement, classification, and variation of vitamin D (24-26). Therefore, this study aims to analyze the vitamin D levels of individuals who have sought treatment at KHSU-ECTR Hospital, taking into account factors such as age, gender, and season.

MATERIAL AND METHODS

Geographical features of the region

Kütahya, located in the Aegean Region in the western part of Turkey in the northern hemisphere, is situated between 38°70’ and 39°80’ north latitudes and 29°00’ and 30°30’ east longitudes. Although it is not situated on the coastline, Kütahya has a central population of 277,270 and a total population of 578,640 as of 2021. Of the central population, 49.31% are men and 50.69% are women (27,28). The average sunshine duration in this region is approximately 3 hours in winter and 10 hours in summer, with an annual average of 6 hours. During winter, the lowest average temperature is -6.8°C, and the highest temperature is 6°C. In summer, the average lowest temperature is 12.4°C, and the average highest temperature is 27.16°C (29).

Study Sample

The study obtained ethical approval from the Committee of Local Ethics (2022/07-22, 22.06.2022), and the ethical principles stated in the 1964 Declaration of Helsinki were adhered to. The study retrospectively analyzed patients who sought treatment at KHSU-ECTR Hospital between 01.01.2017 and 31.12.2021, focusing on individuals whose 25-OH VitD levels were measured, using data from the hospital database system.

Analysis of Vitamin D

To measure the vitamin D levels of the patients, serum samples were promptly delivered to the biochemistry laboratory within the first half hour, ensuring they were not exposed to sunlight. Peripheral venous blood samples were then centrifuged at 3500 rpm for 10 minutes to obtain serum samples. The total 25-OH VitD levels were measured using the immunoassay method with the Unicel DXI 800/Beckman Coulter autoanalyzer device. For patients with multiple 25-OH VitD measurements, the initial measurement was considered. A total of 328 patients with 25-OH VitD levels exceeding 100 ng/ml and those with insufficient sample results were excluded from the study. The study included 121,727 patients, ranging from the smallest value of 0 ng/ml to the largest value of 100 ng/ml for 25-OH VitD levels. The study utilized data on variables such as the patients’ age, gender, season, year, and 25-OH VitD levels. In accordance with the classification used in the National Health and Nutrition Examination Surveys (NHANES), the age variable was categorized as follows: 0, 1-3, 4-8, 9-13, 14-18, 19-30, 31-50, 51-70, and 71+. Furthermore, the 25-OH Vitamin D levels were classified into two categories based on the Endocrine Society Guideline: <20 ng/ml (deficient) and ≥20 ng/ml (no deficiency) (30).

Statistical Analysis

The data obtained from the hospital information system was transferred to the computer environment for analysis. Statistical evaluations were conducted using IBM SPSS Statistics 20. For categorical data such as age, gender, season, and year, frequency tables were created, presenting the frequency (n) and percentage (%) values. In order to analyze the numerical data of 25-OH VitD levels across age groups, gender, season, and year variables, a test for conformity to normal distribution was initially performed. Since the p-values from the Kolmogorov-Smirnov and Shapiro-Wilk tests were less than 0.05, indicating non-normal distribution, non-parametric hypothesis tests were used. The Mann-Whitney U test was employed when comparing two groups, while the Kruskal-Wallis test was utilized when there were more than two groups. The results included mean, minimum, maximum, median, interquartile range values, standard deviation, and 95% confidence interval. To examine the 25-OH VitD levels in the two categories of <20 ng/ml and ≥20 ng/ml, cross-tables and chi-square test statistics were applied. Bar graphs were created to visually represent the mean values and percentage distributions of 25-OH VitD levels based on the variables under consideration. Logistic Regression

Analysis (Backward Stepwise) was employed to identify factors influencing vitamin D deficiency, and odds ratios (OR) were calculated. A statistical significance level of p<0.05 was adopted.

RESULTS

Approximately 33% of the patients included in the study belonged to 2017, while 14% belonged to 2021. The lowest percentage of patients was observed in 2020, at 8%. Among the participants, 65.3% were women and 34.7% were men, with a mean age of 39.83±22.81 years. The mean age for men was 38.45±24.79 years, and for women, it was 40.57±21.63 years. The distribution of patients across seasons was relatively balanced. The range of 25-OH VitD levels varied from 0 ng/ml to 100 ng/ml, with a mean level of 16.73±11.11 ng/ml. A statistically significant difference in 25-OH VitD levels was found between genders (p=0.000). Women had a mean 25-OH VitD level of 15.84±11.52 ng/ml, whereas men had a mean level of 18.40±10.08 ng/ml, indicating that men had higher vitamin D levels than women. Seasonal variation also showed a statistically significant difference in vitamin D levels (p=0.000). The mean 25-OH VitD level was highest in summer, with a value of 18.35±11.25 ng/ml, and lowest in winter, with a value of 15.36±10.62 ng/ml. The autumn season had the second-highest level of 25-OH VitD, indicating the carryover effect of sunlight exposure from summer. Moreover, there was a statistically significant difference in vitamin D levels between years (p=0.000). The highest average 25-OH VitD level was observed in 2017, while a decline in levels was observed for 2019 and 2020, respectively (Table 1).

The vitamin D status was categorized as <20 ng/ml and ≥20 ng/ml, with 71.5% of the patients having a vitamin D level below 20 ng/ml and 28.5% having a level of 20 ng/ml or above (Figure 1). This indicates that the majority of patients, 71.5%, had vitamin D deficiency. The distribution of vitamin D status was statistically significant across different age groups ($\chi2$=1762.164; p=0.000). Younger age groups, such as 0 (17.5%), 1-3 (32.3%), and 4-8 (56.4%), had lower rates of vitamin D deficiency compared to other age groups. In the remaining age groups, the rate of vitamin D deficiency was over 70%. There was also a statistically significant difference in vitamin D status between men and women ($\chi2$=1506.537; p=0.000). The rate of vitamin D deficiency was 64.6% in men and 75.2% in women. Notably, women had a lower rate of vitamin D deficiency at 24.8%. When considering vitamin D status according to seasons, the rates of patients without vitamin D deficiency were higher in summer (36.2%) and autumn (33.3%) compared to other seasons. Vitamin D deficiency

Table 1: 25-OH VitD levels and vitamin D status by age groups, gender, season and years.

Variables	Categories	Mean±SD	Median (Q1-Q3)	p-value	<20 ng/ml (n(%))	≥20 ng/ml (n(%))	Chi-Square (χ2); df and p-value
Age Groups	0	33.11±14.86	32 (23-42)	0.000*	675 (17.5)	3179 (82.5)	11762.164; 8 and 0.000*
	1-3	25.81±11.85	24 (17-32)		1454 (32.3)	3049 (67.7)	
	4-8	19.46±7.96	18 (14-24)		3145 (56.4)	2436 (43.6)	
	9-13	16.10±7.07	15 (11-20)		3787 (73.5)	1366 (26.5)	
	14-18	14.15±7.82	12 (9-17)		5028 (82.0)	1100 (18.0)	
	19-30	14.13±8.21	12 (9-17)		15706 (81.5)	3574 (18.5)	
	31-50	14.69±9.39	12 (9-18)		25963 (79.0)	6882 (21.0)	
	51-70	17.08±11.64	14 (10-21)		23574 (70.5)	9865 (29.5)	
	71+	17.17±13.71	13 (8-22)		7693 (70.3)	3251 (29.7)	
Gender	Male	18.40±10.08	16 (12-22)	0.000*	27302 (64.6)	14958 (35.4)	1506.537; 1 and 0.000*
	Female	15.84±11.52	12 (9-19)		59723 (75.2)	19744 (24.8)	
Season	Spring	15.93±11.58	13 (9-19)	0.000*	23694 (75.7)	7617 (24.3)	2148.145; 3 and 0.000*
	Summer	18.35±11.25	16 (11-23)		17715 (63.8)	10070 (36.2)	
	Autumn	17.60±10.71	15 (10-22)		19609 (66.7)	9773 (33.3)	
	Winter	15.36±10.62	12 (9-18)		26007 (78.2)	7242 (21.8)	
Year	2017	18.07±12.21	15 (10-22)	0.000*	26669 (66.7)	13306 (33.3)	789.157; 4 and 0.000*
	2018	16.31±10.58	14 (9-20)		23923(73.6)	8590 (26.4)	
	2019	15.51±10.05	13 (9-19)		17009(75.8)	5437 (24.2)	
	2020	15.85±10.71	13 (9-19)		7233 (75.3)	2377 (24.7)	
	2021	16.48±10.58	14 (9-21)		1219 (70.9)	4992 (29.1)	
Total		16.73±11.11	14 (9-21)		8702 (71.5)	34702 (28.5)	

Note: *Comparing 25-OH VitD levels; Mann-Whitney U Test for Gender, Kruskall Wallis Test for Age Groups, Season and Year.*
Chi-Square Tests to compare vitamin D status by age groups, gender, season and year. df: degrees of freedom.
SD: Standard Deviation, Q1: First Quarter, Q3: Third Quarter
**:p<0.001.*

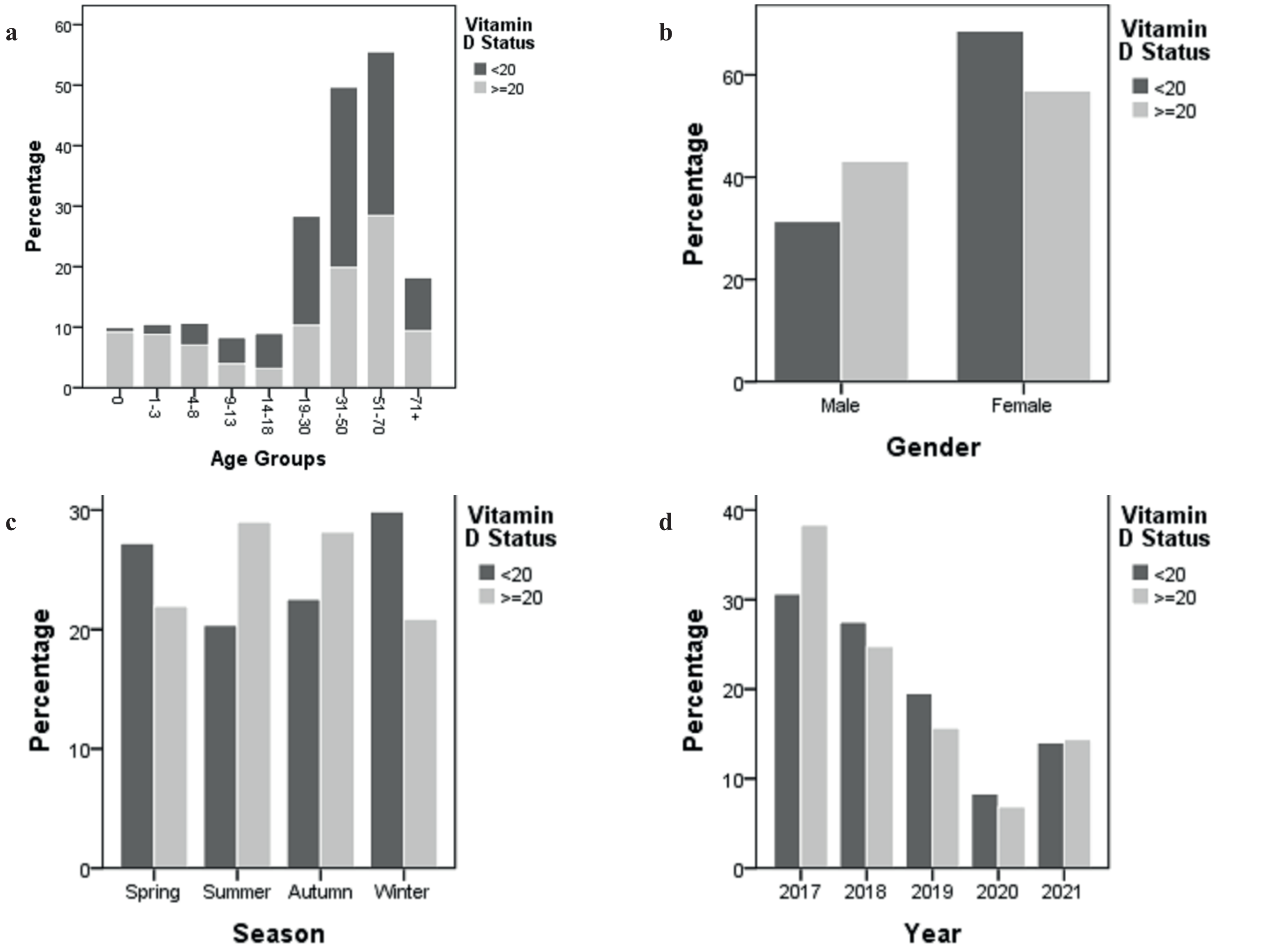

Figure 1: Bar charts of Vitamin D status by age groups (a), gender (b), season (c) and year (d).

Table 2: Determination of factors affecting vitamin D status by logistic regression

Variables in the Equation				
	OR	95% CI for OR		p-value
		Lower	Upper	
Age	1.01	1.00	1.01	0.000*
****Gender**	1.64	1.59	1.68	0.000*
*****Season**				0.000*
Spring	1.77	1.71	1.83	0.000*
Fall	1.14	1.09	1.18	0.000*
Winter	2.06	1.99	2.14	0.000*
Constant	1.67			0.000*

***:Male (reference), ***: Summer (reference) , OR: Odds Ratio, CI: Confidence Interval*
Logistic Regression Analysis (Backward Stepwise); Model significance: p:0.000
**:p<0.001*

was observed in 78.2% of patients during winter and 63.8% during summer. Thus, the difference in vitamin D status between seasons was statistically significant ($\chi 2$=2148.145; p=0.000) (Table 1). When vitamin D status was considered as the dependent variable; the effects of gender, age and seasonal variables on the presence or absence of vitamin D deficiency were evaluated and it was shown that they had significant effects. The odds ratios (OR) were used to interpret the risk coefficients.

The analysis revealed that for every 1 unit increase in age, the risk of Vitamin D deficiency increased by 1.01 times, and this result was statistically significant (p=0.000). Women had a 1.64 times higher risk of Vitamin D deficiency compared to men, and this difference was statistically significant (p=0.000). When the summer season was taken as the reference category, the risk of Vitamin D deficiency was 1.77 times higher in spring, 1.09 times higher in autumn, and 2.06 times higher in winter. These differences were statistically significant (p=0.000). The higher risk of Vitamin D deficiency in winter can be attributed to the lower amount of sunlight available compared to summer. It was also observed that the positive effect of sunlight exposure in summer extended to the autumn season (Table 2).

DISCUSSION

Numerous studies conducted in different countries and continents have consistently shown a high prevalence of vitamin D deficiency (25). The Middle Eastern countries have an approximately 80% deficiency rate, while Western, Southern, and Eastern European countries range from 30% to 60%. In Northern European countries, the deficiency rate is around 20%. Severe vitamin D deficiency, with levels below 12 ng/ml, affects more than 10% of Europeans (31). The incidence of vitamin D deficiency is progressively increasing and has become a significant public health concern (32). A study conducted in Pakistan with 123 patients (70 men and 53 women) reported a mean 25-OH VitD level of 16.44±3.84 ng/ml. When using a cut-off point of 20 ng/ml for vitamin D deficiency, approximately 70% of the participants were found to be deficient (33). In our study, the mean vitamin D level was 16.73±11.11 ng/ml, and using the same cut-off point, vitamin D deficiency was observed in 71.5% of the patients. In a study involving 849 healthy children aged 1-16 years in Turkey, the prevalence of vitamin D deficiency was 8% when using a cut-off point of 20 ng/ml. The deficiency rate was reported as 14.5% for children aged 1-7 years and 8.4% for children ≥7 years old. The higher prevalence of vitamin D deficiency in younger age groups has been attributed to lower daily calcium intake (34). In our study, the prevalence of vitamin D deficiency was calculated as 17.5% in the 0 age group, 32.3% in the 1-3 age group, 56.4% in the 4-8 age group, and 73.5% in the 9-13 age group. These findings suggest that the incidence of vitamin D deficiency in children increases with age. Another study conducted with a large sample size of 108,742 25-OH VitD measurements from an internationally accredited laboratory found higher vitamin D levels, particularly in the 0 to 1-3 age groups, and a lower incidence of vitamin D deficiency in these age groups compared to other age groups. This finding supports the effectiveness of the Ministry of Health program in the Republic of Turkey, which provides 400 U of free daily vitamin D supplementation to all newborns up to the age of 1. In other words, the youngest age groups have the highest 25-OH VitD levels (3). The results of our study are consistent with these findings, confirming the reliability of our evaluation.

A study conducted in Sakarya with 784 patients aged 0-18 years reported a mean 25-OH VitD level of 37.41±10.15 ng/ml. The incidence of vitamin D deficiency was found to be higher in winter compared to summer. The study indicated that vitamin D levels were significantly associated with the year factor but not with gender, age, and season (35). In our study, we also observed a lower rate of vitamin D deficiency in summer compared to winter. Additionally, we found a significant difference in vitamin D levels across all factors, including age, gender, season, and year.

In a study involving 118 office workers aged 21-52 in Ankara, the measured 25-OH VitD level was 28.42±10.44 ng/ml in summer and 13.83±6.62 ng/ml in winter. The vitamin D level was significantly higher in summer compared to winter (36). Similarly, in our study, the mean 25-OH VitD level was 18.35±11.25 ng/ml in summer and 15.36±10.62 ng/ml in winter. The difference in vitamin D levels between summer and winter was statistically significant.

The months when UVB (ultraviolet B) availability is too low to allow the synthesis of vitamin D in the skin, and UVB availability decreases with increasing latitude (from 35 to 69°K), are referred to as the 'vitamin D winter.' It is estimated to last for 7-8 months in the southernmost part of Europe (37). In a study conducted in Manisa, one of the provinces in the Aegean region where sunlight is abundant in our country, a total of 391 people participated, including 119 men and 272 women. The rate of vitamin D deficiency was calculated as 74.9% (22). Similarly, in our study conducted in Kütahya, another province of the Aegean region, the rate of vitamin D deficiency was found to be 71.5%, which is quite close to the previously mentioned rate of 74.9%. The Manisa province study reported a mean 25-OH VitD level of 16.91±13.09 ng/ml, which was similarly low in our study. The rate of vitamin D deficiency in men in Manisa was 66.4%, while it was significantly higher in women at 78.7%. Dressing style and socio-demographic differences were thought to be influential factors in the higher rate among women (22). In our study in Kütahya, there were more women than men, and the rate of vitamin D deficiency in women was found to be significantly higher than in men.

In the study conducted in İzmir, which included 956 individuals over the age of 18, the 25-OH VitD level was categorized into three groups: <20 ng/ml, 20-30 ng/ml, and >30 ng/ml. There was no statistically significant difference in terms of age and gender among the individuals in these three groups (38). However, in our study, we divided the 25-OH VitD levels into two groups: <20 ng/ml and ≥20 ng/ml. We found a significant difference in age and gender between these two groups. A total of 11,734 participants, including 9,142 women and 2,592 men, were enrolled in the research conducted in Bursa. The study reported low vitamin D levels, particularly in women and during the spring season. The mean 25-OH VitD level was calculated as 16.62±11.54 ng/ml. Vitamin D deficiency, defined as a 25-OH VitD level below 20 ng/ml, was observed in 70.6% of all individuals, 57.2% of men, and 74.4% of women. Gender was identified as a significant factor in vitamin D deficiency, with men having 8.4 times lower vitamin D levels compared to women (1). In our study, vitamin D deficiency was observed in 71.5% of all participants, 64.6% of men, and 75.2% of women. Age, gender, and season were reported as important factors in vitamin D deficiency. Another study, which included 1,424 patients over the age of 18, 79.6% of whom were women, who visited the Diyarbakir Internal Medicine outpatient clinic, reported a mean age of 39.17±15.74 and a mean 25-OH VitD level of 16.79±12.58 ng/ml. The rate of patients with vitamin D deficiency was 69.5% (39). In our study, the mean age was 39.80±22.81 years, and the mean 25-OH VitD level was 16.73±11.11 ng/ml. The proportion of patients with vitamin D deficiency was 71.5%. These results are consistent with the existing literature, which estimates that over 1 billion people worldwide will fall into the deficiency category for vitamin D status (40).

CONCLUSION

Between 2017 and 2021, it was found that 71.5% of the patients admitted to the hospital in our region had a vitamin D level of less than 20 ng/ml, indicating a high prevalence of vitamin D deficiency. This deficiency was more common in women and showed an increasing trend with age, especially during winter. However, contrary to this trend, a higher proportion of males, children aged 0-8, and individuals during the summer season had a 25-OH VitD level greater than 20 ng/ml. Considering the seasonal and latitudinal weather conditions in our region, increasing sunlight exposure and making changes in nutrition and lifestyle can help improve vitamin D levels.

Conflict of Interest: No conflict of interest was declared by the authors.
Ethics: This study was approved by the Kütahya Health Sciences University Rectorate Non-Interventional Clinical Research Ethics Committee (Date: 22.06.2022, Number: 2022/07-22).
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