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Relationship Between the Vitamin D Status and the Season, Place of Living, Age, Gender, and Chronic Disease

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ABSTRACT

Objective: The aim of the present study was to investigate the variations in 25-OH Vitamin D levels considering age, gender, the place of living, season, and presence of chronic disease.

Materials and Methods: Individuals whose 25-OH Vitamin D levels were measured in seven state hospitals in the Tokat Province, Turkey, between September 2016 and August 2017 were selected using the hospital information system and included in this retrospective study.

Results: The study included a total of 22,044 individuals aged ≥18 years. Vitamin D deficiency and insufficiency were observed in 89.4% of the individuals surveyed. Of all participants, 78.7% (n=17.328) were female, and 74.3% (n=16.377) were living in urban areas. An average 25-OH Vitamin D level was significantly low in people living in urban areas (15±12.4 ng/ml) compared to those living in rural areas (15.4±11.5 ng/ml; p=0.03). An average seasonal 25-OH Vitamin D level was the lowest in the winter (13.4±11.5 ng/ml) and the highest in the summer season (17±12.1 ng/ml; p<0.001). An average 25-OH Vitamin D level was 15.1±12.2 ng/ml, which was significantly higher in men (17.6±9.9 ng/ml) than in women (14.4±12.6 ng/ml) (p<0.001). The average 25-OH Vitamin D level of subjects who did not have a chronic disease was significantly lower than in those who had only hypertension, heart disease, or multiple sclerosis (14.40±11.73, 15.67±12.72, 17.42±13.13, and 19.50±14.88, respectively; p<0.005).

Conclusion: It was found that Vitamin D deficiency was associated with the place of living, age, gender, and season of the year. An average 25-OH Vitamin D level was significantly higher in individuals with hypertension, heart disease, and multiple sclerosis.

Keywords: Vitamin D, season, living place, gender

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INTRODUCTION

Vitamin D is a fat-soluble vitamin that controls growth and development, maintains the development of musculoskeletal system, and regulates calcium and phosphorus metabolisms. It has been found that low 25-OH Vitamin D levels are associated with cancer, autoimmune diseases, infectious diseases, osteoporosis, and cardiovascular diseases (1, 2). In the study evaluating 35.667 individuals in Turkey, 94.47% had <30 ng/ml serum 25-OH Vitamin D level, while 76.25% had <20 ng/ml (3). Vitamin D is produced by activation of previtamin D3 synthesis in the skin by sunlight, especially by ultraviolet B rays (UVB). Diet is one of the Vitamin D sources, but a limited number of foods contain Vitamin D (2). The 25-OH Vitamin D level is associated with exposure to sunlight, Vitamin D uptake, latitude, season, gender, air pollution, use of sunscreen, skin pigmentation, age, efficiency of intestinal absorption, liver and kidney diseases, and use of medicine (2). In a global study that included 7.564 postmenopausal women from 25 countries on five continents, significant associations were found between the serum 25-OH Vitamin D level and season of the year, and the lowest levels were observed in winter months (4). Another study found that 25-OH Vitamin D levels were higher in men compared to women in all age groups (5). In addition, a non-linear relationship was found between age and the 25-OH Vitamin D level, and a higher prevalence of Vitamin D deficiency was found in the advanced age (6).

The aim of the present study was to evaluate the associations between Vitamin D levels and season of the year, age, gender, living place, and chronic diseases in the Tokat Province, Turkey located, in the 40.31 North Latitude.

MATERIALS and METHODS

Individuals whose 25-OH Vitamin D levels were measured in state hospitals of Tokat Districts during September 2016–August 2017 were included into this retrospective study via a screening by hospital automation system. The place of living, age, gender, chronic diseases, and 25-OH Vitamin D levels of the subjects were recorded. When multiple measurements of 25-OH Vitamin D were available for a given patient, only the first measurement was used. Adults were divided into three groups based on age (18–50, 51–64, and ≥65). The seasons were summer (June–August), winter (December–February), autumn (September–November), and spring (March–May). The locations of town and district centers were grouped as urban, while villages were grouped as rural. The patients with chronic kidney failure, chronic liver disease, epilepsy, and cancer were excluded. In the evaluation of the association between the 25-OH Vitamin D level and chronic diseases, the patients with two or more chronic conditions were not included in statistical analyses.

Laboratory Tests

Serum 25-OH Vitamin D levels were determined via the electrochemiluminescence method with a Roche Cobas e601 auto-analyzer (Roche Diagnostics, Mannheim, Germany; measuring range 3–70 ng/mL, functional sensitivity 4.01 ng/mL, and coefficient of variation 18.5%). Serum 25-OH Vitamin D levels <10 ng/ml were considered to indicate severe deficiency, 10–19 ng/ml deficiency, 20–29 ng/ml insufficiency, while levels ≥30 ng/ml were considered sufficient (2, 7).

The study was approved by the local University Hospital Clinical Research Ethical Committee (17-KAEK-112/: 83116987).

Statistical Analyses

Descriptive analyses were used for general characteristics of the study population. Quantitative data were analyzed using the arithmetic mean and standard deviation. Qualitative data were expressed as the frequency and percentage. The Shapiro–Wilk test was used to assess the normality of the data. The independent samples t-test or one-way analysis of variance was used to compare groups for continuous data. Tukey's Honest Significant Difference test was used for multiple comparisons. A chi-squared test was used to compare study groups for categorical data. A p-value <0.05 was considered significant. Statistical analyses were performed using the SPSS software (IBM SPSS Statistics ver. 19, SPSS Inc., an IBM Co., Somers, NY).

RESULTS

The study included 22.044 people whose average age was 49.1±16.9 (range 18–98). Vitamin D deficiency was found in 75.4% of all participants (n=16.613), and 14% (n=3.092) had Vitamin D insufficiency (20–29 ng/ml). Only 10.6% of participants (n=2.339) had sufficient 25-OH Vitamin D levels (≥30 ng/ml). The most common three diseases observed in the study were hypertension, heart disease, and chronic obstructive pulmonary disease in the decreasing order, while 11.278 people had no chronic disease. On the other hand, 1.149 people had more than one chronic condition.

Data regarding gender, age, the place of living, seasons, and chronic diseases based on average 25-OH Vitamin D levels are presented in Table 1. An overall mean of 25-OH Vitamin D level was 15.1±12.2 ng/ml, which was significantly higher in men (17.6±9.9 ng/ml) compared to women (14.4±12.6 ng/ml; p<0.001). In terms of age groups, the highest level of 25-OH Vitamin D was measured in participants aged 51–64 years (median 17±13.5 ng/ml) followed by the group ≥65 years of age (median 16.1±12.6 ng/ml), while the 18–50 years of age group had the lowest 25-OH Vitamin D level (median 13.7±11.1 ng/ml; p<0.001). Of all participants, 78.6% (n=17.328) were women, and 74.3% (n=16.377) of them were living in urban areas. The 25-OH Vitamin D levels of people living in towns (15.0±12.4 ng/ml) were significantly lower than of those living in villages (15.4±11.5 ng/ml; p=0.03). In terms of season of the year, 23.9% of the study data (n=5.273) were

Table 1. 25-OH Vitamin D level variation depending on gender, age, place of living, season, and chronic disease

	25-OH vitamin D level			
	Count (%)	**Mean±SD (ng/ml)**	**t, F**	**p**
Gender				
Women	17328 (78.6)	14.40±12.60	16.138	<0.001
Men	4716 (21.4)	17.60±9.90		
Age				
18–50	11496 (52.1)	13.70±11.10[a]	166.673	<0.001
51–64	6059 (27.5)	17.00±13.50[b]		
≥65	4489 (20.4)	16.10±12.60[c]		
Place of living				
Rural	5667 (25.7)	15.40±11.50	2.132	0.030
Urban	16377 (74.3)	15.00±12.40		
Season				
Winter	5401 (24.5)	13.40±11.50[a]	151.305	<0.001
Spring	6895 (31.3)	13.60±11.70[a]		
Summer	4475 (20.3)	17.00±12.10[b]		
Autumn	5273 (23.9)	17.00±13.10[b]		
Hypertension				
Yes	8493 (24.7)	15.67±12.72	7.187	<0.001
No	11278 (75.3)	14.40±11.73		
Chronic obstructive pulmonary disease				
Yes	241 (2.1)	15.82±10.98	1.830	0.067
No	11278 (97.9)	14.40±11.73		
Diabetes mellitus				
Yes	7 (0.1)	13.34±10.58	0.241	0.809
No	11278 (99.9)	14.40±11.73		
Parkinson's disease				
Yes	12 (0.1)	17.39±13.51	0.878	0.380
No	11278 (99.9)	14.40±11.73		
Multiple sclerosis				
Yes	25 (0.2)	19.50±14.88	2.165	0.030
No	11278 (99.8)	14.40±11.73		
Heart disease				
Yes	839 (6.9)	17.42±13.13	7.091	<0.001
No	11278 (93.1)	14.40±11.73		

a, b, c: Means with the same letter are not statistically different. Yes: Only those with one chronic disease. No: Those without chronic disease; SD: Standard deviation

Table 2. Distribution of variables based on the classification of the 25-OH vitamin D level

	Classification of 25-OH vitamin D level					
	Severely deficiency Count (%)	Deficiency Count (%)	Insufficiency Count (%)	Sufficiency Count (%)	χ^2	p
Gender						
Women	8805 (50.8)[a]	4612 (26.6)[b]	2047 (11.8)[b]	1864 (10.8)[c]	1425.654	<0.001
Men	1033 (21.9)[a]	2163 (45.8)[b]	1045 (22.2)[b]	475 (10.1)[c]		
Age						
18–50	5684 (49.4)[a]	3498 (30.4)[b]	1377 (11.0)[c]	937 (8.2)[d]		
51–64	2334 (38.5)[a]	1896 (31.3)[b]	1000 (16.5)[c]	829 (13.7)[c]	339.649	<0.001
≥65	1820 (40.5)[a]	1381 (30.8)[b]	715 (15.9)[c]	573 (12.8)[c]		
Place of living						
Rural	2321 (41.0)[a]	1875 (33.0)[b]	896 (15.8)[b]	575 (10.2)[a]	55.649	<0.001
Urban	7517 (45.9)[a]	4900 (29.9)[b]	2196 (13.4)[b]	1764 (10.8)[a]		
Season						
Winter	2785 (51.6)[a]	1613 (29.9)[b]	575 (10.6)[c]	428 (7.9)[c]		
Spring	3565 (51.7)[a]	1940 (28.1)[b]	767 (11.1)[c]	623 (9.1)[c]	674.304	<0.001
Summer	1499 (33.5)[a]	1571 (35.1)[b]	835 (18.7)[c]	570 (12.7)[c]		
Autumn	1989 (37.7)[a]	1651 (31.3)[b]	915 (17.4)[c]	718 (13.6)[c]		

a, b, c: Means with the same letter are not statistically different. Pearson Chi-Square test was used

from people whose measurements were performed in autumn, while 24.5% (n=5.401) in winter, 31.3% (n=6.895) in spring and 20.3% (n=4.475) in summer. The 25-OH Vitamin D levels were lowest in winter (median 13.4±11.5 ng/ml) and highest in summer (median 17±12.1 ng/ml; p<0.001). An average 25-OH Vitamin D level of people who did not have a chronic disease was significantly lower compared to the people who had only hypertension, heart disease, or multiple sclerosis (14.40±11.73, 15.67±12.72, 17.42±13.13, and 19.50±14.88, respectively; p<0.005).

Distributions of variables based on the classification of 25-OH Vitamin D levels are presented in Table 2. Severe deficiency, deficiency, and insufficiency were significantly higher than sufficiency in both women and men (p<0.001). Of all participants, 89.5% with severe deficiency, 68.1% with deficiency, and 66.2% with insufficiency were observed in women. Severe deficiency, deficiency, and insufficiency of Vitamin D were significantly higher than Vitamin D sufficiency in the 18–50 years of age group (p<0.001). Similarly, severe deficiency and deficiency of Vitamin D were significantly higher in both 51–64 and ≥65 years of age groups (p<0.001). The 25-OH Vitamin D level was <30 ng/ml in 91.8% of people in the 18–50 years of age group. Vitamin D insufficiency and deficiency were significantly higher than sufficiency in people living in rural areas (p<0.001). On the other hand, severe deficiency was significantly higher than Vitamin D deficiency and insufficiency in people living in towns (p<0.001). Severe deficiency was most frequent in winter and spring months (51.6 and 51.7%, respectively), while sufficiency was most frequent in autumn and summer months (13.6 and 12.7%, respectively). In terms of months, the highest average 25-OH Vitamin D level was observed in August (19.7±12.4 ng/ml) and the lowest in February (12.8±11.5 ng/ml) (Fig. 1).

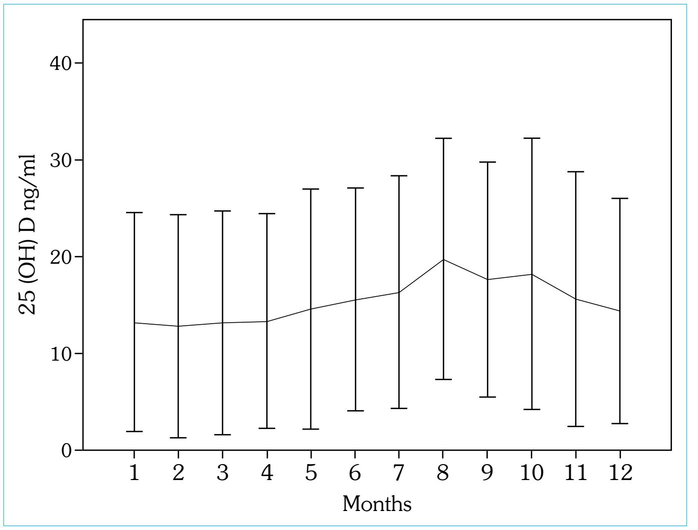

Figure 1. Monthly averages of vitamin D levels

DISCUSSION

Vitamin D deficiency and insufficiency were observed in 89.4% of 22.044 participants in the present study. In a study that examined the deficiency in Greece (latitude 35-40 N), the prevalence of Vitamin D insufficiency was 87.7% (8), while in another study carried out in Spain (latitude 40.46 N) about one-third of the population had 25-OH Vitamin D levels <20 ng/ml (9). Thus, it is clear that Vitamin D deficiency represents a global public health problem. Differences in 25-OH Vitamin D levels could vary depending upon the latitude, season, clothing habits, sunlight exposure, and dietary differences (2).

In the present study, severe deficiency, deficiency, and insufficiency rates were significantly lower than sufficiency in both men and women. Deficiency and insufficiency rates were quite high in both women and men (89.2% and 89.9%, respectively). Similar to previous studies (10), the 25-OH Vitamin D level in women was lower than that in men in the present study. Unlike our findings, Sanghera et al. found lower 25-OH Vitamin D levels in men compared to women (11). These gender differences could be associated with gender-related variations in the body fat contents. A great sequestration effect of subcutaneous fat tissue could lead to decreases in the 25-OH Vitamin D level. Vitamin D deficiency is more common in overweight and obese individuals compared to those with normal weight (12, 13). Gender-associated variations in 25-OH Vitamin D levels could be related to androgen-associated changes in the concentration of Vitamin D-binding protein, precursor production by skin, and 25-hydroxilation in the liver (14).

Another variable affecting the 25-OH Vitamin D level is age. The 25-OH Vitamin D level was significantly lower in the 18–50 years of age group compared to the group aged ≥50 years. Similarly, Al Quaiz et al. found that the prevalence of Vitamin D deficiency in both men and women was higher in the 30–50 years age group compared to the older age group (15). In a study conducted in Turkey, Vitamin D deficiency was more prevalent in the 10–40 years of age group compared to the group >40 years, and this finding was attributed to the fact that the older age group in Turkey took Vitamin D replacement treatment (16). Findings of the present study appear to support such as a conclusion. In the present study, Vitamin D deficiency and insufficiency in women aged 18–50 years were significantly more prevalent than sufficiency, while no association was observed between the 25-OH Vitamin D level and age in men in this age group. Similarly, Schramm et al. found the lowest 25-OH Vitamin D level in the oldest age group (25-OH Vitamin D levels of 19.7, 20.1, and 16.7 ng/ml for 45–54, 55–64, and 65–75 years of age, respectively), while no significant association was found between the 25-OH Vitamin D level and age in men (25-OH Vitamin D levels of 20.4, 21.6, and 20.2 ng/ml for 45–54, 55–64, and 65–75 years of age, respectively) (17). Decreasing 25-OH Vitamin D levels along with aging could be due to a decreases in the Vitamin D synthesis by the skin, malabsorption, a decrease in the conversion into active form of Vitamin D in the kidney, decreases in Vitamin D receptors, and less exposure to sunlight (18). Nevertheless, the prevalence of Vitamin D deficiency was not associated with age in a study conducted on 143 healthy individuals (19).

The amount of UVB in sunlight varies greatly with the season, latitude, and hour of the day, and it could have a considerable effect on Vitamin D synthesis (20). Severe Vitamin D deficiencies were observed in spring and winter months. Winter was the season with the lowest 25-OH Vitamin D level measured in all subjects followed by spring, while the highest level was observed in summer. In terms of months, August was the month in which an average 25-OH Vitamin D level of all participants was the highest (19.7±12.4 mg/dl), while February was the one with the lowest level (12.8±11.5 mg/dl). The highest 25-OH Vitamin D level observed in the last month of summer could be explained by the fact that the synthesis of Vitamin D was high as a result of the exposure to sunlight during summer months. Similarly, decreasing 25-OH Vitamin D levels at the end of winter months could be explained by a lower Vitamin D synthesis as a result of exposure to less sunlight during these months. It is possible that due to lack of the sunbathing habit during summer months and clothing style of individuals in the region, the 25-OH Vitamin D level increased toward the end of summer months, and stored 25-OH Vitamin D level stayed high in autumn months. In line with the present study, there are reports in the literature mentioning that the serum 25-OH Vitamin D levels vary considerably among seasons, peak 30–60 days following the exposure to sunlight in summer months and drop to the lowest level toward the end of winter months (1, 20). In a study by Wyskida et al., sufficient vitamin levels were most frequent in August in both men and women, while the lowest values were observed in women in January and in men in March (21). Results of the present study are similar to the results of the study by Gonzalez Molero et al., conducted in Spain to examine seasonal variations in the 25-OH Vitamin D levels (9). However, our results were in conflict with the ones from a study conducted in Saudi Arabia (15). Unlike many studies reporting that 25-OH Vitamin D levels change with seasons, a study found a consistently high level of Vitamin D deficiency throughout the year without any major change. This finding was attributed to the use of traditional clothing all year round, which hinders sunlight from reaching the skin (22). A high level of Vitamin D deficiency and insufficiency observed in the present study throughout the year in the Tokat Province could be due to the failure of sunlight exposure at an appropriate time of the day and for enough time with appropriate clothing.

Another variable affecting the 25-OH Vitamin D level in the present study was the place of living. The 25-OH Vitamin D level was found to be lower in people from urban areas compared to people from rural areas. In a study reporting lower Vitamin D prevalence in people from suburbs than people living in towns, it was mentioned that such a variation could be attributed to differences in the lifestyle, such as more outdoor activities of people living in suburbs and an extensive use of sunscreen in urban areas (23). Vitamin D deficiency was observed in 75.8% of people in urban communities and in 74.0% of people in rural communities. A study conducted in India reported Vitamin D deficiency in 91.3% of people living in towns (24). Another reason for a higher incidence of Vitamin D deficiency in urban areas could be the air pollution (25). Air pollution is the main factor determining the amount of UVB reaching the surface of Earth. Therefore, atmospheric pollution could play a crucial role in the development of Vitamin D deficiency (26).

An average 25-OH Vitamin D level was significantly higher in individuals with hypertension, heart disease, and multiple sclerosis. Similar to our findings, the studies comparing hypertensive individuals with healthy controls found a significantly higher 25-OH Vitamin D level in people with hypertension compared to the control group (27, 28). The reason for this could be that 25-OH Vitamin D could induce vascular resistance, change the sensitivity of vascular muscle cells to vasoconstrictive factors, and thus lead to hypertension (29). An average 25-OH Vitamin D level of individuals with multiple sclerosis was higher than individuals who did not have a chronic condition. Similarly, a study comparing calcium homeostasis and 25-OH Vitamin D regulation in the multiple sclerosis patients with healthy controls found a lower average 25-OH Vitamin D level in the control group (30).

The strength of the present study lies in the sampling size, wide age range, and its covering the entire year. Major limitations of the study, on the other hand, were that no data were available on wearing characteristics, dietary habits, sun exposure, and use of Vitamin D supplements since the data were obtained retrospectively from hospital records. In addition, only individuals present in the hospital system were evaluated, which limited generalizations about all individuals living in the region. Simultaneous calcium and parathormone levels were not included, and therefore, it was not possible to evaluate hyperparathyroidism and calcium metabolism. Liquid chromatography mass spectrometry, the gold standard for 25-OH Vitamin D measurement, was not used in the present study. Instead, a faster and perfectly sensitive electrochemiluminescence immune assay method was employed. As a result, it was not possible to distinguish different forms such as 25-OH D3 and 25-OH D2. In addition, the gene polymorphisms of the Vitamin D gene were not evaluated in the present study.

CONCLUSION

The 25-OH Vitamin D level should be evaluated and treated not only in the postmenopausal period, but also in the premenopausal period. It should be kept in mind that Vitamin D deficiency is important in men, as well as in women. Education campaigns should be launched to emphasize these problems and prevent them. Health professionals should inform general public about the necessity of enough sunlight exposure in summer months, and physical activity programs should be organized. In addition, Vitamin D supplement programs should be planned for risk groups during winter months to prevent Vitamin D deficiency and eliminate associated health problems. The 25-OH Vitamin D level was higher in patients with hypertension and chronic heart disease. Thus, studies dealing with the effect of the 25-OH Vitamin D level on the pathogenesis of hypertension and chronic heart disease. The 25-OH Vitamin D level was not associated with chronic obstructive pulmonary disease, diabetes mellitus, and Parkinson's disease, while the 25-OH Vitamin D level was higher in patients with multiple sclerosis. These findings need to be supported by additional larger-scale studies.

Ethics Committee Approval: The study was approved by the Gaziosmanpaşa University Clinical Research Ethics Committee (date: 18.07.2017, number: 17-KAEK-112/: 83116987).

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