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Retrospective Analysis of Vitamin D Levels in Patients with Chronic Renal Failure, Obesity, and Cancer

Kronik Böbrek Yetmezliği, Obezite ve Kanser Hastalarında Vitamin D Düzeylerinin Retrospektif İncelemesi

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ÖZET

AMAÇ: Çalışmamızda 2018-2021 yılları arasında İnönü Üniversitesi Turgut Özal Tıp Merkezine başvuran kronik böbrek yetmezliği, obezite ve kanser tanılı hastaların yaş, cinsiyet ve mevsimlere göre vitamin D düzeylerinin dağılımının incelenmesi amaçlandı.

GEREÇ VE YÖNTEM: Tanımlayıcı tipte olan çalışmamızda 01.01.2018-01.01.2021 tarihleri arasında İnönü Üniversitesi (İÜ) Turgut Özal Tıp Merkezine başvuran kronik böbrek yetmezliği, obezite ve kanser tanılı vitamin D seviyeleri ölçülen hastaların dosyaları taranarak retrospektif olarak değerlendirildi. Hastalar; yaş, cinsiyet ve örneklerin alındığı mevsimlere göre gruplandırıldı. 25(OH)D vitamini düzeyleri LC-MS/MS yöntemi ile analiz edilmişti. Hastalar vitamin D düzeyi bakımından eksik, yetersiz ve normal olarak sınıflandırıldı.

BULGULAR: Hastanemize başvuran 882 kronik böbrek yetmezliği hastasının %63,3'ünde (n=558), 2894 obezite hastasının %65,8'inde (n=1903) ve 1787 kanser hastasının %54,9'unda (n=981) vitamin D eksikliği tespit edildi. Hastalıklara göre vitamin D düzeyleri arasında anlamlı bir fark vardı (p<0.001).

SONUÇ: Hastanemize başvuran toplam 5563 kronik böbrek yetmezliği, obezite ve kanser hastasının; %61,9'unda (n=3442) vitamin D eksikliği, %23,1'inde (n=1284) vitamin D yetersizliği tespit edilirken, sadece %15'inde (n=837) vitamin D seviyesi normal olarak bulundu. Vitamin D eksikliği bakımından %57 oranla en fazla eksiklik obezite hastalarında görüldü. Çalışmamızda vitamin D düzeylerinin incelenen hastalıklara, mevsimlere ve yaş gruplarına bağlı olarak değiştiği görüldü.

Anahtar Kelimeler: vitamin D, kanser, kronik böbrek yetmezliği, obezite

ABSTRACT

OBJECTIVE: In our study, it was purposed to research the distribution of vitamin D according to age, sex, and seasons of the patients diagnosed with obesity, cancer, and chronic renal failure who applied to Inonu University Turgut Ozal Medical Center between 2018-2021.

MATERIALS AND METHODS: In our descriptive study, vitamin D measurements from 01.01.2018-01.01.2021 users who visited Inonu University Turgut Ozal Medical Center and were diagnosed with obesity, cancer, and chronic renal failure were scanned in their files and assessed retrospectively. The patients were grouped according to their sex, age, and seasons in which the samples were taken. 25(OH)D levels were analyzed by LC-MS/MS method. The patients were classified as deficient, inadequate, and normal in terms of vitamin D level

RESULTS: Vitamin D deficiency was monitored in 54.9% (n = 981) of 1787 cancer patients admitted to our hospital, 63.3% (n = 558) of 882 chronic renal failure patients, and 65.8% (n = 1903) of 2894 obese patients.

CONCLUSION: Of the 5563 obesity, cancer, and chronic renal failure patients who applied to our hospital; vitamin D deficiency was found in 61.9% (n = 3442), vitamin D deficiency was found in 23.1% (n = 1284), while vitamin D level was found to be normal in only 15% (n = 837). In terms of vitamin D deficiency, the highest deficiency was seen in obese patients with a rate of 57%. In our study, it was observed that vitamin D levels vary depending on the diseases, seasons, and age groups examined.

Keywords: vitamin D, cancer, chronic kidney failure, obesity

INTRODUCTION

Vitamin D deficiency (VDD) is considered a global common epidemic not only in our country (Turkey) but also in the world (1). Although it has been known for many years that VDD plays a role in diseases for instances osteomalacia and rickets. Today, it is recorded that VDD has a part in the progress of diabetes mellitus, multiple sclerosis, chronic kidney disease, metabolic syndrome, epilepsy, and many diseases. It is thought that the benefits of its use as a supplement and vitamin D may play a part as an auxiliary factor in treatment (2,3). Apart from these, it is also linked with a diagnosis of cancers, cardiovascular diseases, and

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Type 1 diabetes, and together with them simultaneously increased (3). These studies have also resulted in the study of the extraskeletal effects of vitamin D. It is stated that any improvement in the human body's vitamin D level will significantly influence the regulation of genes associated with cancer and cardiovascular diseases (4).

There are different assumptions regarding reference ranges of Vitamin D. The American Endocrine Society, one of the international health authorities, defines Vitamin D levels which below 20 ng/mL as a deficiency, which between 20-29 ng/mL as insufficiency, and which 30ng/mL and above as normal. (5). On the other hand, the World Health Organization defines vitamin D levels below 20 ng/mL as insufficiency and vitamin D levels below 10 ng/mL as a deficiency. (6).

Chronic Renal Failure, (CRF), cancer, and obesity are also diseases in which VDD is common and thought to be linked with VDD. Our work aims to report the 25(OH)D deficiency by examining the vitamin D levels in CRF patients, obesity, and cancer who applied to our hospital from Malatya city and neighboring provinces and to determine its change in terms of age, sex, and season.

MATERIAL & METHODS

This research was planned as a descriptive, cross-sectional analytical study. Before starting the study, ethical approval was obtained from Inonu University (IU) Health Sciences Non-Interventional Clinical Research Ethics Committee with decision number 2018/12-10, This study was carried out by retrospectively scanning the files of CRF, obesity, and cancer patients who applied to IU Turgut Ozal Medical Center between 01.01.2018 and 01.01.2021. In the study, all patients diagnosed by the relevant polyclinics were screened without any age restrictions. The intersection of the three groups in the study hadn't any patient. Patients with any two diseases were not included in the study. The youngest patient was 2 years old and the oldest patient was 96 years old in our study. In our study, 25(OH)D levels were measured by our biochemistry laboratory using the LC-MS/MS method. The measurement range for serum 25(OH)D was in the range of 20-70 ng/mL. The ranges determined by the American Endocrine Society were taken as a reference for Vitamin D cut-off values. According to this, in our study, 25(OH)D levels for ranges <20 ng/mL, 20-30 ng/mL, and >30 ng/mL were accepted as a deficiency, insufficiency, and normal, respectively.

Statistical Analysis

While evaluating the findings obtained in the study, SPSS (Statistical Package for Social Sciences) for Windows 20.00 program was used for statistical analysis. Descriptive statistics for continuous variables were summarized as mean and standard deviation (SD), and for categorical data in terms of frequency and percentage. For the comparison of categorical data, Pearson Chi-Square and Fisher-Exact tests were used. When there was a difference between groups, Bonferroni correction was applied for paired. Results were considered statistically significant for $p < 0.01$.

RESULTS

The number of patients for vitamin D levels in terms of sex, diseases, and seasons of 5563 patients included in the study, min-max. values, arithmetic mean and SD measures are given in Table 1.

In the literature, VDD was described as serum 25(OH)D level <20 ng/mL and insufficiency between 21 and 29 ng/mL, and vitamin D levels >30 ng/mL were taken as the basis for optimal health (7). In our work, the classification of Vitamin D levels was made by taking these values as a reference. Of the 5563 people in the study, 32% (n = 1783) were men and 68% (n=3780) were women. When the dispersion of vitamin D levels in terms of sex for all patients was examined, there was not a significant difference between men and women as to vitamin D levels ($p > 0.05$).

Considering that the three patients set were evaluated together, the highest VDD was 76.3% in winter (n = 1136), the highest insufficiency was 30.1% (n = 459) in the summer season, and the highest normality was 19.7% in the summer season (n = 301). Of 1263 patients who applied to our hospital in the spring had a deficiency level of vitamin D in 64.7% (n = 817) and an insufficiency level of vitamin D in 21.3% (n = 269). Of 1526 patients who applied to our hospital in the summer had a deficiency level of Vitamin D in 50.2% (n = 766) and an insufficiency level of vitamin D in 30.1% (n = 459). Of 1285 patients who applied to our hospital in autumn had a deficiency level of Vitamin D in 56.3% (n = 723) and an insufficient level of vitamin D in 24.8% (n = 319). It was found deficiency level of Vitamin D in 76.3% (n = 1136) and an insufficient level of vitamin D in 15.9% (n = 237) of 1489 patients who visited our hospital in winter. When these data were reviewed, there was a significant difference between vitamin D levels due to seasons ($\chi^2=248.681$; $p<0.01$).

Table 1. Vitamin D Levels by Sex, Diseases and Seasons

			n	%	Minimum	Maximum	Mean	SD
Spring	**CRF**	Men	92	52,5	,830	48,750	17,586	11,377
		Women	83	47,5	1,000	46,680	14,830	11,997
		Total	175	100	,830	48,750	16,279	11,723
	Obesity	Men	182	28,8	1,000	53,620	16,274	8,853
		Women	448	71,2	,720	63,020	16,565	10,435
		Total	630	100	,720	63,020	16,481	9,998
	Cancer	Men	132	28,8	1,000	52,420	16,782	11,278
		Women	326	71,2	1,000	66,200	21,385	14,284
		Total	458	100	1,000	66,200	20,058	13,635
Summer	**CRF**	Men	125	48,1	,750	58,000	23,256	12,151
		Women	135	51,9	1,040	66,600	20,482	13,575
		Total	260	100	,750	66,600	21,816	12,960
	Obesity	Men	247	31,1	4,370	54,960	23,209	8,761
		Women	547	68,9	,980	60,920	18,855	10,446
		Total	794	100	,980	60,920	20,210	10,149
	Cancer	Men	118	25,0	2,230	69,230	22,073	11,864
		Women	354	75,0	1,000	68,100	22,765	13,227
		Total	472	100	1,000	69,230	22,592	12,891
Autumn	**CRF**	Men	94	51,1	2,940	58,130	21,269	13,089
		Women	90	48,9	1,990	48,790	15,610	11,576
		Total	184	100	1,990	58,130	18,501	12,660
	Obesity	Men	209	31,3	4,340	55,890	22,083	10,486
		Women	459	68,7	1,000	61,200	17,862	9,843
		Total	668	100	1,000	61,200	19,183	10,230
	Cancer	Men	124	28,6	3,480	64,900	24,730	13,388
		Women	309	71,4	1,000	58,120	21,491	12,992
		Total	433	100	1,000	64,900	22,418	13,173
Winter	**CRF**	Men	125	47,5	1,000	65,050	16,295	11,607
		Women	138	525	,950	67,110	14,789	11,892
		Total	263	100	,950	67,110	15,505	11,759
	Obesity	Men	215	26,8	1,090	69,090	12,880	8,001
		Women	587	73,2	1,000	69,930	12,699	8,520
		Total	802	100	1,000	69,930	12,747	8,379
	Cancer	Men	120	28,3	1,000	54,580	13,010	9,283
		Women	304	71,7	,930	68,480	18,001	12,537
		Total	424	100	,930	68,480	16,589	11,912

SD: standard deviation, n: number

When the ages included in the study were examined, the lowest age in the CRF group was 2, the highest age was 92; in the obesity group, the lowest age was 3, the highest age was 81; in the cancer group, the lowest age was 3 and the highest age was 96. In terms of age groups, the highest VDD among the total patients was in the ages group of 18-34 which constitute 14% of all patients (n = 775) and the highest deficiency was 4.4% in the 0-17 age group (n = 245) and the highest normality was detected in the 55+ age group with a frequency of 5.8% (n = 326). In the 0-17 age group, 54.9% (n = 467) of 850 patients received to our hospital had deficiency of vitamin D levels and 28.8% (n = 245) of them had insufficiency levels of vitamin D. In the 18-34 age group, 73.4% (n = 775) of 1056 patients admitted to our hospital had deficiency levels and 17.3% (n = 183) of them had insufficiency levels of vitamin D. In the 35-54 age group, 61% (n = 1151) of 1886 patients received to our hospital had deficiency levels and 22.4% (n = 460) of them had insufficiency levels of vitamin D. In the 55+ age group, 59.2% (n = 1049) of 1771 patients admitted to our hospital had deficient levels and 22.4% (n = 396) of them had insufficient levels of vitamin D. There was a significant difference between vitamin D levels according to age groups (p <0.01).

VDD was found in 63.3% (n = 558) of 882 CRF patients, 65.8% (n = 1903) of 2894 obese patients and 54.9% (n = 981) of 1787 cancer patients. While VDD levels were higher than both insufficiency and normal levels in terms of diseases (p <0.01), no significant difference was found between insufficiency and normal levels.

Vitamin D levels of CRF patients were founded according to sex, seasons, and age groups, and a significant difference was found among vitamin D levels in respect of all three factors (Table 2).

Vitamin D levels of obese patients were founded in terms of sex, seasons, and age groups, and a significant difference was found between vitamin D levels as regards all three factors (Table 3).

Vitamin D levels of cancer patients were also analyzed in terms of sex, seasons, and age groups; while we found a significant difference between vitamin D levels in terms of sex and seasons, no significant difference as regards age groups (Table 4).

Table 2. Vitamin D Levels in Chronic Renal Failure Patients by Sex, Seasons, and Age Groups

		Vitamin D Levels									
		Deficiency		Insufficient		Normal		Total			
		n	%	n	%	n	%	n	%	χ^2	p
Sex	Men	253	58,0	89	20,4	94	21,6	436	100		
	Women	305	68,4	73	16,4	68	15,2	446	100	10,487	0,005
	Total	**558**	**63,3**	**162**	**18,4**	**162**	**18,4**	**882**	**100**		
Seasons	Spring	119	68,0	30	17,1	26	14,9	175	100		
	Summer	128	49,2	66	25,4	66	25,4	260	100		
	Autumn	118	64,1	28	15,2	38	20,7	184	100	37,471	0,000
	Winter	193	73,4	38	14,4	32	12,2	263	100		
	Total	**558**	**63,3**	**162**	**18,4**	**162**	**18,4**	**882**	**100**		
Age Groups	0-17	31	44,3	15	21,4	24	34,3	70	100		
	18-34	64	75,3	9	10,6	12	14,1	85	100		
	35-54	134	64,1	47	22,5	28	13,4	209	100	24,618	0,000
	55+	329	63,5	91	17,6	98	18,9	518	100		
	Total	**558**	**63,3**	**162**	**18,4**	**162**	**18,4**	**882**	**100**		

χ^2: chi-square, p: probability, n: number %: percentage

Table 3. Vitamin D Levels in Obesity Patients by Sex, Seasons and Age Groups

		Vitamin D Levels									
		Deficiency		Insufficient		Normal		Total			
		n	%	n	%	n	%	n	%	χ^2	p
Sex	Men	510	59,8	235	27,5	108	12,7	853	100		
	Women	1393	68,3	466	22,8	182	8,9	2041	100	20,494	0,000
	Total	**1903**	**65,8**	**701**	**24,2**	**290**	**10**	**2894**	**100**		
Seasons	Spring	435	69,0	143	22,7	52	8,3	630	100		
	Summer	419	52,8	252	31,7	123	15,5	794	100		
	Autumn	390	58,4	190	28,4	88	13,2	668	100	183,079	0,000
	Winter	659	82,2	116	14,5	27	3,4	802	100		
	Total	**1903**	**65,8**	**701**	**24,2**	**290**	**10**	**2894**	**100**		
Age Groups	0-17	362	55,7	200	30,8	88	13,5	650	100		
	18-34	624	75,4	147	17,8	57	6,9	828	100		
	35-54	703	65,9	255	23,9	109	10,2	1067	100	67,232	0,000
	55+	214	61,3	99	28,4	36	10,3	349	100		
	Total	**1903**	**65,8**	**701**	**24,2**	**290**	**10**	**2894**	**100**		

χ^2: chi-square, p: probability, n: number %: percentage

DISCUSSION

The prevalence of VDD in the community is 20-50%, and deficiency levels have been reported up to 70-80% in CRF patients (8). A group of researchers aiming to assess the vitamin D status of hemodialysis patients in Germany found that approximately one-third (32.7%) of the patients had severe VDD and 47% had insufficiency. They stated that the incidence of cancer is also high among the same individuals, emphasizing the cancer-affecting properties of vitamin D for the risk of cancer disease seen in kidney patients, and stated that more studies are needed (9). Epidemiological studies have indicated that low 25(OH)D levels are free predictors of disease progression and mortality in patients with CKD (Chronic Kidney Disease) and End-Stage Renal Disease (ESRD) (10). Grahame found that 39% of 257 CRF patients had low serum 25(OH)D levels and lower levels were linked with women's sex (p=0.000 for each). In the study, 25(OH)D levels also differed in terms of the season (p = 0.018), peaking in autumn and reaching the lowest level in spring (11). Li et al. demonstrated the relationship between vitamin D and the renin-angiotensin system using animal models. Accordingly, it has been hypothesized that vitamin D plays a key role in the renocardiovascular system and acts as a negative endocrine regulator in the renin-angiotensin system. In this respect, it has been illuminating the molecular effects of vitamin D analogs, the renin-angiotensin system, and the therapeutic renin inhibitors that control blood pressure (12).

Table 4. Vitamin D Levels in Cancer Patients by Sex, Seasons and Age Groups

		Vitamin D Levels									
		Deficiency		Insufficient		Normal		Total			
		n	%	n	%	n	%	n	%	χ^2	p
Sex	Men	306	61,9	94	19,0	94	19,0	494	100		
	Women	675	52,2	327	25,3	291	22,5	1293	100	14,131	0,001
	Total	**981**	**54,9**	**421**	**23,6**	**385**	**21,5**	**1787**	**100**		
Seasons	Spring	263	57,4	96	21,0	99	21,6	458	100		
	Summer	219	46,4	141	29,9	112	23,7	472	100		
	Autumn	215	49,7	101	23,3	117	27,0	433	100	52,344	0,000
	Winter	284	67,0	83	19,6	57	13,4	424	100		
	Total	**981**	**54,9**	**421**	**23,6**	**385**	**21,5**	**1787**	**100**		
Age Groups	0-17	74	56,9	30	23,1	26	20,0	130	100		
	18-34	87	60,8	27	18,9	29	20,3	143	100		
	35-54	314	51,5	158	25,9	138	22,6	610	100	6,118	0,410
	55+	506	56,0	206	22,8	192	21,2	904	100		
	Total	**981**	**54,9**	**421**	**23,6**	**385**	**21,5**	**1787**	**100**		

χ^2: chi-square, p: probability, n: number %: percentage

In our study, we found that 63.3% of the patients followed up with the diagnosis of CRF had deficient, 18.4% insufficient, and 18.4% normal serum 25(OH)D levels. In addition, the vitamin D levels of the patients were examined in terms of sex, seasons, and age groups, and a significant difference was “found among vitamin D levels” in terms of all three factors. For 25(OH)D deficiency in this patient group; the highest rate in terms of sex was found in men (68.4%), the highest rate in terms of seasons was found in winter (73.4%), and the highest rate in terms of age was found in the age group of 18-34 (75.3%). Although there are studies on VDD in CRF patients, there is no study focusing on VDD in these patients in terms of age, sex, and seasonality. There is an impaired vitamin D metabolism in patients with CRF. Although there are many unanswered questions on this issue, what is apparent is that VDD is severe in kidney patients and that the use of supplements can be beneficial in these patients.

Obesity occurs when many factors come together. Although diet, genes, or other lifestyles are thought to have a major effect on the development of obesity, the role of vitamins cannot be neglected in this process. It is a controversial issue whether VDD is a result/cause of obesity (13). In the study conducted by Vimaleswaran et al., it was suggested that while high BMI causes low 25(OH)D level, while low 25(OH)D has little effect on obesity (14). McGill et al. were realized that obese patients have rarely vitamin D sufficiency, and there is an adverse “relationship between serum” 25(OH)D levels and body weight, BMI (body mass index), waist circumference, and total body fat mass (15). The relationship “between vitamin D and” obesity can be declared by the effect of vitamin D on adipogenesis regulating factors in adipose tissue and on inflammation and energy homeostasis in adipocytes (16). In a meta-analysis study on VDD in obese patients, the prevalence of VDD was 35% higher in obese than in the control group. (17). It has been stated that increased PTH level secondary to hypovitaminosis D stimulates lipid anabolism by increasing Ca2+ directed to adipose tissue (18,19), and treatment with VD in 3T3-L1 preadipocytes has been shown to inhibit adipogenesis through down-regulation of transcription factor C/EBPbeta. In addition, it was emphasized that 1,25(OH)D activates the WNT/beta-catenin pathway, resulting in the blockade of adipogenesis (19–21). In the work by Lagunova et al., the seasonal change and prevalence of VDD were assessed in different BMI, sex, and age categories in a population of 2126 patients in Norway. For sex and age groups (<50 years and ≥50 years), an adverse relationship was found between BMI and serum 25(OH)D levels. The results show that one-third of women with a BMI ≥40 and one-two of men are vitamin D deficient (22).

Most of the studies reporting VDD in obese individuals have not been methodically evaluated for seasonal variations. However, Ernst et al. reported that there are significant seasonal changes in serum 25(OH)D levels and the prevalence of VDD in obese patients (23). A meta-analysis study also reported that VDD is linked with age, latitude, and obesity (17). Bischof et al. observed a seasonal change in 25(OH)D serum levels of 483 adults in 2002-2004. In this study, it was stated that 25(OH)D levels were minimum in January and increased until July. While evaluating the vitamin D status of the obese, it was recommended to consider BMI, age and seasons, and to consider more aggressive vitamin D supplements for obese individuals (24). Lagunova et al. found that patients with a BMI≥30 had serum 25(OH)D concentration approximately 20% lower than those of normal weight through the year, not just in summer. In addition, seasonal changes of 25(OH)D were not affected by BMI in women, while obese men had much smaller seasonal change and higher VDD than non-obese men. Obese men and women in the young age group have been reported to have low vitamin D status not only in winter but also in summer. It has also been emphasized that about 40% of obese women and 75% of men have VDD in winter and spring, and about 25% still have deficient levels in the summer. As the age group, the elder people (over 50 years old) with low BMI have found higher 25(OH)D values through the year, although the seasonal variation is not very large (22). In our study, it was found that serum 25(OH)D levels were insufficient and deficient in 90% of patients who were followed up with a diagnosis of obesity. In addition, vitamin D levels were analyzed in terms of sex, seasons, and age groups, and a significant difference was found between vitamin D levels in terms of all three factors. For 25(OH)D deficiency in this patient group; the highest rate in terms of sex was found in women (68.3%), the highest rate in terms of seasons was found in winter (82.2%), and the highest rate in terms of age was found in the age group of 18-34 (75.4%). Although vitamin D supplementation has not been clearly shown to benefit the negative metabolic profile in obese patients, based on the results of our study, only 10% of 2894 obese patients had normal vitamin D levels; for this reason, it strengthens the possibility that VDD is a major agent that has not been revealed in the occurrence of the metabolic pattern in these patients.

In addition to being associated with important public health problems such as vitamin D, obesity, diabetes, and hypertension, there are many studies recently showing the link between VDD and cancer types (25). In the study of Öngen et al., it was stated that as one goes to the north pole, sun exposure decreases, and cancer and cancer-related mortality rates increase. This case strengthens the hypothesis that there may be a relationship between cancer and vitamin D levels. (26). Li et al stated that in recent studies and epidemiological studies, the protective role of vitamin D against the risk of developing many kinds of cancer has been investigated. In these studies, it was emphasized that VDD causes an up in the risk of breast, lung, pancreatic, colorectal, ovarian bladder, thyroid, and kidney cancers. (27). Vitamin levels below 20 ng/mL, which is the cut-off value for deficiency, have been linked with a rised risk of 30-50%, especially for colon, prostate and breast cancer development, and an increased mortality rate from these cancers (26). In addition to the anti-cancer effects of vitamin D and its analogs, some studies have also been carried on the impacts of suppressing the proliferation of human cancer cells mediated by vitamin D receptors. (28). It has been looked into that Vitamin D has a control function on genes that control cell proliferation, differentiation, apoptosis, and angiogenesis. In this respect, the result of vitamin D on cancer can be explained by the mechanism of inhibition of signals that trigger cell growth, cell proliferation, metastasis, and angiogenesis (29). In a recent study, it was shown that patients with serum 25(OH)D levels lower than 20 ng/mL have a high probability of having breast cancer (30). When vitamin D and cancer disease are evaluated, there are studies in which values of 25(OH)D are lower in individuals with cancer than in healthy individuals. In the study that Shi et al. investigated vitamin D levels in individuals with cancer, it was stated that serum 25(OH)D levels were insufficient and deficient in 71% of 1940 people diagnosed with cancer. (31). In our study, in parallel with the findings of Shi et al., it was determined that 78.5% of the patients who were followed up with a diagnosis of cancer disease had insufficient and deficient serum 25(OH)D levels. In observational studies demonstrating the relationship between breast cancer and vitamin D, it has also been shown that the risk of breast cancer significantly decreases with high 25(OH)D levels (32). In a comprehensive meta-analysis study by Zhang et al. with 74655 participants, vitamin D supplementation found a significant 16% reduction in cancer-related mortality. More notably, the study reported that the reduction in cancer mortality was not seen with supplementation of the vitamin D2 form, but only with supplementation of the vitamin D3 form (33). In epithelial cells, the vitamin D receptor (VDR) and its ligand 1,25D contribute to the maintenance of the differentiated phenotype and support pathways that protect cells against endogenous and exogenous stresses. This provides a reduced risk for carcinogenic transformation (34). Tangpricha et al. injected colon cancer cells to mice whose predetermined plasma vitamin D levels. It was observed mice with vitamin D sufficiency had 40% smaller tumors (35). Leyssens et al. observed that 1,25(OH)2D3, the active form of vitamin D, reduced cell proliferation at certain concentrations in Caco-2, SW1417, and SW480-ADH colon cancer cell lines (36).

In one of the epidemiological studies focusing on latitudinal relationships while reported the link between sunlight and cancer, John et al. noticed significant decreases in prostate cancer risk in the south of the United States, where sun exposure is higher (37). Hanchette and Schwartz founded that there was an adverse correlation between the geographical spread of solar UV intensity and prostate cancer mortality in North America, and also there was a lower cancer mortality rate in the South compared to the North. (38). Freedman et al. explored that exposure to sunlight was linked together with a decrease in mortality rates due to some kind of cancer. (39). A study conducted on Norwegian patients with prostate, breast, and colon cancer patients by Robsahm et al it found that patients in seasons with much sun exposure had much better survival than in other seasons (40). However, randomized controlled trials of vitamin D supplementation are required to define the causality of the relationship between vitamin D and cancer risk. Since our study was retrospective, it was not possible to determine whether cancer patients took vitamin D supplements or not. However, despite the possibility that there may be cancer patients taking vitamin D supplementation in the population, only 21.7% of the patients had normal vitamin D levels. In addition, while vitamin D levels do not show a significant difference in cancer patients in terms of age groups; there was also a significant difference in terms of sex and seasons. In this patient group, the sex with the highest deficiency in men (61.9%), and the season in which it is most prevalent in winter (67.0%). For this reason, we think that there can be a contrary correlation between vitamin D level and cancer, although the benefits of vitamin D for some cancers are controversial, deficiency of vitamin D should be seen as a risk for many types of cancer, and normal levels of it have a protective effect. In this context, it is critical to ensure normal blood levels of vitamin D to protect against cancer.

In studies conducted in our country and abroad, it has been reported that 25(OH)D levels of females are lower than men, and 25(OH)D deficiency is more common in women. This difference between the sex in 25(OH)D levels are thought to be because women benefit less from sunlight due to religious and socio-cultural reasons, which determine their dressing style, and the limitation of the time spent in open areas (41). In the study conducted by Mansoor et al. in Pakistan, the average vitamin D level in 123 healthy adults was found to be 41.1±9.6 nmol/L (16.44 ng/mL). In the same study, 69.9% of the participants in the study found that 25(OH)D levels were deficient and 21.1% were insufficient (90% in total) (42). Hekimsoy et al. on people living in a region that generally receives sunlight throughout the year, such as the Aegean region of our country, found 25(OH)D deficiency as 74.9% and 25(OH)D deficiency as 13.8%. Moreover, 25(OH)D deficiency was observed with a higher rate in women (78.7%) than men (66.4%) (41). In some studies, it has been reported that serum 25(OH)D levels varies seasonally and reaches their highest levels in the summer months (43). In the article studied by Öğüş et al. in Ankara, they found the mean of vitamin D levels of 3242 patients as 22.80 ± 13.27 ng/mL, and vitamin D levels <20 ng/mL on 47% of the patients (50% in women, 38% in men). (44). In our study, the distribution of all 5563 patients in terms of sex, diseases, seasons, and age groups was also examined. There was no significant difference between the levels of vitamin D between women and men. Telo et al., in their study examining the change of vitamin D concentration in the Elazığ region as to age, season, and sex, found the lowest 25(OH)D levels in both women and men in winter and the highest level in summer and found a significant difference between seasons (45). In a study by Çatak et al., in which 2742 people looked at vitamin D levels, the lowest of it was observed in winter and the highest of it in summer (46). In our study, seasonally the highest levels were monitored in the summer season and the lowest levels were observed in the winter season for vitamin D. Considering the age group, the highest deficiency in vitamin D was seen in 14% (n=775) in the 18-34 age group, and the highest deficiency in the 0-17 age group among all patients.

CONCLUSION

In conclusion, while vitamin D levels were deficient and insufficient in obesity, cancer, and CKD patients, there was no difference in terms of gender. We also found that vitamin D levels differed in terms of season and age groups. There are literature studies in which VDD is present even in healthy individuals. In this respect, especially in diseases such as cancer, obesity, CKD that require vitamin D supplementation, supplementation doses should be adjusted in terms of the age of the patient and season. Therefore, we think that our study will make an important contribution to the literature.

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