

## Research Article

# Vitamin D Levels of Hospitalized Patients in Internal Medicine Clinic and Its Relationship with Clinical Parameters

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## Abstract

**Objectives:** This study was conducted to determine the frequency of Vitamin D (VD) deficiency and to investigate whether there is a significant difference between sociodemographic and clinical characteristics of patients and 25-OH VD levels by examining 25-OH VD levels in patients 18 years and older admitted to our internal medicine clinic.

**Methods:** This retrospective study was carried out in Haydarpaşa Numune Training and Research Hospital Internal Medicine clinic between May and June 2014, and the patients whose VD levels were measured were examined retrospectively through the hospital information system. Forty-nine patients with type 2 diabetes mellitus and 96 non-diabetic patients were included in the study. A control group of 51 healthy individuals was formed.

**Results:** A total of 145 patients and 51 healthy controls were included in the study. When the study group was classified according to the level of VD, severe deficiency in 76 cases, deficiency in 55 cases, failure in 14 cases were detected. We found that being over 75 years of age, female gender and malignancy predicted vitamin deficiency. When the VD levels of diabetic and non-diabetic patients were compared, VD levels of diabetic patients were found to be lower than non-diabetic patients, but not statistically significant. VD levels between diabetic, non diabetic female patients and healthy female volunteers were statistically different ( $p < 0.001$ ,  $p = 0.001$ ). When VD levels of diabetic and nondiabetic female patients were compared, no statistically significant difference was found ( $p = 0.216$ ).

**Conclusion:** VD deficiency and failure are common problems threatening healthy adults in our country, and VD levels are significantly lower in hospitalized patients. This seems to be related to many comorbid diseases. There is a need for more controlled work in this area.

**Keywords:** Acute renal failure, autoimmune diseases, chronic renal failure, cirrhosis, coronary artery disease, diabetes mellitus, heart failure, hypertension, malignancy, sepsis, Vitamin D.

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Vitamin D (VD) has important effects on calcium homeostasis and bone metabolism in the body.<sup>[1,2]</sup> Under normal conditions, 90-95% of the VD in the human body is caused by the effects of sunlight. Any condition that prevents Ultraviolet B (UVB) rays from reaching the earth

or any condition that interferes with human exposure will result in VD deficiency.<sup>[2]</sup> VD is synthesized in the skin after exposure to sunlight (Vitamin D3) and also taken as an exogenous diet (Vitamin D3 and Vitamin D2).<sup>[3]</sup>

25-Hydroxy Vitamin D (25-OH D) is usually measured to as-

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sess the level of VD. The reason for the measurement of 25-OH D level; The half-life of 1,25 dihydroxy vitamin D, which is the active form, is 4-6 hours whereas the half-life of 25-OH D is about 2–3 weeks.<sup>[3]</sup>

Subclinical VD deficiency and inadequacy affect a large proportion of men and women in all age groups in many geographical regions. This is the result of inadequate dietary supplementation, which involves a small amount of calcium consumption with limited sunlight exposure. Adequate solar exposure to avoid VD deficiency and the consumption of foods containing VD are prudent. Despite all precautions, VD deficiency leads to major health problems in many countries, especially in the elderly.<sup>[4]</sup>

Until the early 1980s, VD was only engaged in research on calcium, phosphorus, bone mineralization, while studies conducted over the last 20–25 years have shown that they function outside of bone metabolism. Today, VD is known to be necessary for optimal health and it is reported that it prevents the development of many diseases such as inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, diabetes, various types of cancer, heart diseases, osteoporosis, infectious diseases.<sup>[5,6]</sup>

Despite uncertainty about the VD ideal level, many studies have shown that VD inadequacy is widespread worldwide, especially in winter.<sup>[4]</sup> In addition, in studies it has been shown that VD deficiency is not only seen in the risk group but also in the Middle East and Asian countries.<sup>[7]</sup> Indeed, the VDR levels were investigated in several studies conducted in Turkey.<sup>[8,9]</sup> Serum 25OHD3 levels are generally regarded as a determinant of the VD status. But there is no consensus on what level of qualification will be accepted.<sup>[10-12]</sup> Conditions in which the 25OHD3 level measured in serum is <20ng/mL (50 nmol/L) is defined as VD deficiency by many experts. Up to 30–40ng/mL 25OHD3 levels have an inverse relationship with PTH levels. In the light of recent data, serum iPTH levels are considered to rise significantly when serum 25OHD3 level is 30ng/mL (or 75nmol/L).<sup>[13]</sup> Based on this data, levels of 21–29ng/mL (50–75nmol/L) 25OHD3 are considered to be relative VD deficiency.

This study was conducted to determine the frequency of VD deficiency and to investigate whether there is a significant difference between sociodemographic and clinical characteristics of patients and 25-OH VD levels by examining 25-OH VD levels in patients 18 years and older admitted to our internal medicine clinic.

## Methods

In this retrospective study, patients who were hospitalized in the Internal Medicine Clinic of Haydarpaşa Numune Education and Research Hospital between May and June 2014 and whose VD levels were measured were retrospec-

tively examined through the hospital information system. In addition, a control group of healthy volunteers with VD levels was formed. Those under 18 years of age and using VD preparations were excluded from the study. Forty-nine patients with type 2 diabetes mellitus and 96 non-diabetic patients were included in the study. A control group of 51 healthy individuals was formed. Serum VD levels of all patients were assessed by High Performance Liquid Chromatography (HPLC) method in our hospital's central laboratory by transferring fasting blood within 24 hours after admission. Blood samples measured within 3 hours. Routine biochemical, bacteriological examinations, microalbuminuria/creatinine in spot urine, protein / creatinine ratio and HbA1c were recorded in diabetic patients. The GFR was calculated as 6 ml MDRD/ml/min/1.73m<sup>2</sup>. ECG, telegraphy, echocardiography, abdomen ultrasonography examination, ophthalmic examination, cardiologic and neurological evaluations with advanced radiological examinations if necessary. Hypertension, acute renal failure, chronic renal failure, malignancy, autoimmune diseases, coronary artery disease, heart failure, sepsis, cirrhosis were recorded.

## Results

A total of 145 patients and 51 healthy controls were included in the study.

When the study group was classified according to the level of VD, severe deficiency in 76 cases, deficiency in 55 cases, failure in 14 cases were detected (Table 1). There were no patients with normal VD levels. When control group was classified according to VD level in 51 healthy volunteers, VD deficiency was detected in 24 volunteers and severe deficiency was detected in 13 volunteers. VD failure was determined in 12 volunteers. In 2 cases, VD levels was within the normal range (Table 2).

Comparison of vitamin D levels between patients according to comorbid status and control group has shown in Table 3.

**Table 1.** Classification of the study group based on Vitamin D levels

Vitamin D level (ng/ml)	Mean±SD (Range)	Number of cases
<10	6.53±2.29 (0–10)	76
10–20	13.68±2.79 (10.30–19.70)	55
20–30	23.15±2.08 (20.10–27.20)	14
>30	-	-

The group with Vitamin D levels <10 ng/ml has 76 cases with a mean level of 6.53±2.29 ng/ml; The group with Vitamin D levels between 10–20 ng/ml has 55 cases with a mean level of 13.68±2.79 ng/ml; The group with Vitamin D levels between 20–30 ng/ml has 14 cases with a mean level of 23.15±2.08 ng/ml.

**Table 2.** Classification of the control group based on Vitamin D levels

Vitamin D level (ng/ml)	Mean±SD (Range)	Number of cases
<10	8.57±1.10 (7.02–9.90)	13
10–20	14.22±2.87 (10–19.80)	24
20–30	23.22±2.32 (20.20–26.80)	12
>30	34.95, 38	2

The group with Vitamin D levels <10 ng/ml has 13 cases with a mean level of 8.57±1.10 ng/ml; The group with Vitamin D levels between 10–20 ng/ml has 24 cases with a mean level of 14.22±2.87 ng/ml; The group with Vitamin D levels between 20–30 ng/ml has 12 cases with a mean level of 23.22±2.32 ng/ml; The group with Vitamin D levels >30 ng/ml includes 2 cases with levels of 34.95 and 38 ng/ml.

**Table 3.** Comparison of patients' Vitamin D levels by comorbid conditions with the control group Vitamin D levels

Comorbid conditions	Vitamin D level (ng/ml)	p
Hypertension	12.11±5.96 (4.36–26.70)	0.024
Type 2 Diabetes Mellitus (DM)	9.60±4.87 (0–20.80)	<0.001
Malignancy	8.88±5.32 (0–23)	<0.001
Heart failure	9.73±5.04 (3.70–22.90)	<0.001
Coronary artery disease	11.13±5.93 (2.79–24.10)	0.009
Chronic Obstructive Pulmonary Disease (COPD)	10.70±6.28 (4.36–22.90)	0.019
Acute kidney disease	8.04±4.85 (0–20)	<0.001
Chronic kidney disease	12.03±5.73 (3.79–27.20)	0.010
Sepsis	9.95±6.73 (0–27.20)	0.002
Cirrhosis	8.10±2.75 (4.67–10.70)	0.021
Autoimmune diseases	10.99±6.99 (2.70–23.90)	0.034
Exitus (Death)	5.62±3.17 (2.06–11.70)	<0.001

Vitamin D (ng/ml): Mean vitamin D level ± standard deviation (range) for each group.

In multivariant logistic regression analysis, we found that being over 75 years of age, female gender and malignancy predicted vitamin deficiency.

Of the diabetic patients, VD deficiency was detected in 47 (96%) and VD failure was detected in 2 (4%). Severe VD deficiency was detected in 28 (57.1%) patients. Of the non-diabetic patients, VD failure was found in 12 (12.5%) patients, VD deficiency was in 84 (87.5%) patients and severe VD deficiency was in 48 (50%) patients (Table 5). Also, the VD levels of diabetic and non-diabetic patients were statistically lower than the control group ( $p<0.001$ ,  $p=0.003$ ). However, when the VD levels of diabetic and non-diabetic patients were compared, VD levels of diabetic patients were found to be lower than non-diabetic patients, but not statistically significant (Table 4).

VD levels between diabetic, non diabetic female patients and healthy female volunteers were statistically different ( $p<0.001$ ,  $p=0.001$ ). When VD levels of diabetic and nondiabetic female patients were compared, no statistically significant difference was found ( $p=0.216$ ).

A statistically significant difference was found VD levels between diabetic, non diabetic male and healthy man control group ( $p<0.001$ ,  $p=0.038$ ). VD levels of diabetic and nondiabetic male patients were compared, no statistically significant difference was found ( $p=0.143$ ). There was no significant different VD levels between diabetic and non-diabetic patients according to sepsis, infection, intensive care need and exitus (death) status. A significant difference was found in the comparison of vitamin D levels in diabetic and non-diabetic patient groups with the healthy control group in terms of sepsis, infection, need for intensive care and death (Table 6).

**Table 4.** Demographic characteristics of the study groups

Demographic characteristic	Diabetic patient group (n=49)	Non-diabetic patient group (n=96)	Healthy control group (n=51)	p
Gender (M/F)	25/24	47/49	18/33	p1=0.164 p2=0.100 p3=0.957
Age (years)	66.37±14.39 (36–92)	59.60±21.00 (18–91)	37.45±13.14 (19–71)	p1=0.002 p2<0.001 p3=0.017
Vitamin D (ng/ml)	9.60±4.87 (0–20.80)	11.48±6.15 (1.60–27.20)	15.78±7.09 (7–38)	p1<0.001 p2=0.003 p3=0.064

Gender (M/F): The number of males/females in each group; Age (years): Mean age ± standard deviation (range) for each group; Vitamin D (ng/ml): Mean vitamin D level±standard deviation (range) for each group. p1: Comparison of diabetic patient group with healthy control group; p2: Comparison of non-diabetic patient group with healthy control group; p3: Comparison of diabetic patient group with non-diabetic patient group.

**Table 5.** Classification of Vitamin D levels in diabetic patients, non-diabetic patients, and healthy control groups

Vitamin D Level (ng/ml)	Diabetic Patient Group (n=49)	Non-Diabetic Patient Group (n=96)	Healthy Control Group (n=51)
<10	6.20±2.59 (0–10) (28 cases)	6.72±2.10 (1.60–9.90) (48 cases)	8.57±1.10 (7.02–9.90) (13 cases)
10–20	13.46±2.53 (10.30–19.60) (19 cases)	13.80±2.95 (10.40–19.70) (36 cases)	14.22±2.87 (10–19.80) (24 cases)
20–30	20.10, 20.80 (2 cases)	23.60±1.88 (20.70–27.20) (12 cases)	23.22±2.32 (20.20–26.80) (12 cases)
>30	- -	- -	34.95, 38 (2 cases)

Vitamin D Levels (ng/ml): Mean vitamin D level±standard deviation (range) for each group; Number of Cases: Number of individuals in each vitamin D level category.

**Table 6.** Comparison of Vitamin D levels in diabetic and non-diabetic patient groups according to sepsis, infection, intensive care need, and exitus compared to the healthy control group

	Vitamin D level (ng/ml)	p
Diabetic patient group		
Sepsis (n=9)	9.65±7.30 (0–20)	p=0.021
Infection (n=31)	9.01±5.09 (0–20.80)	p<0.001
Intensive Care Need (n=13)	10.90±5.66 (3.70–20.80)	p=0.025
Exitus (n=5)	5.23±3.10 (2.79–10.60)	p=0.002
Non-diabetic patient group		
Sepsis (n=11)	10.19±6.59 (4–27.20)	p=0.020
Infection (n=45)	10.80±6.66 (1.60–27.20)	p=0.001
Intensive Care Need (n=17)	10.98±7.57 (2.06–27.20)	p=0.020
Exitus (n=7)	5.88±3.43 (2.06–11.70)	p=0.001
Healthy control group (n=51)	15.78±7.09 (7–38)	

Vitamin D Level (ng/ml): Mean vitamin D level ± standard deviation (range) for each condition; P-Value: Statistical significance of the difference in vitamin D levels between the specified condition and the healthy control group.

## Discussion

In our study, we found VD deficiency or failure in all hospitalized patients at the Internal Medicine Department. VD levels of the study group were significantly lower than control group. This suggests that VD deficiency and failure in our country is a common problem that concerns all of our society and it is a more obvious problem in patients who need to be hospitalized. The VD levels of patients with heart failure, hypertension, type 2 DM, malignancy, coronary artery disease, acute renal disease, chronic kidney disease, sepsis, cirrhosis, autoimmune disease, exitus were significantly lower than those of healthy control group. Our results were consistent with other studies in the literature.<sup>[14–18]</sup>

In our study, VD levels of male and female patients with diabetes mellitus were lower than men and women without

diabetes mellitus. The presence of diabetes independently of gender appears to be a factor predicting VD deficiency.<sup>[19,20]</sup> VD has an immunomodulator effect, and there are also several studies in which deficiency may be a predisposing factor for type-2 DM.<sup>[21–23]</sup>

Studies in the literature indicate that VD is associated with cardiovascular disease, neuropathy, liver fatigue, and diabetic nephropathy in DM patients.<sup>[24–27]</sup> In our study, VD deficiency was found in 47 (96%) and VD failure was found in 2 (4%), with severe VD deficiency in 28 (57.1%) of the diabetic cases. VD failure was detected in 12 (12.5%), VD deficiency in 84 (87.5%) and severe VD deficiency in 48 (50%) of the non-diabetic cases.

The VD levels of diabetic and non-diabetic patient groups were significantly lower than the VD levels of the healthy control group. This indicated that VD deficiency and fail-

ure were a common problem in the community. According to our results; the VD levels of female patients in the non-diabetic patient group are significantly lower than the VD levels of the male patients, and this gender difference is almost absent in the presence of diabetes. Patients who were found to have deficiency and failure were replenished with the recommendations of the Turkish Endocrine Society.

## Conclusion

VD deficiency and failure are common problems threatening healthy adults in our country, and VD levels are significantly lower in hospitalized patients. This seems to be related to many comorbid diseases. There is a need for more controlled work in this area. It has been shown in advanced age, malignancy, and female gender predisposition to VD deficit regardless of other factors. VD deficiency is a widespread problem in both diabetic and nondiabetic patients, and there is a need for wider, controlled studies to fully demonstrate the clinical outcome of this condition. In the clinic, the patient's risk factors should be assessed, appropriate replacement must be done, patients should be informed about the necessity of sun exposure and nutrition.

## Disclosures

**Ethics Committee Approval:** This retrospective study was carried out in Haydarpaşa Numune Training and Research Hospital Internal Medicine clinic between May and June 2014.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – N.İ., F.M.T.; Design – N.İ., F.M.T.; Supervision – F.M.T.; Materials – N.İ., S.B.; Data collection and processing – N.İ., S.B.; Analysis and interpretation – N.İ., S.B.; Literature search – N.İ.; Writing – N.İ.; Critical Review – N.İ., F.M.T.

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