

## Research Article

# Assessment of Relationship Between Serum Vitamin D Levels and Metabolic Syndrome Components in Hemodialysis Patients

Sevil Karahan Yılmaz<sup>1\*</sup> , Cuma Mertoğlu<sup>2</sup> , Aylin Ayaz<sup>3</sup> **Abstract**

**Aim:** This study is aimed to evaluate the relationship between serum vitamin D levels and metabolic syndrome in hemodialysis patients.

**Materials and Methods:** This study was conducted with participation of 80 patients undergoing hemodialysis for more than 6 months three times a week, aged > 18 years. Their height, dry weight, waist circumference were measured. Biochemical parameters such as serum 25-hydroxyvitamin D, lipid profile, and fasting blood glucose were analyzed. Metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III criteria. Severe vitamin D deficiency, 25 (OH) vitamin D < 5 ng/ml; mild vitamin D deficiency, 25 (OH) vitamin D 5-15 ng/ml; vitamin D insufficiency, 25 (OH) vitamin D 16-30 ng/ml, and vitamin D sufficiency, 25 (OH) vitamin D > 30 ng/ml were categorized. Statistical analysis of the data was performed with the use of SPSS version 21.0.

**Results:** 48.4% of hemodialysis patients were identified to have metabolic syndrome. According to the serum levels of vitamin D; 35.0% of patients had severe vitamin D deficiency, 37.4% of patients had mild vitamin D deficiency, 18.8% of patients had vitamin D insufficiency and 8.8% of patients had vitamin D sufficiency (> 30 ng/ml). Vitamin D insufficiency was significantly associated with metabolic syndrome and central obesity.

**Conclusions:** Deficiency/insufficiency is observed in serum 25-hydroxyvitamin D levels in hemodialysis patients. Vitamin D insufficiency is associated with metabolic syndrome.

**Keywords**

Hemodialysis; 25-Hydroxyvitamin D; Metabolic Syndrome

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## Problem statement and analysis of the latest research

Metabolic syndrome is defined as a set of risk factors that include insulin resistance, hypertension, high triglyceride levels, lower high-density lipoprotein cholesterol levels, and obesity (particularly central adiposity) [1]. Metabolic syndrome has risk factors for cardiovascular diseases, type 2 diabetes, and progression of hepatic and renal disorders [2].

Vitamin D is a steroid-derived hormone that is obtained from 7-dehydrocholesterol with ultraviolet light in the skin. Approximately 95% of vitamin D is synthesized in the skin under the influence of sunlight exposure [3]. Non-classical

effects of vitamin D are grouped under 3 main headings: regulation of hormone secretion, immune function, and proliferation and differentiation of the cell. Active vitamin D plays an important role in maintaining normal bone mineral homeostasis and insulin secretion [4]. Vitamin D intake and serum 25-hydroxyvitamin D (25 (OH) D) levels are associated with obesity, metabolic syndrome, insulin resistance, diabetes, hypertension, cardiovascular diseases, polycystic ovary syndrome, fatty liver disease, and chronic renal failure [5].

Vitamin D deficiency is a worldwide public health problem, it increases the risk of metabolic syndrome [6]. Vitamin D deficiency plays a key role in the pathophysiology of risk factors of metabolic syndrome which affects the cardio-

vascular system, increases insulin resistance and obesity, stimulates the renin-angiotensin-aldosterone system that causes hypertension. The discovery of vitamin D receptor expressed ubiquitously in almost all body cells such as immune, vascular and myocardial cells, pancreatic beta cells, neurons, and osteoblasts suggests involvement of vitamin D mediated effects on metabolic syndrome. Moreover, vitamin D deficiency as well as cardiovascular diseases and related risk factors, frequently co-occur. This underlines the importance of understanding the role of vitamin D in the context of metabolic syndrome [7]. A decrease in serum 25 (OH) D vitamin level in hemodialysis is known [8] and the study that shows the relationship between vitamin D levels and metabolic syndrome is linked in a recent study only [9–11].

**Objective:** We aimed at the assessment of the relationship between serum vitamin D levels and metabolic syndrome components in hemodialysis patients.

## Materials and Methods

This study was performed with the participation of 80 patients between September 2017-December 2017; patients have been undergoing hemodialysis in the dialysis unit of Erzincan Mengücek Gazi Education and Research Hospital for at least 6 months three times a week, and their mean age was  $56.27 \pm 15.80$  years. Patients were excluded if they had acute or chronic inflammation/infection, liver failure, and cancer. All patients received Vitamin D supplements (treatment of secondary hyperparathyroidism) and phosphorus binding agent, included in the study.

A questionnaire technique was used to collect data regarding patients' general information, medical history, and physical activity. Their height, dry weight, and waist circumference were measured. Dry weight measurements were conducted at the end of hemodialysis. Their body mass index (BMI) was calculated by dividing their body weight by the square meter of height [12]. Doing or not doing regular sports/exercise, sport/exercise type, frequency, and duration were investigated for physical activity status.

The blood samples were collected in advance of the hemodialysis. Biochemical parameters as serum 25 (OH) D, lipid profile, fasting blood glucose (FPG), phosphorus (P), albumin, hemoglobin, parathyroid hormone (PTH), and C-reactive protein (CRP) were extracted from patient files. 25 (OH) D and parathyroid hormone were analyzed in Siemens Advia-Centaur XP using a chemiluminescent immunometric assay method [13]; lipid profile, FBG, calcium (Ca), P, and albumin were analyzed in a Beckman Coulter with model number AU640 using a photometric method [14]. C-reactive protein was analyzed in Siemens Bn II using the nephelometer method [15].

The metabolic syndrome status was defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III). According to NCEP-ATP III guidelines, metabolic syndrome was diagnosed with abdominal obesity (waist circumference > 102 cm for men or > 88 cm for

women), fasting triglyceride levels  $\geq 150$  mg/dl, reduced high-density lipoprotein cholesterol (HDL-C < 50 mg/dl for women or < 40 mg/dl for men), blood pressure of systolic  $\geq 130$  mmHg and diastolic ones  $\geq 85$  mmHg, fasting blood glucose  $\geq 100$  mg/dl as three or more out of five factors to establish the diagnosis of metabolic syndrome [16].

Vitamin D status was evaluated by serum 25 (OH) vitamin D levels according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI). Severe vitamin D deficiency with 25 (OH) vitamin D < 5 ng/ml; mild vitamin D deficiency with 25 (OH) vitamin D 5-15 ng/ml; vitamin D insufficiency with 25 (OH) vitamin D 16-30 ng/ml and vitamin D sufficiency with 25 (OH) vitamin D > 30 ng/ml were categorized [17].

## Statistical analysis

Statistical analysis of the data was performed with the use of SPSS version 21.0 (SPSS Inc., Chicago, USA). Data are presented as mean  $\pm$  standard deviation (SD) for numeric variables and percentages for categorical variables. The "Mann-Whitney U Test" and "Kruskal Wallis H-Test" were used for group comparisons. The Pearson correlation analysis was used to find the relationship between two variables. To examine the relationship between vitamin D status and metabolic syndrome and metabolic syndrome components, multivariate logistic regression models were used. Results at 95% confidence interval, p values of < 0.05 were accepted as statistically significant [18].

## Results

The study included 51 (63.7%) male and 29 (36.3%) female hemodialysis patients whose average age was  $56.27 \pm 15.80$  years. Patients were on dialysis for a median of  $4.22 \pm 2.86$  years. According to NCEP-ATP III criteria, metabolic syndrome was identified in 48 (48.4%) patients. Age, duration of dialysis, anthropometric measurements, and biochemical parameter levels of hemodialysis patients with and without metabolic syndrome are represented in Table 1. A statistically significant difference was observed in dry weight, BMI, waist circumference, triglyceride, and HDL-C levels in hemodialysis patients with and without metabolic syndrome ( $p < 0.05$ ). Dry weight, BMI, waist circumference, serum triglycerides were significantly higher and HDL-C levels were lower in patients with metabolic syndrome than in other groups.

According to physical activity status, 30.7% of patients performed regular sports/exercise, it was seen that it takes > 30 minutes/day and 3 days/week in patients who do regular sports/exercise.

Serum 25 (OH) vitamin D levels were evaluated according to National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI); 35.0% of patients had severe vitamin D deficiency, 37.4% of patients had mild vitamin D deficiency, 18.8% of patients had vitamin D insufficiency and 8.8% of patients had vitamin D sufficiency (> 30 ng/ml),

**Table 1.** Anthropometric measurements and biochemical parameter levels of hemodialysis patient with and without metabolic syndrome.

Parameters	Metabolic syndrome(+) 39 (49%)	Metabolic syndrome(-) 41 (51%)	p-value
Age (year)	55.92±13.99	56.61±17.51	0.413
Duration of dialysis (year)	3.76±2.68	4.67±2.98	0.151
Dry weight (kg)	76.34±13.12	63.30±12.82	<0.001*
Body mass index (kg/m <sup>2</sup> )			
Male	26.32±3.31	23.76±3.81	0.009*
Female	30.38±5.70	21.77±3.68	0.010*
Waist circumference (cm)			
Male	100.35±8.64	91.90±9.78	0.001*
Female	100.89±12.18	81.50±13.04	0.002*
Systolic blood pressure(mmHg)	127.94±27.35	122.68±23.56	0.300
Diastolic blood pressure (mmHg)	73.74±20.03	69.51±10.23	0.230
Fasting plasma glucose (mg/dL)	133.73±58.24	115.14±85.43	0.300
Cholesterol (mg/dL)	183.00±40.56	166.36±43.10	0.052
Triglycerides (mg/dL)	231.67±103.06	159.97±120.50	<0.001*
Low density lipoprotein cholesterol (mg/dL)	106.14±35.61	93.73±32.36	0.103
High density lipoprotein cholesterol (mg/dL)	33.78±6.76	38.67±9.76	0.042*
Uric acid (mg/dL)	6.44±1.34	6.07±1.89	0.310
Albumin (mg/dL)	3.95±1.02	3.95±0.85	0.999
Phosphoros (mmol/L)	4.91±1.15	5.19±1.42	0.334
25(OH)D (nmol/L)	12.30±1.49	11.21±1.41	0.601
Hemoglobin (g/L)	11.86±1.27	11.77±2.01	0.487
Parathyroid hormone (pg/mL)	579.95±82.54	798.44±92.07	0.061
C-reactive protein (mg/dL)	11.75±2.85	10.40±1.92	0.703

Notes: \*p < 0.05, Mann-Whitney U Test.

serum 25 (OH) D as a deficiency (mean 11.74 ± 81.42 nmol) was determined. Anthropometric measurements and biochemical parameter levels of hemodialysis patients according to serum 25 (OH) D level are represented in Table 2. There was no statistically significant difference in age, dialysis duration, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood glucose, cholesterol, triglycerides, HDL-C, low-density lipoprotein cholesterol (LDL-C), uric acid, PTH, and CRP levels (p > 0.05); only there was a significant difference in waist circumference (p < 0.05) in patients whose Vitamin D status was evaluated according to severe deficiency, mild deficiency, insufficiency and sufficiency. There was no significant relationship between serum 25 (OH) D level and waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood sugar, triglycerides, and HDL-C.

As shown in Table 3, vitamin D insufficiency was significantly associated with metabolic syndrome and central obesity. No associations between severe deficiency, mild deficiency, and insufficiency and raised triglycerides, reduced HDL-C, raised blood pressure, or raised fasting plasma glucose were identified.

## Discussion

In the study which planned to evaluate the relationship between serum 25 (OH) D and metabolic syndrome components in hemodialysis patients, metabolic syndrome was identified in 48 (48.4 %) patients. In a study of hemodialysis patients, metabolic syndrome was identified in 61 (56.5%) of patients according to NCEP-ATP III criteria [19]. In another study, according to the International Diabetes Federation (IDF) criteria for metabolic syndrome, 241 (38.2%) hemodialysis patients had metabolic syndrome [20]. There were 115 hemodialysis patients evaluated by NCEP-ATP III and the International Diabetes Federation (IDF) criteria; metabolic syndrome was identified according to NCEP-ATP III 41.7 % and IDF 42.6% [21]. Metabolic syndrome was 50.0% in 100 hemodialysis patients according to NCEP-ATP III criteria [22]. Vogt and others identified metabolic syndrome in 98 (74.5%) patients according to IDF criteria [23]. In another study, according to NCEP-ATP III 80 (24.7%) hemodialysis patients had metabolic syndrome [24]. Ahmadi and others performed a study with the participation of 145 hemodialysis patients, and provided that metabolic syndrome was identified according to IDF criteria 53.1 % [9]. In 143 hemodialysis patients, metabolic syndrome was identified according to IDF criteria 45.5% [10]. In another study, according to IDF cri-

**Table 2.** Anthropometric measurements and biochemical parameter levels of hemodialysis patients according to serum 25 (OH) D level.

Parameters	Vitamin D status				p-value
	Severe deficiency 28(35%)	Deficiency 30(38%)	Insufficiency 15(19%)	Sufficiency 7(8%)	
Age (year)	54.64±15.61	56.43±15.83	58.13±17.10	58.14±16.44	0.965
Duration dialysis (year)	4.67±2.65	4.41±2.60	3.38±0.92	3.42±1.18	0.107
Body mass index (kg/m <sup>2</sup> )	24.87±3.87	25.12±6.15	24.56±5.82	24.16±6.78	0.809
Waist circumference (cm)	94.75±10.43	92.43±15.52	96.34±18.42	93.36±14.70	0.006*
Systolic blood pressure (mmHg)	124.35±31.10	117.56±18.78	124.46±24.56	116.62±25.13	0.844
Diastolic blood pressure (mmHg)	69.34±9.91	71.23±9.54	73.01±14.13	70.12±10.89	0.847
Fasting plasma glucose (mg/dL)	117.89±57.96	104.09±36.12	120.55±64.56	117.12±59.73	0.920
Cholesterol (mg/dL)	159.86±32.67	175.18±44.12	182.45±58.80	183.89±74.32	0.154
Triglycerides (mg/dL)	159.30±81.33	154.29±58.54	194.77±111.34	188.09±113.93	0.425
High density lipoprotein cholesterol (mg/dL)	37.24±9.55	36.18±10.29	37.24±9.21	38.39±14.10	0.444
Low density lipoprotein cholesterol (mg/dL)	95.98±24.06	109.78±34.13	107.67±69.18	102.68±36.64	0.225
Uric acid (mg/dL)	5.81±1.27	6.58±2.49	6.25±1.35	6.20±0.66	0.734
Parathyroid hormone (pg/mL)	843.70±484.56	727.58±614.66	707.98±707.89	157.64±71.25	0.299
C-reactive protein (mg/dL)	17.96±14.70	23.11±18.87	12.58±10.29	15.24±12.72	0.582

Notes: p > 0.05, Kruskal Wallis Test.

**Table 3.** Association of vitamin D status with the metabolic syndrome and components of the metabolic syndrome among the hemodialysis patients.

	Vitamin D status					
	Severe deficiency		Mild deficiency		Insufficiency	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
	Adjusted for age and sex					
Metabolic syndrome	2.70 (1.02-9.36)	0.300	2.41 (0.5-9.96)	0.921	3.34 (1.20-8.60)	0.030*
Central obesity	0.65 (0.39-1.28)	0.816	0.72 (0.50-1.49)	0.218	0.98 (0.65-1.78)	0.002*
Raised triglycerides	1.54 (1.36-1.80)	0.148	1.45 (0.95-2.21)	0.090	1.53 (1.15-2.48)	0.876
Reduced high-density lipoprotein cholesterol	0.85 (0.63-1.80)	0.645	1.05 (0.84-2.12)	0.432	0.93 (0.61-1.98)	0.149
Raised blood pressure	1.57 (0.20-1.71)	0.078	0.95 (0.23-2.38)	0.110	1.51 (1.30-1.88)	0.315
Raised fasting plasma glucose	1.13 (0.56-2.05)	0.322	1.22 (0.76-2.49)	0.087	0.92 (0.58-2.23)	0.675

Notes: In all models, vitamin D sufficiency was designated as the reference category (odds ratio = 1.00).

teria, 90 (25.3%) hemodialysis patients had metabolic syndrome [11]. In studies, the prevalence of metabolic syndrome in hemodialysis patients varies according to the diagnostic criteria for metabolic syndrome and the number of patients [9–11, 19–23]. It appears, that the prevalence of metabolic syndrome among patients on hemodialysis was nearly half in different studies [9, 10, 21, 22] and metabolic syndrome identified in this study (48.4%), were similar.

A recent meta-analysis showed that different components in the metabolic syndrome negatively affect the kidney in different proportions in terms of proteinuria, and it showed their effect in descending order to be hypertension, hypertriglyceridemia, low HDL-C, abdominal obesity, and impaired glucose intolerance [25]. Also supporting studies made

in [9, 10, 21, 24, 26], dry weight, BMI, waist circumference, serum triglycerides were significantly higher and HDL-C levels were lower in patients with metabolic syndrome than other groups. As in this study, BMI is also high in patients with metabolic syndrome (p < 0.05), is an independent predictor of metabolic syndrome in hemodialysis patients without diabetes and dyslipidemia [9, 15, 22, 24, 27]. These discrepancies in the results of different studies could be attributed to the different populations and healthcare settings between these studies and the current study.

Vitamin D deficiency is a worldwide public health problem seen in hemodialysis patients. In this study, according to the serum levels of vitamin D 35.0% of patients had severe vitamin D deficiency, 37.4% of patients had mild vitamin D



deficiency, 18.8% of patients had vitamin D insufficiency and 8.8% of patients had vitamin D sufficiency ( $> 30$  ng/ml), serum 25 (OH) D as a deficiency (mean  $11.74 \pm 81.42$  nmol) was determined and vitamin D deficiency/insufficiency is found in near almost all of the patients (91.2%). To determine the vitamin D deficiency in hemodialysis patients in another study performed with the participation of 187 patients, mean serum 25 (OH) D level was  $11.7 \pm 7.5$  ng/ml; just sufficiency in 4%, deficiency in 73%, insufficiency in 23% of patients was found [8]. In a study with the participation of 47 patients to determine serum vitamin D level in hemodialysis patients, deficiency in 72.4% of patients, insufficiency in 23.4% of patients, and sufficiency in 4.3% of patients were identified [28]. In a study with the participation of 145 patients, mean serum vitamin D levels of  $24.7 \pm 16.1$  ng/ml, severe deficiency in 3.4% of patients, deficiency in 31% of patients, insufficiency in 36.6% of patients, and sufficiency in 29% of patients were found [9]. Pinghua and others found that according to the levels of 25 (OH) D<sub>3</sub>, patients were included into sufficient group 33 (23.1%), insufficient group 69 (48.2%), and deficient group 41 (28.7%) [10]. Kara and others showed that patients with serum 25 (OH) D levels  $< 20$  ng/ml, were classified as those having a vitamin D deficiency 83 (64.3%) and those with serum 25 (OH) D levels  $\geq 20$  ng/ml were classified as having normal vitamin D levels 46 (35.7%). The mean serum 25 (OH) D levels were  $11.13 \pm 3.60$  ng/ml in the deficient group and  $27.04 \pm 7.20$  ng/ml in the normal group [29]. The results of this study are in line with the results of studies on this issue [8].

Although it is known that vitamin D deficiency increases the risk of metabolic syndrome [6], low serum vitamin D levels in were found to be associated with the metabolic syndrome in studies [9, 10], but another study concluded that there is a lack of association between serum 25 (OH) vitamin D concentrations and metabolic syndrome in hemodialysis patients [11]. There was a relationship between vitamin D deficiency and components of metabolic syndrome as central obesity and fasting blood glucose [9]. Low 25 (OH) D<sub>3</sub> level negatively correlated with abnormal metabolic factors central obesity, raised TG, reduced HDL-C, raised SBP, and raised FBG [10]. In another study, both vitamin D mild deficiency and insufficiency were found to be significantly associated with central obesity [11]. In this study, vitamin D levels in hemodialysis patients were deficiency/insufficiency and vitamin D insufficiency was significantly associated with metabolic syndrome and central obesity.

Vitamin D deficiency is lower in obese individuals due to insufficient intake of vitamin D, dressing more closed than normal-weight individuals, and due to less outdoor physical activity, and because of their high fat mass, vitamin D storage rate and consequently decrease in bioavailability, obese individuals are in subcutaneous adipose tissue. The levels of 25-hydroxylase and 1-alpha hydroxylase, which are the enzymes that activate vitamin D, are considered to be decreased. In addition, vitamin D deficiency in obese individuals can

support lipogenesis and weight gain [30].

## Conclusions

An increase was seen in BMI, waist circumference, triglyceride, and HDL levels which components of the metabolic syndrome in hemodialysis patients. Deficiency/insufficiency of serum vitamin D levels was in hemodialysis patients, and vitamin D insufficiency was significantly associated with metabolic syndrome and central obesity. Appropriate nutrition programs to patients should be prepared for hemodialysis patients to achieve their ideal weight and to control which is a component of metabolic syndrome, blood sugar, and triglyceride levels and follow-up should be done regularly. The physician gave vitamin D supplements to patients who diagnosed deficiency/insufficiency of vitamin D in hemodialysis patients, overcoming deficiency/insufficiency of vitamin D. Sun exposure is the most important determinant of vitamin D in hemodialysis patients. Seasonal variation is an important parameter affecting sun exposure. Peak vitamin D levels are in autumn or the end of summer and the lowest levels are in spring or the end of winter. Sun exposure level is also important. Sun exposure time  $> 6$  hours/week or active physical activity  $> 30$  min/day and 3 days/week may have a positive impact on both their vitamin D levels and the metabolic syndrome.

## Prospects of Further Researches

The limitations of this study, small sample and to conduct this study in a single-center, unfavorable evaluation of sun exposure conditions are the shortcomings of this investigation. Long-term randomized controlled trials are needed to determine the relationship between metabolic syndrome components and vitamin D levels.

## Ethical Statement

All procedures were performed in studies involving human participants, were conducted in accordance with the ethical standards of the Institutional Research Committee (Erzincan University Ethics Committee approved this study on the 14 September, 2015, the number of 09/13) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Informed Consent

Informed consent form was obtained from the subjects before the study.

## Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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