Research Article

The relation between Vitamin D and obesity in hemodialysis patients at Minia University Hospital.

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Abstract

Background: Vitamin D deficiency has a critically important role in the pathophysiology of metabolic syndrome, which complicates the cardiovascular system, increases insulin resistance and obesity, and cause hypertension. Also, vitamin D deficiency, as well as ischemic heart diseases and related risk factors, frequently co-occur. Aim of the work: to identify the relationship between serum concentrations of vitamin D and metabolic syndrome and in hemodialysis patients and compare between metabolic and nonmetabolic patient. Patients and methods: This study was carried out in the hemodialysis unit of Minia University Hospital from May 2016 to May 2018. One hundred eighty patients on hemodialysis were included in this study. Results: The prevalence of vitamin D insufficiency and mild deficiency in hemodialysis patients enrolled in this study was 21.1% and 78.8% respectively. Patients with vitamin D deficiency were significantly associated with central obesity (waist circumference ≥90 cm in both sexes or BMI > 30 kg/m2). Conclusion: There is a significant relation between serum 25(OH) vitamin D concentrations and central obesity in hemodialysis patients.

Keywords: Vitamin D; metabolic syndrome; hemodialysis patients

Introduction

Metabolic syndrome is an assemblage of interconnected metabolic risk factors that are present together far more frequently than what is expected by chance alone.^[1]

The co-occurrence of central obesity, insulin resistance, raised blood pressure, and dyslipidemia places an individual at higher risk for type 2 diabetes, coronary artery disease, cerebrovascular disease, chronic kidney disease, and cognitive decline. [2]

1, 25-Dihydroxy vitamin D is a steroid-derived hormone, and through binding its omnipresent nuclear receptors is involved in the regulation of more than 200 genes in humans.^[3]

Accumulating evidence suggests that vitamin D plays a pivotal role in cardiovascular health, and its deficiency is associated with cardiovascular diseases. [4]

Vitamin D supplementation has been shown to confer benefits against cardiovascular mortality, in particular in the group of patients with a positive history for vitamin D deficiency.^[5]

Based on community-level epidemiological studies and also clinical studies on patient groups, low levels of vitamin D have been implicated in the pathogenesis of metabolic syndrome and its components. [6] In patients with end-stage renal disease (ESRD) undergoing hemodialysis, vitamin D deficiency is highly prevalent.

Patients and Methods Patients:

This cross-sectional study was conducted from May 2016 to May 2018 in the hemodialysis unit of Minia University Hospital. One hundred eighty patients on regular dialysis were included in this study. We obtained Informed consent from all patients in this study. All procedures dealing with human subjects were conducted in keeping with the ethical guidelines laid down by the latest revision of the Helsinki declaration.

Assessment:

Before a dialysis session, detailed medical history was obtained and recorded in predesigned questionnaires. After a dialysis session and with only light clothing allowed, weight was measured using a digital scale and was recorded with 0.1 kg precision. Without shoes on, height was measured using a wall-mounted stadiometer and was recorded to the nearest 0.1 cm. The Ouetelet formula measured body mass index (BMI) as weight in kilograms divided by height in meter squared. Using an inflexible tape and at the end of normal expiration, waist circumference was measured midline between the inferior costal margin and the anterior superior iliac crest and was recorded to the nearest 0.1 cm. The blood pressure was measured when the patients were seated and adequately prepared and positioned with the arm extended along the body. The arm chosen for the measurement was the one contralateral to the HD vascular access (i.e., the arteriovenous fistula).

We were using a proper sized adult cuff attached to a standard sphygmomanometer. Three blood pressure readings were obtained before, during, and after dialysis. The readings were then averaged.

To obtain an accurate BP measurement, the following steps were performed: (1) the arm circumference was obtained and the cuff was adjusted; (2) the cuff was placed 2-3 cm above the cubital fossa, leaving no gaps; (3) the cuff was placed over the brachial artery; (4) the systolic pressure level was estimated by palpating the radial pulse; (5) the brachial artery was palpated in the cubital fossa and the stethoscope's bell or diaphragm was placed without applying too much pressure; (6) the cuff was inflated until the pressure is 20-30mm Hg higher than the estimated systolic pressure, obtained by palpation; (7) slow deflation was proceeded (at a speed of 2-3mmHg/s); (8) the systolic pressure was determined by auscultating the first sound (Korotkoff Phase I) and then the deflation speed was increased slightly; (9) the diastolic pressure was deter-mined when the sounds disappear (Korotkoff Phase V); (10) auscultation for approximately 20-30mm Hg after the last sound to confirm its disappearance and then fast and complete deflation has proceeded.

Laboratory evaluation:

Informed consent for the collection of 5 ml of blood for laboratory tests was obtained from all study.

5 ml of blood was withdrawn by sterile venipuncture after fasting for 12 hours, left to be clotted then centrifuged, and the separated serum was divided into aliquots.

One was designated for the immediate assessment of lipid profile [Serum concentrations of (triglycerides, HDL-c, LDL-c, and total cholesterol), FPG, albumin, calcium, and phosphorus.

The rest of the serum was stored at -20 c for subsequent assay of Serum 25(OH)-vitamin D and PTH.

Routine chemistry tests (lipid profile, FPG, albumin, calcium, and phosphorus) were assayed using fully automated clinical chemistry auto-analyzer system Konelab 2011 (Thermo electron incorporation, Finland).

Definitions:

The metabolic syndrome defined according to the criteria of the International Diabetes Federation (IDF). [7]

Patients are diagnosed with metabolic syndrome in the presence of central obesity (waist circumference ≥90 cm in both sexes or BMI > 30 kg/m2) plus at least two of the following four criteria:

- (1) Raised triglycerides (≥150 mg/dL) or treatment for this lipid abnormality.
- (2) Reduced HDL-c (<40 mg/dL in men and <50 mg/dL in women) or under medications for this dyslipidemia.
- (3) Elevated blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg) or treatment of previously diagnosed hypertension.
- (4) Raised FPG (FPG \geq 100 mg/dL) or previously diagnosed type 2 diabetes.

The following categories of vitamin D status are defined according to National Kidney Foundation Kidney Disease Outcome Quality Initiative guidelines: [Eknoyan G. et al. 2003]

- (1) Severe vitamin D deficiency, 25(OH) vitamin D < 5 ng/mL.
- (2) Mild vitamin D deficiency, 25(OH) vitamin D between 5 ng/mL and 15 ng/mL
- (3) Vitamin D insufficiency 25(OH) vitamin D between 16 ng/mL and 30 ng/mL.
- (4) Vitamin D sufficiency, 25(OH) vitamin D > 30 ng/mL.

Statistical Study

The data of our study were coded, tabulated, and statistically analyzed using the SPSS program (Statistical Package for Social Sciences) software version 20.

Descriptive statistics were done for numerical data by mean, standard deviation, and minimum & maximum of the range, while they were done for categorical data by number and percentage. Comparison between two means was made using the t-test. Correlation between non-parametric variables was done using Spearman's rho correlation test.

Multiple linear regression analysis was done for detection of the association between vitamin D status and components of the metabolic syndrome and metabolic syndrome as a single entity among the hemodialysis patients. The level of significance was taken at (P-value < 0.05).

Results

Table (1) the relations between metabolic and non-metabolic syndrome in hemodialysis patients in this study:

	Metabolic syndrome	Non metabolic syndrome	
	N=64	N=116	P value
Age	25.72	10.69	0.01*
Range	25-72	19-68	0.01*
Mean ± SD	52.1±12	44.6±14.5	
Sex	11(24.40/)	32(55.2%)	0.05
Male Female	11(34.4%)		0.03
	21(65.6%)	26(44.8%)	
Duration of dialysis (m)	9-192	6-360	0.2
Range Mean ± SD		86.5±69.8	0.2
	68.2±53.8	80.3±09.8	
Weight (kg)	47-110	40-101	0.0001*
Range			0.0001*
Mean ± SD	73±15.8	60.4±14.8	
Height (cm)	147.176	125 172	0.2
Range	147-176	135-173	0.3
Mean ± SD	158.2±8.1	156.3±9	
Body mass index	10.2.49.9	17.2.42.7	0.0001*
Range	19.3-48.8	17.3-43.7	0.0001*
Mean ± SD	29.1±6.2	24.5±4.8	1
Waist circumference	05.122	(7.122	0.0001*
Range	85-133	67-122	0.0001*
Mean ± SD	104.1±11.9	87.6±12.8	
SBP	00.150	00.100	0.014
Range	90-170	90-180	0.01*
Mean ± SD	137.8±20.4	125.6±23.1	
DBP			
Range	60-100	60-100	0.03*
Mean ± SD	84.3±10.4	78.9±12	
PTH (pg\ml)			
Range	113-1600	108-1779	0.4
Mean ± SD	776.7±485.5	853.2±517.9	
Vitamin D (ng\ml)			
Range	8-23	7-27	0.5
Mean ± SD	12.1±3.7	12.7±4.3	
FBS (mg\dL)			
Range	60-180	60-163	0.03*
Mean ± SD	87.4±31.7	76.7±15.5	
Total cholesterol			
(mg\dL)	125-306	91-257	0.005*
Range	199.4±46.8	173.9±35.6	
Mean ± SD			
Triglycerides (mg\dL)			
Range	90-343	48-279	0.0001*
Mean ± SD	177.2±61.9	122.2±47.7	
HDL-c (mg\dL)			
Range	28-47	29-49	0.0001*
Mean ± SD	36.2±6.2	41.5±5.8	
LDL-c (mg\dL)			
Range	53-239	33-194	0.02*
Mean ± SD	127.7±47.8	107.2±35.4	
Total calcium (mg\dL)			
Range	7.8-8.9	7.8-8.9	0.4
Mean ± SD	8.3±0.2	8.4±0.2	
Phosphorus (mg\dL)			
Range	4.8-7.6	4.3-8.5	0.3
Mean ± SD	6.1±0.7	6.2±0.8	
Albumin (g\dL)			
Range	3.1-4.4	3-4.2	0.9
Mean ± SD	3.6±0.3	3.6±0.3	

P-value calculated by t-test (p < 0.05) is considered to be significant.

When moving from the cases of vitamin D mild deficiency to vitamin insufficiency, HDL-c linearly increased (P-value for trend <0.05 by t-test).

There is a linearly decreasing trend in total cholesterol, but not reaching statistical significance (P-value = 0.07). Additionally, age, triglycerides, and LDL-c linearly decreased but

not reaching statistical significance (P-value = 0.1 in all tests).

For other variables examined; namely, diastolic blood pressure, BMI, FPG, systolic, and waist circumference, no linear increasing or decreasing patterns across categories of vitamin D were identified.

Table (2): correlation analysis between vitamin D level and demographics, clinical characteristics, and laboratory investigations of the hemodialysis patients enrolled in this study:

Variables	Vitamin D status		
	Insufficiency	Mild deficiency	
	(n=38)	(n= 142)	P value
	Mean ± SD	Mean ± SD	
Age	42.5±15.3	48.5±13.6	0.1
Waist circumference (cm)	93.1±11.9	93.6±15.5	0.8
BMI (kg\m²)	25.9±4.9	26.2±6	0.8
Cholesterol	168±34	187±42.6	0.07
Triglycerides	124.3±41.3	146.4±62.5	0.1
HDL	42.3±6.1	38.9±6.4	0.04*
LDL	101±34.4	118.1±42.3	0.1
FBS	85.6±27.3	79.2±21.8	0.2
SBP	134.7±25.4	128.7±22.1	0.3
DBP	83.1±14.1	80.2±11	0.3

Table (3): correlation analysis between vitamin D level and demographics, clinical characteristics, and laboratory investigations of the hemodialysis patients enrolled in this study:

	Vitamin D Pearson's rho	
	r	P value
Age	-0.17	0.1
Sex	0.18	0.09
Duration of dialysis (months)	0.02	0.8
Weight (kg)	0.04	0.7
Height (cm)	-0.004	0.9
Body mass index(kg\m2)	0.04	0.6
Waist circumference (cm)	0.02	0.7
Central obesity	0.08	0.4
Systolic blood pressure (mmHg)	0.1	0.3
Diastolic blood pressure (mmHg)	0.1	0.2
PTH (pg\ml)	0.08	0.4
FBS (mg\dL)	0.04	0.6
Total cholesterol (mg\dL)	-0.2	0.05
Triglycerides (mg\dL)	-0.18	0.08
HDL cholesterol (mg\dL)	0.24	0.01*
LDL cholesterol (mg\dL)	-0.18	0.08
Total calcium (mg\dL)	0.01	0.9
Phosphorus (mg\dL)	-0.03	0.7
Albumin (g\dL)	-0.13	0.2
Metabolic syndrome	-0.05	0.6

As shown in table 3, vitamin D level was positively correlated with HDL-c.

No significant correlation between vitamin D level and all these factors (age, sex, duration of dialysis, weight, height, BMI, waist circum-

ference, central obesity, systolic blood pressure, diastolic blood pressure, 25(OH) vitamin D, FBS, total cholesterol, LDL-c, total calcium, triglycerides, phosphorus and albumin).

Table (4): The association of vitamin D status with components of the metabolic syndrome among the hemodialysis patients enrolled in this study is explored using logistic regression:

	Vitamin D status	Vitamin D status			
	Insufficiency	Insufficiency		Deficiency	
	OR (95% CI)	P value	OR (95% CI)	P value	
	Adjusted for age	Adjusted for age and sex			
Central obesity	0.1(0.01-0.8)	0.02*	8.1(1.2-54)	0.02*	
Raised TG	0.5(0.1-2.7)	0.4	1.8(0.3-9.2)	0.4	
Reduced HDL-c	5.1(0.3-68.3)	0.2	0.1(0.01-2.5)	0.2	
Raised BP	0.2(0.05-1.2)	0.08	4.01(0.8-19.5)	0.08	
Raised FPG	0.1(0.01-1.04)	0.05	8.9(0.9-83.9)	0.05	

OR: Odds Ratio, CI: confidence interval, TG: Triglycerides, HDL-c: High-density lipoprotein cholesterol, BP: Blood pressure, FPG: Fasting plasma glucose P value (p < 0.05) is considered to be significant.

As shown in Table 4, both vitamin D deficiency and insufficiency were significantly associated with central obesity. Compared with vitamin D insufficiency, patients with vitamin D deficiency were 8.1 times more likely to be centrally obese (OR, 95% confidence interval [CI] = 8.1, 1.2–54, P-value = 0.02). An

association between both vitamin D deficiency and insufficiency and raised FPG was also observed but failed to reach statistical significance (P = 0.05). No associations between both vitamin D deficiency and insufficiency and raised triglycerides reduced HDL-c or raised blood pressure were identified.

Table (5): The association of vitamin D status with metabolic syndrome as a single entity among the hemodialysis patients enrolled in this study is explored using logistic regression: Independent variables

Independent	Vitamin D status			
variables	Insufficiency		Deficiency	
	OR (95% CI)	P value	OR (95% CI)	P value
Metabolic syndrome	Adjusted for age and sex			
	4.5(0.4-49.9)	0.2	0.2(0.02-2.3)	0.2
Metabolic syndrome	Adjusted for age, sex and PTH			
	0.9(0.2-2.9)	0.9	1.06(0.3-3.3)	0.9

OR: Odds ratio, CI: confidence interval, PTH: Parathyroid hormone; P value (p < 0.05) is considered to be significant.

As shown in Table 5, No association between both vitamin D deficiency and insufficiency and metabolic syndrome (P-value = 0.2 and 0.9, respectively) even after adjustment for age, sex, and parathyroid hormone levels.

Discussion

Metabolic syndrome is a clustering of risk factors, as dyslipidemia, insulin resistance, central obesity, and hypertension that together culminate in the increased risk of type 2 diabetes mellitus and cardiovascular disease. As

these conditions are among the leading causes of mortality. [8]

Vitamin D is a fat-soluble vitamin that is essential for optimal health. It is essential for the regulation of calcium and phosphorus

absorption, maintenance of healthy bones and teeth, and is suggested to supply a protective role against multiple diseases. ^[9]

Vitamin D deficiency plays a key role in the pathogenesis of risk factors of metabolic syndrome, which affect the cardiovascular system, increase insulin resistance and obesity, stimulate rennin-angiotensin-aldosterone system that causes hypertension. Moreover, vitamin D deficiency, as well as cardiovascular diseases and related risk factors, frequently co-occur. [10]

Metabolic syndrome has a high prevalence in ESRD patients and is a risk factor for cardiovascular disease, the leading cause of mortality in chronic kidney disease. [11]

As per National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines, the following categories for vitamin D status were defined: severe vitamin D deficiency, 25(OH) vitamin D < 5 ng/mL; mild vitamin D deficiency, 25(OH) vitamin D between 5 ng/mL and 15 ng/mL; vitamin D insufficiency 25(OH) vitamin D between 16 ng/mL and 30 ng/mL, and vitamin D sufficiency, 25(OH) vitamin D > 30 ng/mL. [12]

In the present study, we searched for whether serum levels of 25(OH) vitamin D have associations with the prevalence of metabolic syndrome and its components in a group of ESRD patients undergoing maintenance hemodialysis.

Our study showed that the prevalence of metabolic syndrome as defined by the International Diabetes Federation (IDF) criteria among the hemodialysis patients enrolled in this study was 35.6%.

Similar results were reported by Alswat K. A. et al. [15].

In their studies, the incidence of metabolic syndrome in hemodialysis patients was 38.2 % and 42.6% respectively.

In our study, reduced HDL-c emerged as the most frequent diagnosed abnormality affecting nearly 67.8% of the hemodialysis patients.

Ahmadi F. et al., [14] reported similar results with reduced HDL-c affecting nearly 80% of the hemodialysis patients.

These results differed from the study by Vigan J. et al., [13], who reported that the most frequent metabolic syndrome criteria observed were hypertensively affecting 66.67% of the hemodialysis patients.

Our study showed that age, weight, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, FBS, total cholesterol, trigly-cerides, and LDL-c were significantly higher and HDL-c was significantly lower among hemodialysis patients with metabolic syndrome compared to those without metabolic syndrome.

Since all these parameters are considered criteria for the metabolic syndrome, it is not surprising to find their values significantly higher among metabolic syndrome patients (except for serum HDL, which was significantly lower).

Similar to our findings but differently from our study that was done on hemodialysis patients, Yasin N. A., et al., [16] reported that all risk factors except hypertension were significantly more frequent among elderly Jordanian patients with metabolic syndrome compared to those without metabolic syndrome. Similar to our findings but differently from our study that was done on hemodialysis patients, Yasin N., et al., [17] reported that waist circumference, body mass index, triglycerides and fasting blood higher among were significantly osteoporotic postmenopausal Jordanian female patients with the metabolic syndrome, and serum HDL was significantly lower.

In our study, the percentage of vitamin D insufficiency and mild deficiency in hemodialysis patients was 21.1% and 78.8% respectively.

In our study, it was found that hemodialysis patients who had a mild deficiency of vitamin D and insufficiency were found to have a significantly lower level of HDL-c.

Contrary to our study that was done on hemodialysis patients, Yasin N. et al., reported that vitamin D deficiency and insufficiency were associated with significant a higher level of serum triglycerides and serum LDL among osteoporotic postmenopausal Jordanian female patients.

Contrary to our study that was done on hemodialysis patients, Vacek J. L. et al., [5] also found an association between serum vitamin D and triglycerides in a large cohort of patients.

Our study concluded that there were no significant correlations between PTH level and metabolic factors included in the MetS in hemodialysis patients.

In our study, both vitamin D mild deficiency and insufficiency in hemodialysis patients were significantly associated with central obesity (waist circumference ≥ 90 cm in both sexes or BMI > 30 kg/m2).

In this study, we did not find a significant association between the concentration of serum 25(OH) vitamin D and metabolic syndrome in hemodialysis patients.

In contrast to our results, Ahmadi, F., et al., [14] found that both vitamin D insufficiency and deficiency were significantly associated with metabolic syndrome in Iranian patients undergoing maintenance hemodialysis.

The association for vitamin D deficiency was stronger than for insufficiency.

Our study has certain limitations. Firstly, it is a cross-sectional study, and direct relations between the variables of interest could not be determined.

Additionally, The lack of association between vitamin D concentrations and metabolic syndrome can be attributed to the relatively small number of patients undergoing hemodialysis in this study.

Therefore, the study might have been inadequately powered to detect the minute between-group differences for metabolic syndrome components. In a few instances, a marked difference or trend was evident; however, it failed to pass the threshold of P < 0.05, and as a result, the null hypothesis was retained. Furthermore, we could not consider factors such as calcium intake, amounts of sunlight exposure, and vitamin D intake which could have affected the serum levels of 25(OH)D because of the limited data.

Finally, measurements were performed only once for each patient, and serial measurements over a year would be required for more accurate studies.

This study was approved by the Institutional Ethics Committee of Medicine, Minia University, Egypt.

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Conflict of Interest: the authors declare that there is no conflict of interests.

Generalizability:

Our external validity of this study we recommend to investigate the vit D in all patient on hemodialysis, who have abnormal BMI and also assess the risk of obesity and treatment of hypovitaminosis D..

Disclosure:

- 1. I haven't any kind of financial support (funding, grants, sponsorship).
- 2. I haven't any commercial or financial relationship.
- 3. I have not signed any agreement with any one that will bias the results of my research in any way.

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