

Prevalence of vitamin D deficiency in patients with type 2 diabetes and its relationship with glycemic control

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Abstract

Aim: The aim of our study is to investigate serum 25-hydroxy (OH) vitamin D levels in patients with type 2 diabetes, determine the prevalence of vitamin D deficiency, and reveal the potential relationship between vitamin D deficiency and glycemic control.

Material and Methods: A total of 100 patients (50 females, 50 males) diagnosed with type 2 DM were included in the study. Data used in the study were retrospectively acquired from the records in the files of patients who had presented to the General Internal Medicine polyclinic and clinic at Firat University Hospital.

Results: Mean vitamin D levels were determined as 11.8 ± 5.8 nmol/l in females and 13.5 ± 7.3 nmol/l in males. 57 patients (57%) in total demonstrated vitamin D deficiency. Vitamin D deficiency was detected in 31 (62%) female patients and 26 (52%) male patients. A significant negative correlation was determined between diabetic patients with and without vitamin D deficiency with regard to HbA1c, fasting blood glucose, post-prandial blood glucose ($p < 0.001$). Diabetic patients with vitamin D deficiency and diabetic patients without vitamin D deficiency demonstrated no significant differences with regard to retinopathy, nephropathy, and neuropathy ($p > 0.05$). A significant negative correlation was determined between diabetic patients with and without vitamin D deficiency with regard to BMI and patient weight ($p < 0.001$).

Conclusion: Our study concludes that vitamin D has a negative significant correlation with FBG, PPBG, HbA1C, and BMI. These results indicate that, as vitamin D levels decrease in patients with type 2 diabetes, insulin resistance increases, and consequently, glycemic control is disrupted. Although, along with our study, other studies too have reported an increased risk for Type 2 diabetes in the presence of vitamin D deficiency, evidence suggesting a causal relationship is limited as not an adequate number of high-quality randomized controlled studies exist.

Keywords: Vitamin D; Type 2 Diabetes; Prevalence.

INTRODUCTION

Vitamin D is a group of sterols that regulates calcium and phosphorus metabolisms, is among fat-soluble vitamins, and differently from other vitamins, has hormone and hormone-precursors that can be produced in the body (1,2). Vitamin D consists of two forms; ergocalciferol (Vitamin D2) that is derived from plants, and cholecalciferol (Vitamin D3) that is derived from animal source foods and is also produced as a result of the exposure of 7 dehydrocholesterol found in the human skin to sunlight (ultraviolet B) (1-3).

Numerous studies have been conducted to investigate the relationship between vitamin D and Diabetes Mellitus and these showed that 25 (OH) D, which is a vitamin D indicator, was lower in individuals with Type 2 diabetes

compared to those without diabetes, that plasma vitamin D levels affected insulin resistance, that insulin sensitivity and release decreased in cases where these levels were low, and also that insulin receptors in promonocytic cells were reduced (4). It was shown by another study that supplemental vitamin D resulted in a decrease in insulin resistance in patients with Type 2 diabetes (5). Studies have shown that Vitamin D3 has antioxidant effects (6). The relationship of oxidative stress with vitamin D and calcium balance was investigated and it was found that calcium balance and mitochondrial membrane potentials were altered under oxidative stress. This change causes damage to the mitochondria and DNA, and leads the cell to undergo programmed death; apoptosis. Apoptosis may be induced by disruption of intracellular electron balance, oxidative stress, mitochondrial defects, and

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inadequate antioxidant stress (7). Vitamin D receptors are found in beta cells and peripherally in target tissues such as skeletal muscles and adipose tissue that respond to insulin, as well as certain cells (8-10). By stimulating the receptors in beta cells, vitamin D promotes insulin release and activation of vitamin D-dependent calcium-binding proteins found in the pancreas (11,12). In vitro and in vivo studies showed that vitamin D was responsible for normal insulin release required for glucose tolerance to be maintained in response to glucose.

Certain studies reported that low levels of vitamin D resulted in more macro vascular complications than microvascular complications (12). Vitamin D receptors are found in adipose tissue and skeletal muscles, and are involved in the determination of peripheral insulin sensitivity (8). Vitamin D either influences the function of insulin directly by bolstering the function of insulin receptors or indirectly by altering calcium influx and efflux (9). Calcium is influential on intracellular processes in skeletal muscles that react with insulin and in tissues such as the adipose tissue that respond to insulin, and variations in Ca^{+2} levels to be rather restricted ensures that insulin is processed at an optimal level. For this reason, changes to intracellular Ca^{+2} , primarily in the target tissues of insulin, disrupt insulin signalization by causing peripheral insulin resistance and may result in a decrease in the activity of GLUT-4, which transports glucose into the cell (13-15). As calcium absorption decreases in vitamin D deficiency, parathormone is released secondarily; and calcium reabsorption in the kidneys increases. This situation inhibits the calcium influx required for insulin to be processed at target cells and decreases insulin sensitivity by increasing intracellular levels of calcium (8). The decrease in insulin sensitivity causes an increase in parathormone release (16). Therefore, increased parathormone as a result of low vitamin D levels negatively affects insulin release from beta cells (12). Table 1 presents vitamin D statuses based on serum 25 (OH) D3 levels (8).

Table 1. Vitamin D status based on serum 25 (OH) D3 levels

Serum ng/mL	25(OH)D3 nmol/L	Levels Vitamin D status
<12	< 30	Vitamin D insufficiency
12-20	30-50	Vitamin D insufficiency
≥30	≥75	Sufficient vitamin D levels

MATERIAL and METHODS

A total of 100 patients diagnosed with Type 2 DM were included in the study. 50 patients were females and 50 were males. Patients with liver disease, acute infection, hypothyroidism, chronic kidney disease, and medication use that could affect vitamin D levels were not included in the study. Patients with serum creatinine levels exceeding 2.0 mg/dl were excluded from the study. Again, patients

with mental retardation and those aged below 18 or above 65 years were not included in the study. Firat University ethics committee granted approval for this study (approval number: 06, date: July 19,2018).

Physical examination data of the patients were acquired from the record system. Results of measurements performed following a minimum fasting period of 8 hours including 25-(OH) vitamin D levels, fasting blood glucose, HbA1c, creatinine, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride and post-prandial blood glucose were acquired for all patients from data in their patient files. 25-(OH) vitamin D levels were measured with the HPLC method. Fasting blood glucose and post-prandial blood glucose were measured with the enzymatic method, and HbA1c was measured with HPLC-UV detector. Lipid levels were measured using an Abbott-Aeroset auto-analyzer with their original kits. LDL cholesterol was calculated using the Friedewald formula. The threshold 25-(OH) level for vitamin D deficiency was considered <30 nmol/l (12 ng/ml) (8).

Statistical Analysis

Statistical evaluations were conducted using the SPSS-22 packaged software. Data were analyzed using descriptive statistical methods, student's t-test, equivalence, and variance analysis. A p-value <0.05 was considered the threshold for significance.

RESULTS

Mean vitamin D levels were determined as $11,8 \pm 5,8$ nmol/l in females and 13.5 ± 7.3 nmol/l in males. 57 patients (57%) had vitamin D deficiency. Vitamin D deficiency was detected in 31 female patients (62%) and 26 male patients (52%). Table 2

Table 2. Comparison of parameters obtained from patients with and without vitamin D deficiency

	Patients with vitamin D deficiency	Patients without vitamin D deficiency	P value
Age	55.4 ± 11	57.5 ± 14.3	
N	57	43	
Female	31	19	
Male	26	24	
HbA1c	10.6 ± 1.9	8.3 ± 1.8	p < 0.001
FBG	325.1 ± 89.5	238.3 ± 61.6	p < 0.001
PPBG	238.5 ± 69.8	168.7 ± 49.1	p < 0.001
Weight	76,2 ± 5.4	71,6 ± 4.2	p < 0.001
BMI	28.3 ± 3.1	26.3 ± 1.8	p < 0.001
Retinopathy	10	6	p > 0.05
Nephropathy	6	4	p > 0.05
Neuropathy	38	32	p > 0.05
Hyperlipidemia	33	22	p > 0.05

A significant negative correlation was determined between diabetic patients with and without vitamin D deficiency with regard to HbA1c, FBG, PPBG ($p < 0.001$). Diabetic patients with vitamin D deficiency and diabetic patients without vitamin D deficiency demonstrated no significant differences with regard to retinopathy, nephropathy, and neuropathy ($p > 0.05$).

A significant negative correlation was determined between diabetic patients with and without vitamin D deficiency with regard to BMI and patient weight ($p < 0.001$).

DISCUSSION

We determined vitamin D deficiency at a rate of 57% in our patients with Type 2 diabetes. Deficiency was more prevalent in females than in males. We think the lower levels of vitamin D manifested by females may be linked to the covered dressing style of women in the area where the study was conducted. The threshold of vitamin D deficiency was accepted as < 30 nmol/l (12 ng/ml) in our study. Earlier studies have used various thresholds for vitamin D deficiency. A study conducted in Italy accepted a vitamin D deficiency threshold of ≤ 37.5 nmol/l (15 ng/ml) and reported the prevalence of vitamin D deficiency in patients with type 2 diabetes mellitus as 34% (17). A study done in Japan (18) reported this rate as 70.6% and a study done in the United States (19) as 63.5%. Another study that considered the threshold of vitamin D deficiency as < 5 ng/ml reported a vitamin D deficiency prevalence of 39% in female patients with type 2 diabetes (20). Studies have determined vitamin D deficiency to be connected to the development of type 2 diabetes (21).

Although studies have used different thresholds to define vitamin D deficiency and obtained different results, the increased prevalence of vitamin D deficiency in patients with type 2 diabetes emphasizes the importance of investigating vitamin D levels in these patients for the treatment of the disease and the necessity of measures to be taken in the pre-diabetic period.

In line with this result, our analyses revealed that vitamin D was negatively correlated with FBG, PPBG, and HbA1C. This result shows that insulin resistance increases in parallel to the decrease in vitamin D levels in patients with type 2 diabetes, consequently disrupting glycemic control.

Targher et al. (17) reported that diabetic patients with vitamin D deficiency had high levels of HbA1c, CRP, and fibrinogen. In our study, the glycemic control parameters of patients with vitamin D deficiency were found to be significantly negatively correlated ($p < 0.001$). Also, one study found that high-dose vitamin D therapy had no significant effect on glycemic control (22).

Obesity may influence vitamin D levels. Earlier studies done on this topic reported that patients with BMI ≥ 30 had low vitamin D levels and that vitamin D bioavailability was also low in these individuals (23). Moreover, it was determined in previous years that vitamin D levels decreased as body fat increased (17). In the study we

conducted, we determined a negative correlation between patients with and without vitamin D deficiency with regard to BMI.

Vitamin D levels were shown to be affected by seasonal changes (24). Furthermore, physical activity was found to be related to vitamin D levels and low physical activity was reported to be associated with the lowest levels of vitamin D in a comprehensive study (25). Therefore, we believe that regular exercise and sufficient exposure to sunlight comprise the fundamental principles of preventing vitamin D deficiency.

In summary, we determined in this study that vitamin D deficiency was more prevalent in type 2 diabetes patients with poor glycemic control compared to patients with better glycemic control. In addition, vitamin D deficiency was found to be significantly negatively correlated in diabetic patients with a high BMI.

CONCLUSION

In conclusion, comprehensive studies are needed to reveal the relationship between vitamin D and glycemic control, excess weight, and insulin resistance and produce more effective solutions for the treatment of type 2 diabetes and obesity, which are becoming increasingly more prevalent in the world population.

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