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Original Article

Evaluation of 25-hydroxy Vitamin D Serum Levels and Thyroid-related Parameters in Patients with Type 2 Diabetes Mellitus and Healthy People in Shiraz, Iran

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Abstract

Background and Aim: The prevalence of type 2 diabetes mellitus (T2DM) is increasing globally. There is increasing evidence in the correlation between altered vitamin D levels, thyroid dysfunction, and T2DM. The goal of this study was to evaluate the association between serum 25-hydroxy vitamin D (25(OH) D), lipid profile, glucose and thyroid-related parameters among patients with T2DM and non-diabetic individuals.

Methods: This case-control study was conducted on 228 individuals (110 type two diabetics and 118 healthy controls). The serum concentration of 25(OH) D was determined by chemiluminescence assay. Photometric methods measured serum levels of fasting blood glucose (FBG), calcium, phosphorous, total Cholesterol (TC), triacylglyceride (TG), high-density lipoprotein (HDL). Low-density lipoprotein (LDL) and VLDL levels were estimated from the Friedewald equation (LDL-C=TC–HDL-*C*–(TG/5)). The Elisa kit measured serum T4 and TSH.

Results: 80% of Patients with T2DM and 71% of healthy individuals were suffering from vitamin D insufficiency. A non-significant relationship between TG (P=0.36), HDL (P=0.33), VLDL (P=0.36), T4 (P=0.56) calcium (P=0.39) and phosphorus (P=0.41) levels were showed in control and diabetic groups. The levels of FBG (P=0.000), TC (P=0.001), LDL (P=0.004), TSH (P=0.000) were significantly higher, and the levels of 25 (OH) D (P=0.001) was significantly lower in the T2DM group compared to the non-diabetic group.

Conclusion: We revealed that the serum level of 25 (OH) D is lower in patients with T2DM, and the TSH level is significantly higher compared to the non-diabetic group. Thyroid dysfunction and a low level of 25 (OH) D are associated with a high risk of T2DM.

Keywords: Type 2 diabetes mellitus**;** 25-hydroxy Vitamin D**;** High-density lipoprotein; Low-density lipoprotein**;** Thyroid-stimulating hormone.

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Introduction

The global incidence of diabetes mellitus will be increased from 285 million people in 2010 to 439 million individuals in 2030 (1). Type 2 diabetes mellitus (T2DM) accounts for about 90% of adult diabetes (2). T2DM is usually determined by a relative or absolute deficiency in insulin secretion and insulin resistance, which is associated with glucose and lipid metabolism abnormalities (2, 3).

This endocrine disorder resulting from the combination of multiple risk factors, including nutritional, genetic, environmental, and behavioral factors (4).

Vitamin D is a multifunctional hormone and an essential nutritional factor for human health (5, 6). The significant well-known action of 25 (OH) D in bone metabolism and calcium homeostasis (7). However, accumulating evidence suggests that vitamin D and calcium are associated with numerous skeletal and non-skeletal disorders in the clinic (8). Several epidemiological reports have focused on the potential action of vitamin D in insulin secretion and glucose metabolism (9). The supplementation of vitamin D and calcium can improve glucose homeostasis and T2DM risk (10). The serum 25-hydroxyvitamin D [25(OH) D] level is accepted as an index of vitamin D status in the human body, which is inversely related to diabetes prevalence (11, 12).

Also, several clinical research has shown that vitamin D deficiency is considered a risk factor in the pathogenesis of thyroid disorders among patients with T2DM (13, 14). Therefore, effective control of vitamin D status is a necessary manner to alleviate the incidence of thyroid diseases and T2DM (10, 15). Thyroid hormones have multiple functions in the regulation of glucose and lipid metabolism. The abnormalities of thyroid hormones are associated with insulin resistance and lipid metabolism disorders among patients with T2DM (16, 17).

Therefore, this study aimed to investigate the serum levels of 25 (OH) D, thyroid-related parameters, lipid profiles, calcium, phosphorus, and blood glucose levels between patients with T2DM and healthy individuals in Doran Hospital of Shiraz.

Methods

Briefly, in this case-control study, 110 patients with T2DM based on clinical findings, whose diabetes was confirmed by a physician, were randomly selected from patients referring to Doran Hospital. Also, we included 118 healthy individuals randomly as the control group among the relatives of diabetic patients with no history of diabetes and confirmed by fasting blood glucose (FBG) test. The inclusion criteria included: the diagnosis of T2DM for at least three years prior, the use of blood glucose-lowering drugs, willingness to participate, and a complete written questionnaire. Exclusion criteria included: displeasure or inability to participate in the study, liver disorder, known renal diseases or creatinine > 2 mg/dL, malabsorption, infertility, oligomenorrhea, Pregnancy, lactation, use of drugs that may affect bone metabolism (Estrogen, Calcitonin, etc.), smoking, alcohol Abuse, inactivity for more than one week, the use of calcium and vitamin D supplementation and severe obesity (BMI > 40 kg/m^2). After overnight fasting, 10 ml of fasting blood sample was taken and carried to the laboratory of Doran Hospital to determine 25-(OH) vitamin D level, lipid profile, FBG, calcium, phosphorous, T4, and TSH parameters. The serum concentration of FBG, calcium, phosphorous, total cholesterol (TC), triacylglyceride (TG), High-Density Lipoprotein (HDL) were measured by photometric methods using a commercial kit (Pars Azmoon kit, Tehran, Iran). LDL and VLDL levels were estimated from the Friedewald equation (LDL-C=TC–HDL-C–(TG/5)). We also measured the serum levels of T4 and TSH using the Elisa kit (Pishtazteb, Iran). Serum 25(OH) D was measured by chemiluminescence kits manufactured by DiaSorin Company (Italy) with a normal range of 30-100 ng/mL. Vitamin D insufficiency and sufficiency were defined with serum 25(OH) D <30 ng/mL and 25(OH)D ≥ 30 ng/mL, respectively (18). Statistical analyses were performed using SPSS software, version 16 (Chicago, USA). All results were expressed as mean ± standard deviation (SD). The student's t-test determined the differences between the mean of continuous variables among experimental groups. The p-value<0.05 was considered statistically significant.

Results

In our study, 128 individuals (39% men and 61% of women) were enrolled. 110 patients (mean age 49.33) with T2DM and 118 healthy individuals (mean age 47.84) as a control group were included.

All data among two diabetic and non-diabetic groups are presented as mean ± SD. The mean age of individuals, 25(OH) D, calcium, phosphorous, T4, TSH, FBG, and lipid profile in both control and diabetic groups are shown in Table 1.

As shown in Table 1, there was a statistically significant association between mean FBS (P=0.000), TC (p=0.001), LDL (P=0.004), 25(OH) D (p=0.001), and TSH (p=0.000). FBS, TC, LDL, and TSH levels were significantly higher in the diabetic group compared to the control group and 25(OH) D was significantly lower in the diabetic group compared to the control group. There was not any statistically significant association between mean age (p=0.31), TG (p=0.36), HDL (P=0.33), VLDL (p=0.36), calcium (p=0.39) and phosphorus (p=0.41) levels in control and diabetic groups. Also, the results of Table 1 showed that there was no significant difference in the T4 level (p=0.56) between the two diabetic and non-diabetic groups. Given that the TSH level (p=0.000) in the diabetic group is significantly higher than in the control group, it seems that diabetic patients have a way to increase this level in the body but not to increase the level of the thyroid hormone.

The mean level of 25-(OH) vitamin D in the diabetic group was 22.76 ng/mL, and in the control group was 27.18 ng/ml. There was a significant difference between the two diabetic and control groups (Table 1).

Table 1. The mean values of biochemical parameters FBG, TG, LDL, HDL, VLDL, TC, T4, TSH, calcium, phosphorous, and VitD3

Variable	groups	N	Mean	Std. Deviation	p-value
Age (year)	Control	118	47.8429	12.45843	0.31
	Diabetes	110	49.3333	12.31540	
FBG (mg/dL)	Control	118	86.2429	8.02951	0.000
	Diabetes	110	١٥٤.32	35.53244	
TG (mg/dL)	Control	118	134.39	64.12440	0.36
	Diabetes	110	141.45	64.72751	
Cholesterol (mg/dL)	Control	118	162.84	29.73253	0.001
	Diabetes	110	174.57	28.90835	
HDL (mg/dL)	Control	118	40.9000	6.47219	0.33
	Diabetes	110	41.7826	8.57065	
LDL (mg/dL)	Control	118	95.0571	27.31392	0.004
	Diabetes	110	104.49	27.59358	
VLDL (mg/dL)	Control	118	26.8786	12.82488	0.36
	Diabetes	110	28.2899	12.94550	
TSH (µIU/mL)	Control	118	3.2950	2.02340	0.000
	Diabetes	110	7.1043	3.16239	
T4 (µg/dL)	Control	118	7.4791	1.77227	0.56
	Diabetes	110	7.3493	1.98973	
VitD$_3$ (ng/mL)	Control	118	27.1٨	7.91	0.001
	Diabetes	110	22.76	8.31	
Calcium (mg/dL)	Control	118	8.67	0.54	0.39
	Diabetes	110	8.61	0.53	
Phosphorous (mg/dL)	Control	118	3.91	0.76	0.41
	Diabetes	110	3.84	0.65	

All results were expressed as mean ± standard deviation (SD) and p <0.05 was considered statistically significant. Abbreviations: FBG, fasting blood glucose; HDL, high-density lipoproteins; LDL, low-density lipoproteins; VLDL, Very low-density lipoproteins; TSH, thyroid-stimulating hormone; TG, triglyceride; TC, total cholesterol. VitD$_3$, Vitamin D3

Table 2. Frequency of participants based on vitamin D levels.

Vitamin D levels	Frequency	Percent
Insufficient	172	75.44
Sufficient	56	24.56
Toxicity	0	0

Vitamin D insufficiency and sufficiency were defined with serum 25(OH) D <30 ng/mL and 25(OH) D ≥30 ng/mL, respectively. The prevalence rate of vitamin D of sufficient and insufficient categories in all individuals was 56 (24.56%) and 172 (75.44), respectively.

As shown in Table 3, the prevalence rate of vitamin D insufficiency and sufficiency in the diabetic group were 88 (80%) and 22 (20%), respectively. These numbers for the control group were 84 (71%) and 34 (29%), respectively.

Table 3. The prevalence rate of vitamin D insufficiency in both diabetic and control groups

(OH) Vit D levels	Diabetic group		Control group	
	mean±Sd	N	mean±Sd	N
30 ng/mL <(OH) Vit.D	19.2273±4.20334	88 (80%)	23.0714±3.37883	84(71%)
(OH) Vit.D≥ 30 ng/mL	36.9091±4.65735	22(20%)	37.3235±6.65022	34(29%)
Total	22.7636±8.30877	110 (100%)	27.1780±7.91151	118(100%)

The results were dysplayed as mean ± standard deviation (SD) and percents. $P < 0.05$ was set as statistically significant.

Discussion

We reported that the serum 25-(OH) D level in patients with T2DM was significantly lower than in the control group, but the serum levels of FBS, cholesterol, LDL, and TSH were significantly higher in the diabetic group compared to the control group. There is any significant association between TG, T4, HDL, VLDL, calcium, and phosphorous levels in the control group and patients with T2DM.

Based on animal and human studies, altered 25 (OH) D status and calcium levels were associated with glycemic status and type 2 diabetes risk (19). Laboratory studies provide evidence for an association between vitamin D status and insulin resistance and hyperglycemia. A study on 100 patients with T2DM suggested that the treatment with vitamin D was significantly improved the serum insulin, FBS levels, and insulin resistance (10). So, Adequate amounts of vitamin D can be associated with a significant reduction in the risk of diabetes (19, 20). In the present study, we analyzed serum levels of 25(OH) D, calcium, phosphorus, FBG, TC, TG, LDL, and HDL in patients with T2DM compared to the health group. Compared to the control group, patients with T2DM had higher levels of TC, LDL, and FBG. There was not any statistically significant association between mean TG, HDL, and VLDL levels among the control and diabetic groups. The serum 25 (OH) D levels were found significantly lower in diabetic groups than non-diabetics. All individuals were divided into two categories on the base of their measured 25-(OH) vitamin D serum levels. 25(OH) D levels are classified as sufficient (> 30) and insufficiency (<30 ng/mL). Vitamin D insufficiency has the highest rate among both T2DM and control groups. Also, in this study, there was not any statistically significant association between serum calcium and phosphorus levels in non-diabetic and diabetic groups. This result agreed with the previous study reported by Marwa et al., who showed that the levels of calcium and phosphorus don't alter among patients with T2DM and vitamin D deficiency (21, 22). A study has also reported a significant relationship between saliva calcium and phosphorus healthy and diabetic persons according to gender (23).

Many studies reported that vitamin D deficiency is related to thyroid disorders among patients with T2DM (13, 24). An association between T2DM and hypothyroidism has been reported, and these

endocrine disorders are often co-existing (25). Interestingly, low levels of thyroid hormones may affect lipid and glucose metabolism. Higher thyroid hormone levels are significantly associated with the improvement of insulin secretion in pre-diabetic individuals (25). Several studies indicated that the serum TSH levels in T2DM individuals were higher than non-diabetic controls (26, 27).

Our results showed that TSH levels were significantly higher in the diabetic group compared to the healthy group. We also evaluate the relationship between plasma. T4 levels were decreased, but no significant association between T4 levels in control and the diabetic group was observed.

Conclusion

In conclusion, the findings of the present research suggested that there is a significant relation between T2DM with 25(OH) D and TSH levels, but no significant association between T4 levels in the two groups was observed. Low serum levels of T4 within the normal range in people with subclinical hypothyroidism may be associated with the prevalence of T2DM.

Conflict of Interest

The authors declared that they have no conflict of interest.

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Ethics

This investigation was constructed, acquired, and gathered based on the data recorded in the laboratory of Shahid Doran Hospital in Shiraz through the following approved code: 1398/17.

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