ORIGINAL ARTICLE

Relation of obesity with serum 25 hydroxy vitamin D3 levels in type 2 diabetic patients

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Background: Hypovitaminosis D is associated with diabetes mellitus (DM). Aim of our study was to determine the relation of obesity with vitamin D levels in type 2 diabetic patients. **Materials and Methods:** We examined 101 type 2 diabetic patients and made a correlation analysis in all parameters. Then we classified our diabetics according to their body-mass indices and compared their 25 hdroxy vitamin D3 levels. **Results:** We found negative correlation between 25O HD and body mass index (BMI) (*P*: <0.001, r: –0.23). When we classified our diabetics according to their body mass indices as normal, overweight and obese, and compared their 25 hydroxy vitamin D3 levels, we determined that in every BMI group 25 hydroxy vitamin D levels were not found to be significantly different. **Conclusion:** These results suggest that at least in a Turkish population with type 2 DM vitamin D levels are low and correlate with BMI, but when vitamin D levels are so low, as obesity worsens vitamin D levels does not lessen.

Key words: Obesity, type 2 diabetes mellitus, vitamin D

INTRODUCTION

Hyperglycemia was shown to be independently associated with low vitamin D levels.[1] The relationship between vitamin D deficiency and risk of diabetes both type 1[2-6] and type 2[7-10] has also been reported in the literature.

A high prevalence of hipovitaminosis D was noted in diabetics.[11-16] One of the reasons for this is stated to be obesity besides diet, lack of sun exposure, renal impairement and genetic predisposition. Studies have suggested vitamin D insufficiency is associated with increased obesity.[17-26]

It has been shown that in Turkey vitamin D deficiency is an important problem.[27-30] There have been rare studies about obesity and vitamin D levels[26,27,31] in Turkish population. Aim of this study was to show the relation of obesity with vitamin D levels in type 2 diabetic patients.

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MATERIALS AND METHODS

Patients

A total of 101 type 2 diabetes mellitus (T2DM) patients, aged from 30-80 years, were recruited from the outpatient clinic of Ankara Education and Research Hospital from January 2011 to February 2011. Sixty one of them were female (61%), 40 of them were male (29%).

We excluded patients with chronic diseases of renal and liver, skin disorders, malabsorption, inflammatory bowel or celiac disease (in history or nowadays), and once taking medications that may interfere with serum levels of 25 hydroxy vitamin D (25 (OH) D).

After detailed physical examination, we measured body weight and height of all the patients. Waist was measured when fasting, in standing position halfway between costal edge and iliac crest, whereas hip was measured at the greatest circumference around the buttocks, by a non-elastic measure. We calculated body mass index (BMI) as weight in kilograms divided by the square of height in meters (kg/m^2).

Blood was withdrawn after 12 h of overnight fasting, at 08.30 a.m., for fasting plasma glucose (FPG), hemoglobin A1c, fasting insulin (FI), serum total and high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), creatinine, calcium (Ca), phosporous (P), parathyroid

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hormone (PTH), thyroid stimulating hormone (TSH), C-reactive protein (CRP), homocysteine (Hcy), and 25 (OH) D levels.

An indirect measure of insulin resistance was calculated from the fasting plasma insulin (μunite/ml) × FPG (mmol/l)/22.5 formula as homeostasis model assessment-insulin resistance.

Systolic and diastolic blood pressure were measured after a 5 min rest in the semi-sitting position with a sphygmomanometer. Blood pressure was determined at least three times at the right upper arm, and the mean was used in the analysis.

Laboratory methods

Plasma glucose, total cholesterol, TG and HDL-C, Ca, *P* concentrations were determined by enzymocalorimetric spectrophotometric method in a Roche/Hitachi molecular PP autoanalyser. Low density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula (LDL: Total cholesterol-HDL-TG/5). Insulin was measured by DRG Diagnostics (DRG Instruments GmbH, Germany) ELISA kits and FI was measured by TOSOH G7 HPLC system. PTH and TSH were determined with Advia Sentor XP device by chemoluminescence method. High sensitivity CRP was measured by immunnoflowmetric tests by Beckman-Cutler device. Hcy concentrations were determined according to the method of HPLC using Agilend 1100 device. For the measurements of 25 (OH) D, Waters LC-MS/MS device liquid chromatography mass spectrometry was used.

Methods

We made correlation analysis between parameters in type 2 diabetics, then made the comparison of 25 (OH) D levels in three BMI groups. We grouped the patients as normal (BMI < 25 kg/m^2), overweight (BMI 2 5-29.9 kg/m^2), and obese (BMI > 30 kg/m^2).

This study was performed according to the Helsinki decleration 2008. The local ethics comitee approved this study and all the subjects gave written informed consent.

Statistical analysis

Correlation between variables was calculated by Pearson correlation analysis. For the comparison of the groups ANOVA test was used. Data are presented as mean ± SD A *P* value of < 0.05 was considered as statistically significant.

RESULTS

We performed the study with 101 T2DM patients. All the demographic and laboratory findings of the patients are presented in Table 1.

When we made correlation analysis in diabetic patients we found positive correlations between 25 (OH) D and creatinin $P < 0.05$, r: 0.18) and negative correlations between 25 (OH) D and BMI ($P < 0.001$, r: −0.23), HbA1c ($P < 0.05$, r: −0.21), FI ($P < 0.05$, r: −0.01), HOMA-IR ($P < 0.05$, r: −0.20), PTH levels ($P < 0.05$, r: −0.18).

Then we classified our T2DM patients according to their 25 (OH) D levels, as < 12, 12-20 and > 20 ng/ml. All the demographic and laboratory findings of the patients with different 25 (OH) D levels are presented in Table 2. We did not find any difference in any parameters of the patients with different 25 (OH) D levels.

Then we classified our T2DM patients according to their BMI's, as normal (BMI < 25 kg/m^2), overweight (BMI 25-29.9 kg/m^2) and obese (BMI > 30 kg/m^2). We did not notice any statistically significant difference in 25 (OH) D levels of the patients according to their BMI's [Table 3].

DISCUSSION

Vitamin D status is best assessed by serum 25 (OH) D than 1,25 dihdroxy vitamin D (1,25 (OH) $_2$D), because 1,25 (OH) $_2$D has a short half life of 15 h and serum

Table 1: Demographic and laboratory findings of type 2 diabetic patients

Patients	T2DM (*n*=101)
Age (year)	55.8±7.5
BMI (kg/m^2)	29.8±4.1
Waist cir. (cm)	97.4±10.6
Hip cir. (cm)	105.6±9.5
FBG (mg/dl)	172.1±68.6
HbA1c (%)	8.2±2.1
FI (μU/ml)	13.0±6.4
HOMA-IR	5.4±3.6
LDL-C (mg/dl)	127.7±38.4
HDL-C (mg/dl)	44.8±10.0
TG (mg/dl)	202.9±23.5
Creatinine (mg/dl)	0.1±0.04
Ca (mg/dL)	9.4±0.3
P (mg/dL)	3.3±0.4
PTH (pg/mL)	53.6±25.2
TSH (μIU/MI)	1.6±1.0
CRP (mg/dl)	8.4±5.3
Hcy (μmol/ml)	11.2±6.2
SBP (mm Hg)	140.1±10.1
DBP (mm Hg)	92.6±11.5
25 (OH) D (ng/ml)	9.9±7.6

BMI= Body mass index; Waist cir.= Waist circumference; Hip cir.= Hip circumference; FBG= Fasting blood glucose; HbA1c= Hemoglobin A1c; FI= Fasting insulin; HOMA-IR= Homeostasis model assesment index-insulin resistance; LDL-C= Low density lipoprotein cholesterol; HDL-C= High density lipoprotein cholesterol; TG= Triglyceride; Ca: Calcium; P= Phosphorous; PTH= Parathyroid hormone; TSH= Thyroid stimulating hormone; CRP= C-reactive protein; Hcy= Homocysteine; SBP= Systolic blood pressure; DBP= Diastolic blood pressure; 25(OH) D= 25-hydroxy vitamin D. Data are presented as mean±SD, NS= Non-significant; T2DM= Type 2 diabetes mellitus

Table 2: Demographic and laboratory findings of type 2 diabetic patients with different 25-hydroxy vitamin D levels

25 (OH) D (ng/ml)	<12 ng/ml	12-20 ng/ml	>20 ng/ml	*P*
Case number	74	20	7	NS
Age (year)	55.3±7.8	39.7±6.0	58.7±7.4	NS
BMI (kg/m^2)	29.8±4.1	30.0±3.0	29.5±6.4	NS
Waist cir. (cm)	96.4±9.6	88.4±7.6	92.4±9.7	NS
Hip cir. (cm)	105.6±9.5	98.6±8.5	101.6±9.3	NS
FBG (mg/dl)	173.4±71.3	167.4±55.3	192.8±55.8	NS
HbA1c (%)	8.2±2.1	8.3±2.0	8.6±2.1	NS
FI (μU/ml)	13.3±6.9	12.2±4.9	12.1±4.0	NS
HOMA-IR	5.5±4.1	4.8±2.2	5.4±1.5	NS
LDL-C (mg/dl)	129.1±37.6	122.2±41.8	129.4±42.4	NS
HDL-C (mg/dl)	44.6±9.3	43.3±11.6	50.8±11.6	NS
TG (mg/dl)	206.3±126.7	206.0±130.9	158.2±57.7	NS

BMI= Body mass index; Waist cir.= Waist circumference; Hip cir.= Hip circumference; FBG= Fasting blood glucose; HbA1c= Hemoglobin A1c; FI= Fasting insulin; HOMA-IR= Homeostasis model assesment index-insulin resistance; LDL-C= Low density lipoprotein cholesterol; HDL-C= High density lipoprotein cholesterol; TG= Triglyceride. Data are presented as mean±SD NS= Non-significant; 25 (OH) D: 25-hydroxy vitamin D

Table 3: Comparison of 25-hydroxy vitamin D levels of type 2 diabetes mellitus patients according to their body mass indices

BMI	Number of patients	25(OH) D levels
Normal	16	13.1±12.7
Over weight	41	8.5±4.7
Obese	44	10.5±6.9
P	NS	

BMI= Body mass index; 25 (OH) D: 25-hydroxy vitamin D; Normal: BMI<25 kg/m^2, Overweight: BMI 25-29.9 kg/m^2, Obese: BMI>30 kg/m^2. Data are presented as mean±SD; NS= Non-significant

concentrations are closely regulated by PTH, Ca, and P.[32] Some variation exits related to cutoff values for insufficiency and deficiency due to differences in assay methods and population variations. Normal 25 (OH) D levels should be 30-60 ng/mL.[32] Vitamin D insufficiency has been reported to range from levels of 16 to 30 ng/mL.[33] Vitamin D deficiency varies from < 11 to < 20 ng/mL[34,35] but is generally defined as levels of < 15 ng/mL.[36] Whatever value is accepted, it is evident that our diabetics has low values of vitamin D, either totally or when classified according to their BMI's. These results are relavent to those of the studies about DM and decreased serum vitamin D levels.[11-16]

People with diabetes are at significant risk for vitamin D insufficiency or deficiency. Reasons for this include limited intake of foods high in vitamin D - less sun exposure due to possible fatigue, obesity or mobility issues - renal impairement, that results in less biologically active vitamin D, since conversion to the active form occurs in the kidneys and genetic predisposition such as polymorphisms of vitamin D binding protein or polymorphisms of CYP2R1 gene (which is necessary to catalyze the formation of the main circulating vitamin D metabolite).[37] The last reason may be obesity. More vitamin D is stored in the fatty tissues and less is biologically active in the serum. Obesity is also associated with inflammation and low vitamin D levels are related to inflammation. Cytokines and other inflammatory agents have been linked to beta cell damage, which then impaires insulin synthesis and secretion. In studies with diabetic mice, high doses of 1,25 (OH) D have been shown to delay the onset of diabetes.[38] This active form has been shown to protect beta cell function caused by inflammatory cytokines; interleukine-6 and tumor necrosis factor-alpha.[39] Regardeless of the possible underlying mechanisms about the relation of vitamin D with obesity, it is relevant to take into account obesity when dealing with low vitamin D levels in diabetes. In our study according to correlation analysis, we found that vitamin D levels were negatively correlated with BMI.

Hypönen *et al*. showed that in their normal, overweight, obese and severely obese subjects serum 25 (OH) D levels decreased with increasing BMI.[14] Al-Dagri also determined that BMI was a significant predictor of 25 (OH) D.[40] Barchetta *et al*. when classified their patients according to serum 25 (OH) D quartiles, found increasing BMI and waist circumference results, in accordance with decreasing vitamin D levels.[41] Finding a negative correlation between vitamin D levels and body-mass indices of our patients, we hoped to find statistically significant difference in 25 (OH) D levels of our normal, overweight and obese diabetic groups. However, we could not be able to demonstrate any difference in 25 (OH) D levels of our patients according to their BMI's. Relatively small sizes of our groups may be a reason. It may also be said that when 25 (OH) D levels were so low obesity markers may not be affected.

It was also surprising that all parameters, including BMI, waist and hip ratios of the patients did not differ when we grouped our patients according to their 25 (OH) D levels. We think that this astonishing result may be due to the small size of the groups. When we looked the levels of 25 (OH) D in the group with > 20 ng/ml, we found that the level of vitamin D was not very high, the mean level was 21.9 ± 22.3 ng/ml. We worry if we can also consider it a reason why there were no differences in BMIs according to varying vitamin D levels.

Present study has some limitations. First, we carried out our study between January and February. Because the primary source of this vitamin is skin production and seasonal variations in vitamin D status is well known we plan to reperform this study in summer. Second, in our type 2 diabetic patients therapy modalities were not mentioned. Third, enlargements of size of the groups are needed. Fourth, as our examination is a cross-sectional one and we randomized our patients from a part of Ankara we cannot apply our results to all the Turkish population.

CONCLUSION

Grave vitamin D levels were present in type 2 diabetic patients in Turkey. A negative correlation was determined in vitamin D levels and BMI, but as vitamin D deficiency was so low, 25 (OH) D levels did not worsened as obesity increased.

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