



## Original Article

## Vitamin D status of Turkish type 1 diabetic patients

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## ABSTRACT

**Introduction:** Vitamin D was associated with the pathogenesis, treatment and prognosis of type 1 and type 2 diabetes mellitus. The aim of this study is to assess vitamin D status of Turkish adult type 1 DM patients and compare them with health controls and also to assess the relationship of vitamin D and glycemic control.

**Method:** Study was designed as cross-sectional and conducted in a tertiary Hospital diabetes unit. 296 type diabetic patients and 151 healthy controls was included to the study. Venous samples were collected into plain tubes after overnight fasting. Serum 25-hydroxyvitamin D level was measured by radioimmunoassay technique. Statistical analysis was performed with SPSS 15.0.

**Results:** 25-Hydroxyvitamin D levels were similar between patients with type 1 diabetes (22, 9 ± 17, 4 ng/ml) and controls (24, 5 ± 19, 3 ng/ml) ( $p = 0,382$ ). Most of the participants have 25-Hydroxyvitamin D deficiency. As shown in Table 2 serum 25-Hydroxyvitamin D level was not associated with most of the biochemical or anthropometric parameters.

**Conclusion:** As a result there were no difference between type 1 diabetics and healthy controls according to their vitamin D levels. Further studies with a larger sample of patients will improve our understanding of the relation of vitamin D and diabetes.

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## 1. Introduction

Vitamin D has important effects on bone tissue and calcium/phosphate homeostasis. It also plays role in preventing fractures and osteoporosis. But the deficiency of vitamin D also associated with increased risk of cancers, heart diseases and autoimmune diseases [1]. Moreover metabolic disorders, namely Type 1 Diabetes Mellitus (Type 1 DM) and Type 2 Diabetes Mellitus (Type 2 DM), were also being linked to vitamin D deficiency [2].

Recently increased amount of researchers speculated that vitamin D affect beta cells in pancreas directly so it was associated with the pathogenesis, treatment and prognosis of Type 1 DM and Type 2 DM [2]. Type 1 DM incidence follows a seasonal patterns so it was therefore hypostasized that vitamin D deficiency has an impact on pathogenesis [3]. Also increased prevalence of vitamin D deficiency in children and adolescents with Type1 DM compared with non-diabetics individuals were reported in many studies

[4–7]. But there are also some studies that do not show significant difference of vitamin D levels between type 1 diabetics and healthy subjects [8–12].

The aim of this study is to assess vitamin D status of Turkish adult type 1 DM patients and compare them with health controls and also assess the relationship of vitamin D and glycemic control.

## 2. Material and method

This cross sectional study was conducted between 01.02.2013 and 01.05.2013 and approved by Local Ethical Committee (approval date and number 20.12.2012–29/G). Participants were enrolled at the time of regularly medical visit. In total 296 Type 1 DM patients and 151 healthy controls were included to the study. All of the Type 1 DM patients were established diagnose according to International Diabetes Federation (IDF) criteria, (diagnose and follow up > 6 months) and all of them were currently insulin dependent. Control subjects were age and sex matched and their blood glucose values were <126 mg/dl and never taking any diabetic medication. Control group who visited other clinics due to acute diseases were

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**Table 1**  
Basic characteristics and Vitamin D levels in Type 1 DM and Controls.

	Type 1 DM (n = 296)	Control (n = 151)	P value
Gender (M/F)	167/129	91/60	0,835
Age (mean ± SD)(Year)	35,9 ± 10,9	37,1 ± 10,9	0,275
<b>BMI (kg/m<sup>2</sup>)</b>	<b>24,7 ± 5,3</b>	<b>26,5 ± 6,9</b>	<b>0,013</b>
Waist circumference (cm)	86,7 ± 10,7	87,8 ± 14,9	0,461
<b>Fasting Blood Glucose (mg/dl)</b>	<b>199,7 ± 10,2</b>	<b>90,7 ± 13,7</b>	<b>0,000</b>
<b>C-peptide</b>	<b>0,5 ± 1,6</b>	<b>1,9 ± 0,8</b>	<b>0,000</b>
<b>HbA1c (%)</b>	<b>8,7 ± 2,1</b>	<b>5,4 ± 0,4</b>	<b>0,000</b>
Vitamin D (nmol/L)	22,9 ± 17,4	24,5 ± 19,3	0,382
Vitamin D Deficiency			
>30 nmol/L (Normal)	%23,9 (71)	%27,1 (41)	0,445
12,5–30 nmol/L (Mild deficiency)	%45,9 (136)	%48,3 (73)	
<12,5 nmol/L (Severe deficiency)	%24,2 (89)	%24,6 (37)	
Ca (mmol/L)	10,4 ± 7,3	9,7 ± 0,4	0,238
P	3,8 ± 3,3	3,6 ± 2,3	0,490
LDL-Cholesterol	117,0 ± 36,6	117,7 ± 32,9	0,836
HDL-Cholesterol	54,0 ± 14,2	53,3 ± 13,5	0,604
Triglycerid	114,8 ± 80,1	110,7 ± 94,5	0,635

randomly selected. After verbal informed consent blood samples provided for analysis. Patients with liver disorders, renal disorders, diabetes mellitus, metabolic bone disorders, primary hyperparathyroidism, or epilepsy treated by anticonvulsant therapy or on other medications that might alter 25(OH)vitamin D or 1,25(OH)<sub>2</sub> vitamin D metabolism and thyroid functions were excluded from the study.

Venous samples were collected into plain tubes after overnight fasting. serum was separated and stored at 708C for a week until analysis. Serum 25-hydroxyvitamin D level the standard indicator of vitamin D status was measured by radioimmunoassay technique. For that aim a kit 25(OH)<sub>2</sub>D<sub>3</sub>-Ria-CT (Bruxelles-Belgium) was used. Other biochemical parameters included this study with vitamin D were calcium, alkaline phosphates, phosphorus, PTH, Mg and creatinine. Serum levels of these biochemical parameters were determined according to standard laboratory procedures. Serum PTH levels were measured by electrochemiluminescent immunoassay (Modular Analytics E170; Roche Diagnostics). Other biochemical parameters included in this study were albumin, calcium, and phosphorus. Serum levels of these biochemical parameters were determined according to standard laboratory procedures using the autoanalyzer Olympus 2700. Corrected calcium levels were calculated on the basis of albumin levels. The criteria used to define vitamin D sufficiency, insufficiency, and deficiency were 25OHD levels of ≥30 ng/mL, 21–29 ng/mL, and ≤20 ng/mL, respectively [13].

Anthropometric measurements included body mass index (BMI) and waist circumference. Body mass index was calculated as the weight (kg) divided by the height (m) squared. Waist circumference was determined as measurements taken at the midpoint between lowest rib and iliac crest after a normal inspiration and expiration.

Statistical analysis was performed with SPSS 15.0. Means ± SD and percentages are presented unless otherwise indicated. Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables and nonparametric Mann–Whitney test was used. Chi-square analysis was performed to test for differences in proportions of categorical variables between two or more groups. Pearson's correlation coefficient was used to evaluate the strength of association between variables. The level *P* < 0.05 was considered as the cut-off value for significance.

### 3. Results

296 Type 1 DM patients and 151 healthy controls were included to the study. The characteristics of groups was shown in Table 1.

Most of the participants were male in Type 1 DM group (167 male, 129 female respectively). On the other hand 91 of healthy subjects were male and remaining 60 were female. Mean age of type 1 DM group was 35,9 ± 10,9 years versus 37,1 ± 10,9 for healthy controls. Anthropometrically only the mean BMI of both groups was significantly differs (Table 1). On the other hand fasting blood glucose, HbA1c levels were significantly higher in diabetic group, whereas lipid profiles do not show significant difference (Table 1).

25-Hydroxyvitamin D levels were similar between patients with type 1 diabetes (22, 9 ± 17, 4 ng/ml) and controls (24, 5 ± 19, 3 ng/ml) (*p* = 0,382). Most of the participants have 25-Hydroxyvitamin D deficiency. In type 1 diabetic group 24, 2% (*n* = 89) of patients have severe vitamin D deficiency and 45, 9% (*n* = 136) of them have mild vitamin D deficiency. On the other hand the severe vitamin D deficiency reaches up to 24, 6% (*n* = 37) and mild vitamin D deficiency 48, 3% (*n* = 73) in healthy controls (Table 1).

As shown in Table 2 serum 25 Hydroxyvitamin D levels was not associated with most of the biochemical or anthropometric parameters. Only a weak association was seen between BMI and vitamin D levels in overall group and type 1 DM group and also a weak correlation was found between HDL-Cholesterol and vitamin D levels in overall group and healthy controls.

### 4. Discussion

In our study we do not found any significant difference between vitamin D levels of type 1 DM patients and healthy controls. On the other hand it was seen that most of the participants in both groups have mild or severe vitamin D deficiency. Vitamin D deficiency is a prevalent situation in Turkey. Especially studies focused on women,

**Table 2**  
Correlations with vitamin D levels with anthropometric and biochemical parameters.

	Over all		Control		Type 1 DM	
	r	p	r	p	r	p
BMI	<b>-0,102</b>	<b>0045</b>	-0,093	0291	<b>-0,125</b>	<b>0048</b>
Waist circumference	-0,035	0538	-0,019	0834	-0,035	0456
FBG	0,003	0946	-0,084	0306	0,042	0473
c-peptide	-0,003	0959	-0,062	0525	0,016	0788
HbA1c	-0,065	0170	-0,058	0479	-0,051	0385
LDL-Cholesterol	0,043	0362	0,052	0524	0,039	0509
HDL-Cholesterol	<b>0,105</b>	<b>0027</b>	<b>0,182</b>	<b>0026</b>	0,067	0254
Triglycerid	0,039	0413	0,001	0987	0,065	0266
Ca	-0,046	0334	0,085	0298	-0,059	0313
P	-0,010	0839	0,010	0904	-0,016	0788

persons living in nursing homes, and the elderly reveals high prevalence of vitamin D deficiency and insufficiency [14]. In a recent study conducted in Turkey with adult participants, it was revealed no significant difference found in mean vitamin D levels between type 1 DM and health controls although the mean vitamin D levels were higher than our levels [8]. But on the other hand another study conducted in Turkey with type 1 diabetic children and adolescent shows a significant difference in vitamin D levels [15]. This discrepancy may be a result of age difference between study populations. Moreover also some other studies in Italy [10], Germany [9], America [11] and Canada [12] show results concordant with our findings. There are studies addressed the association between vitamin D deficiency and type 1 DM [1–7]. This variations may be a result of the bias of studies geographical distribution, dietary intake, skin color, ethnic features, genetic predisposition or sun avoiding behavior. So future efforts that are larger, prospective, and take into account this bias that may influence serum 25-OH vitamin D would be beneficial.

There are some limitation in this study. First of all the exact duration and time of sun exposure could affect the result. We found out lower levels of vitamin D in diabetics and health controls compared with western studies. This condition reflects insufficiency of vitamin D is a common in Turkish population. But this condition could be related with genetic factors as well as decreased sun exposure.

As a result there were no difference between type 1 diabetics and healthy controls according to their vitamin D levels. Further studies with a larger sample of patients will improve our understanding of the relation of vitamin D and diabetes.

## References

- [1] Holic FM. Diabetes and the vitamin D connection. *Curr Diabetes Rep* 2008;8:393–8.
- [2] Wolden-Kirk H, Overbergh L, Cristesen HT, Brusgaard K, Mathieu C. Vitamin D and diabetes: its importance for beta cell and immune function. *Mol. Cel. Endocrinol.* 2011;347:106–20.
- [3] Kahn HS, Morgan TM, Case LD, Dabelea D, Mayer-Davis EJ, Lawrence JM, et al. Association of type 1 diabetes with month of birth among US youth: SEARCH for diabetes in youth study. *Diabetes Care* 2009;32:2010–2.
- [4] Svoren BM, Volkening LK, Wood JR, Laffel LM. Significant vitamin D deficiency in youth with type 1 diabetes mellitus. *J Pediatr* 2009;154:132–4.
- [5] Greer RM, Rogers MA, Bowling FG, Buntain HM, Harris M, Leong GM, et al. Australian children and adolescent with type 1 diabetes have low vitamin D levels. *Med J Aust* 2007;187:59–60.
- [6] Bener A, Alsaïd A, Al-Ali M, Al-Kubaisi A, Basha B, Abraham A, et al. High prevalence of vitamin D deficiency in type 1 diabetes mellitus and healthy children. *Acta Diabetol* 2009;46:183–9.
- [7] Al-Daghri NM, Al-Attas OS, Alokail MS, Alkharfy KM, Yakout SM, Aljohani NJ, et al. Lower vitamin D status is more common among Saudi adults with diabetes mellitus type 1 than in non-diabetics. *BMC Public Health* 2014 Feb 11;14:153. <https://doi.org/10.1186/1471-2458-14-153>.
- [8] Yavuz DG, Keskin L, Kiyıcı S, Sert M, Yazıcı D, Sahin I, et al. Vitamin D receptor gene BsmI, FokI, ApaI, TaqI polymorphisms and bone mineral density in a group of Turkish type 1 diabetic patients. *Acta Diabetol* 2011;48:329–36. <https://doi.org/10.1007/s00592-011-0284-y>.
- [9] Biershenk L, Alexander J, Wasserfall C, Haller M, Schatz D, Atkinson M. Vitamin D levels in subjects with and without type 1 diabetes residing in a solar rich environment. *Diabetes Care* 2009;32(11):1977–9. <https://doi.org/10.2337/dc09-1089>.
- [10] Verrotti A, Basciani F, Carle F, Morgese G, Chiarelli F. Calcium metabolism in adolescents and young adults with type 1 diabetes mellitus without and with persistent microalbuminuria. *J Endocrinol Investig* 1999;22:198–202.
- [11] Thrailkill KM, Jo CH, Cockrell GE, Moreau CS, Lumpkin Jr CK, Fowlkes JL. Determinants of undercarboxylated and carboxylated osteocalcin concentrations in type 1 diabetes. *Osteoporos Int* 2012;23:1799–806. <https://doi.org/10.1007/s00198-011-1807-7>.
- [12] Masse PG, Pacifique MB, Tranchant CC, Arjmandi BH, Ericson KL, Donovan SM, et al. Bone metabolic abnormalities associated with well-controlled type 1 diabetes (IDDM) in young adult women: a disease complication often ignored or neglected. *J Am Coll Nutr* 2010;29(4):419–29. <https://doi.org/10.1080/07315724.2010.10719859>.
- [13] Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int* 2005;16:713–6.
- [14] Hekimsoy Z, Dinc G, Kafesciler S, Onur E, Guvenc Y, Pala T, et al. Vitamin D status among adults in the Aegean region of Turkey. *BMC Public Health* 2010;10:782. <https://doi.org/10.1186/1471-2458-10-782>.
- [15] Mutlu A, Yeşiltepe G, Özsu E, Çizmecioglu FM, Hatun Ş. Vitamin D deficiency in children and adolescents with type 1 diabetes. *J. Clin. Res. Pediatr. Endocrinol.* 2011;3(4):179–83. <https://doi.org/10.4274/jcrpe.430>.