VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
E-ISSN 2450–8187

This Research Paper is accompanied by an Editorial, see page 222.

Ehsan Aliniagerdroudbari[1], Zahra Farhangian[2], Sepideh Babaniamansour[3], Mahtab Niroomand[4]
[1]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of Internal Medicine, School of Medicine, Imam Khomeini Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[3]School of Medicine, Islamic Azad University Tehran Faculty of Medicine, Tehran, Iran
[4]Department of Internal Medicine, Division of Endocrinology, Clinical Research Development Unit of Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Association between Glycemic Control Status and Serum Level of Vitamin D3 in Patients with Type 2 Diabetes: A Cross-Sectional Study

ABSTRACT

Objective: This study aimed to assess the association between glycemic control status and serum levels of vitamin D3 in Iranian patients with type 2 diabetes (T2D).

Materials and methods: This was a cross-sectional study on 452 patients with T2D in Tehran, Iran, performed between September 2019 and September 2020. We assessed the diabetes laboratory test and vitamin D3 level in all participants using the Enzymatic Glucose Oxidase method. Data were analyzed using SPSS version 24.

Results: a total of 452 patients were enrolled in this study (mean age: 59.4 ± 11.4 years, 63.5% females). Vitamin D deficiency was reported in half of the participants. Deficient vitamin D was significantly associated with higher mean level of hemoglobin A1c, fasting plasma glucose, total cholesterol, and low-density lipoprotein-cholesterol ($p < 0.05$). Multiple regression showed that the level of vitamin D3 could be a good predictor of hemoglobin A1c after adjusting for confounding variables affecting the hemoglobin A1c (regression coefficient: 0.442, 95% CI, 0.072–0.811, $p = 0.063$).

Conclusions: With the alarming rates of vitamin D deficiency in patients with T2D, there was a significant direct association between vitamin D3 and hemoglobin A1c levels before and after adjusting for the associated factors. (Clin Diabetol 2022, 11; 4: 262–268)

Keywords: diabetes mellitus, vitamin D, vitamin D deficiency, glycated hemoglobin A, dietary supplements

Introduction

Diabetes Mellitus is a chronic metabolic disorder that has become one of the most important global health issues. It affected 422 million people worldwide (8.5% of adults) in 2014 and is estimated to increase to 642 million by 2040. The incidence of diabetes showed an increasing trend in the past decades, especially in low- and middle-income countries. The Mediterranean Region has the highest rates of diabetes. A study reported more than four million Iranians have diabetes [1]. An upward trend in the incidence rate among the Iranian population suggests 9.2 million diabetes patients by 2030 [2–5]. Type 2 diabetes (T2D) has high morbidity and mortality rates (fifth leading cause of death in the Iranian population) [6–8].

Address for correspondence:
Dr. Mahtab Niroomand, Associate Professor of Endocrinology
Department of Internal Medicine,
Division of Endocrinology
Clinical Research Development Unit of Shohada Tajrish Hospital
Shahid Beheshti University of Medical Sciences, Tehran, Iran
Address: Arabi Ave, Daneshjoo Blvd, Velenjak, 7th Floor, Bldg. No. 2,
Shahid Beheshti University of Medical Sciences, Tehran, Iran
phone: +989126191851
e-mail: mahtabniroomand@yahoo.com
Clinical Diabetology 2022, 11; 4: 262–268
DOI: 10.5603/DK.a2022.0032
Received: 20.12.2021 Accepted: 10.06.20222

Vitamin D is commonly known as a vitamin that affects bones by the regulation of calcium (Ca) and phosphorus (P) [9]. Adequate sun exposure helps the conversion of 7-dehydrochlostrol (at the lower layer of the epidermis) into vitamin D2 (pre D3) and then into vitamin D3 in healthy skin. The vitamin D is affected by a number of supplements and fortified foods. 1α,25-dihydroxy vitamin D3 [1,25(OH)2D3] is an activated form of vitamin D. Vitamin D deficiency has a high prevalence from 2.5% to 96% in the Iranian population. Studies showed that geographical region, history of some diseases, the intake of vitamin D3, etc., were the causative factors for the high prevalence of vitamin D deficiency [10–14]. Recent studies stated that vitamin D deficiency has a crucial role in patients with T2D. It increases the incidence rate and worsens the patients' clinical condition [15, 16]. The receptor of 1,25(OH)2D3 stimulates the insulin secretion in pancreatic beta-cells via direct or intracellular Ca way. Some studies showed that vitamin D deficiency was accompanied by a decrease in beta cell function in patients with T2D by decreasing the insulin secretion, insulin and C-peptide response, insulin sensitivity, and glucose tolerance [15, 17, 18]. A study among Iranian patients with diabetes showed that hemoglobin A1c (HbA1c) level had a significant inverse association with vitamin D3 level [19]. In contrast, some studies among patients with diabetes showed there was no significant difference in the prevalence of vitamin D deficiency between patients with diabetes and healthy individuals. Also, there was no significant association between HbA1c and vitamin D3 levels [20, 21]. Comparing the vitamin D deficiency between patients with T2D and people without diabetes in Saudi Arabia also showed that although 98% of the studied population had vitamin D deficiency, no significant difference was observed in the serum level of vitamin D3 between the case and control groups [22].

There is no consensus on the findings, and more studies are required to ascertain the results. This study aimed to assess the association between glycemic control status and serum levels of vitamin D3 in patients with T2D and the possible associated factors in an Iranian population.

Materials and methods

Study design

This cross-sectional study was conducted at diabetes clinics affiliated with Shahid Beheshti University of Medical Sciences in Tehran, Iran, between September 2019 and September 2020. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved the executive protocol of the study. The study was conducted in accordance with the Declaration of Helsinki (7th revision 2013). The written consent form was obtained from all participants before the study. The study imposed no additional costs on the patients or the health system.

Data collection

All patients aged 18 years or older, diagnosed with T2D (at least six months ago) or on antidiabetic drugs, entered the study. The exclusion criteria were as follows: T1D, T2D diagnosis within less than six months, any conditions affecting the serum level of vitamin D3 like thyroid or parathyroid disorder, cancer, pregnancy, breastfeeding, anticonvulsant, or corticosteroids.

All patients underwent a face-to-face interview and were asked to fill out the demographic and disease-related questionnaires. Demographic data and baseline information was as follows: age, gender, occupation, education level, regular physical activity (at least 30 minutes a day for five days a week) [23], and Ca intake based on the amount of dairy intake and the use of Ca supplements [24].

Data related to the disease were as follows: duration of DM [25], type of treatment (oral medication or insulin therapy), family history of DM (in first- or second-degree relatives), diabetes micro- or macrovascular complications, and other risk factors, such as history of atherosclerotic cardiovascular disease, hypertension (HTN) and dyslipidemia (based on the patient's medical records).

Diabetes complications were as follows: retinopathy (based on the fundoscopy reports over the past year), neuropathy (based on history, physical examinations, electromyography, and nerve condition velocity), nephropathy, and diabetic foot ulcer (based on history and physical examinations).

HTN is defined as systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg or a history of taking antihypertensive medicines. Dyslipidemia is defined as total cholesterol (TC) $\geq$ 200 mg/dL, triglycerides (TG) $\geq$ 150 mg/dL, high-density lipoprotein-cholesterol (HDL-c) level $<$ 45 mg/dL and low-density lipoprotein-cholesterol (LDL-c) level $\geq$ 100 mg/dL [26]. Patients were asked to provide information on the Ca and vitamin D supplements taken in the last six months.

The researchers measured the height using a wall-mounted stadiometer (Heightronic 235; Measurement Concepts, Snoqualmie, WA). BMI (kg/m^2) was calculated by dividing weight (kg) by the square of height (m^2). Normal weight, overweight, and obesity were defined as BMI $<$ 25 kg/m^2, BMI 25 to 29.9 kg/m^2, and BMI $\geq$ 30 kg/m^2, respectively [27].

Finally, biochemical tests were performed to measure the serum levels of fasting plasma glucose (FPG; enzymatic glucose oxidase method), HbA1c, TG, TC, LDL-c, and 25(OH) vitamin D3 with a coefficient of vari-

ation of less than 5% in all patients as part of routine prediction care program. Laboratory data was noted.

The most recent ADA criteria for diagnosing diabetes were as following: FPG ≥ 126 mg/dL (7.0 mmol/L), HbA1c ≥ 6.5% or 2-hr plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during an OGTT (75-g) or random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) [25]. HbA1c level in the last three months was used to categorize the glycemic control status; good (HbA1c ≤ 7%), moderate (HbA1c = 7–8%), poor (HbA1c = 8–9%) and bad (HbA1c > 9%).

Ca intake was divided into low (< 500 mg/day), moderate (500–1000 mg/day), and high (> 1000 mg/day), based on the estimation of daily dietary Ca intake using a table in the Clinician's Guide to Prevention and Treatment of Osteoporosis [24].

The serum level of 25(OH) D, less than 20 ng/mL (< 50 nmol/L), 20 to 30 ng/mL (50 to 75 nmol/L), and at least 30 ng/mL (≥ 75 nmol/L) was considered as a deficiency, insufficiency, and sufficient, respectively [28].

Statistical analysis

According to the study conducted by Aljabri KS, the prevalence of vitamin D deficiency in T2D was 30–40% [28]. Therefore, the sample size was at least 358, based on the formula below and 95% confidence interval. Sampling was done in six-month and with a convenience method.

$\alpha = 0.05$, Z1-a/2 = 1.96, p = 0.37, q = 0.63, d = 0.05

All data were analyzed with SPSS version 24.0 (SPSS Inc., Chicago, IL., USA). Categorical variables were described using the frequency (percentage) of the data. Continuous variables were described using the mean ± standard deviation of the data. An independent samples t-test was applied to compare continuous variables between different groups of vitamin D3 ranges. The association between categorical variables was assessed using the chi-square test or Fisher's exact test. Different seasonal blood sampling was a confounding factor for the serum level of vitamin D3, which was adjusted by regression. Multiple logistic regression analysis was performed to determine the independent predictor factors with 95% CI. P < 0.05 was considered statistically significant.

Ethics approval

The implementation of the project was approved by the ethics committee of Shahid Beheshti University of Medical Sciences.

Consent to participate

All participants provided informed consent before the study.

Results

The present study included 452 patients (63.5% were females). The mean age was 59.4 ± 11.4 years (ranging from 25 to 89). The mean level of 25(OH) D was 25.3 ± 18.3 ng/mL (ranging from 1.5 to 122). The frequency of vitamin D deficiency, insufficiency, and sufficiency were 217 (48%), 97 (21.5%), and 138 (30.5%), respectively. The frequency of vitamin D deficiency in males and females was 53.9% and 44.6%, respectively. Demographic data and baseline information are shown in Table 1.

Most patients were housewives, obese, with equal or less than twelve years of education, duration of DM of less than five years, good glycemic control, dyslipidemia, HTN, positive family history of DM in first-degree relatives, moderate Ca intake, and on oral medications. History of taking any supplement, regular physical activity, and micro- or macrovascular complications were less frequent in patients. The laboratory data were mostly in fall and winter (Tab. 1).

Figure 1 shows the distribution of glycemic control status based on the vitamin D3 range. In this regard, the prevalence of good glycemic control was higher in those with sufficient vitamin D3 and vice versa in those with deficient vitamin D3.

The vitamin D3 ranges varied significantly by gender, occupation, glycemic control status, history of Ca intake, history of taking any vitamin D and Ca-D supplements, and history of HTN, nephropathy, and neuropathy ($p < 0.05$). Mean of age was significantly higher in patients with sufficient vitamin D3 ($p < 0.05$). However, the mean levels of HbA1c, FPG, TC, and LDL-c were significantly higher in those with deficient vitamin D ($p < 0.05$) (Tab. 1).

Figure 2 shows the distribution of HbA1c values depending on the level of vitamin D3. In this regard, HbA1c was higher in those with lower vitamin D3 levels.

Multiple regression showed that the level of HbA1c still had a significant inverse association with vitamin D range (HbA1c was higher in those with sufficient level of vitamin D3) after adjusting for the confounding variables affecting the HbA1c (regression coefficient: 0.442, 95% CI, 0.072–0.811, p = 0.063). Therefore, vitamin D3 level can be an appropriate and independent factor for predicting the level of HbA1c in diabetes patients (Tab. 2).

Discussion

The present study assessed the vitamin D3 status among patients with T2D. The results showed that an abnormal vitamin D3 level had been a problem for the most studied population. The high prevalence of vitamin D deficiency is not a surprise because this

Table 1. Demographic Data and Baseline Information in Different Groups of Vitamin D3

Variables	Vitamin D3 range				
	Total (n = 452)	Deficient (n = 217)	Insufficient (n = 97)	Sufficient (n = 138)	p-value*
Gender					
Male	165 (36.5)	89 (41)	39 (40.2)	37 (26.8)	0.018
Female	287 (63.5)	128 (59)	58 (59.8)	101 (73.2)	
Occupation					
Unemployed	10 (2.2)	3 (1.4)	0	7 (5.1)	< 0.001[a]
Retired	72 (15.9)	40 (18.4)	13 (13.4)	19 (13.8)	
Housewife	208 (46)	88 (40.6)	40 (41.2)	80 (58)	
Employee	31 (6.9)	16 (7.4)	13 (13.4)	2 (1.4)	
Merchant	46 (10.2)	25 (11.5)	14 (14.4)	7 (5.1)	
Education level (year)					
Illiterate	48 (10.6)	23 (10.6)	8 (8.2)	17 (12.3)	0.410
≤ 12	268 (59.3)	124 (57.1)	57 (58.8)	87 (63)	
> 12	51 (11.3)	25 (11.5)	15 (15.5)	11 (8)	
Glycemic control status					
Good	174 (38.5)	74 (34.1)	38 (39.2)	62 (44.9)	0.004
Moderate	110 (24.3)	47 (21.7)	22 (22.7)	41 (29.7)	
Poor	85 (18.8)	41 (18.9)	23 (23.7)	21 (15.2)	
Bad	83 (18.4)	55 (25.3)	14 (14.4)	14 (10.1)	
Duration of DM, range (year)					
< 5	153 (33.8)	73 (33.6)	33 (34)	47 (34.1)	0.870
5–10	137 (30.3)	66 (30.4)	27 (27.8)	44 (31.9)	
10–20	103 (22.8)	52 (24)	25 (25.8)	26 (18.8)	
≥ 20	59 (13.1)	26 (12)	12 (12.4)	21 (15.2)	
Type of treatment					
None	18 (4)	14 (6.5)	2 (2.1)	2 (1.4)	0.096
Insulin	31 (6.9)	10 (4.6)	7 (7.2)	14 (10.1)	
Oral medications	321 (71)	154 (71)	72 (74.2)	95 (68.8)	
Both	82 (18.1)	39 (18)	16 (16.5)	27 (19.6)	
Family history of DM					
None	145 (32.1)	67 (30.9)	34 (35.1)	44 (31.9)	0.888
In first-degree relative	289 (63.9)	142 (65.4)	58 (59.8)	89 (64.5)	
In second-degree relative	18 (4)	8 (3.7)	5 (5.2)	5 (3.6)	
Ca intake					
Low	42 (9.3)	21 (9.7)	8 (8.2)	13 (9.4)	0.006
Moderate	200 (44.2)	109 (50.2)	40 (41.2)	51 (37)	
High	125 (27.7)	42 (19.4)	32 (33)	51 (37)	
Regular physical activity					
Yes	110 (24.3)	47 (21.7)	24 (24.7)	39 (28.3)	0.366
No	342 (75.7)	170 (78.3)	73 (75.3)	99 (71.7)	
Vitamin D3 supplement					
Yes	28 (6.2)	1 (0.5)	7 (7.2)	20 (14.5)	< 0.001
No	424 (93.8)	216 (99.5)	90 (92.8)	118 (85.5)	
Ca-D supplement					
Yes	46 (10.2)	10 (0.9)	8 (3.1)	28 (11.3)	< 0.001
No	406 (89.8)	207 (99.1)	89 (96.9)	110 (89.9)	
Laboratory date					
Spring and Summer	191 (42.3)	89 (41)	39 (40.2)	63 (45.7)	0.620
Fall and Winter	261 (57.7)	128 (59)	58 (59.8)	75 (54.3)	
HTN (%)	308 (68.1)	136 (62.7)	67 (69.1)	105 (76.1)	0.030
Dyslipidemia (%)	375 (83)	176 (81.1)	83 (85.6)	116 (84.1)	0.574
Retinopathy (%)	89 (19.7)	32 (14.7)	24 (24.7)	30 (21.7)	0.122
Nephropathy (%)	123 (27.2)	50 (23)	24 (24.7)	49 (35.5)	0.032
Neuropathy (%)	174 (38.5)	86 (39.6)	26 (26.8)	62 (44.9)	0.017
DFU (%)	26 (5.8)	9 (4.1)	7 (7.2)	10 (7.2)	0.371
AS-CVD (%)	110 (24.3)	51 (23.5)	19 (19.6)	40 (29)	0.236
Age (year)	59.4 ± 11.4	57.7 ± 11.6	59.5 ± 10	62 ± 11.5	0.002
BMI (kg/m^2)	29.8 ± 5.6	29.8 ± 5.8	29.4 ± 5.7	29.9 ± 5.2	0.718
HbA1c level (%)[a]	7.7 ± 1.7	8.0 ± 1.9	7.7 ± 1.6	7.3 ± 1.4	0.001[b]
FPG (mg/dL)	154.6 ± 59	163.8 ± 65.9	150.1 ± 51.1	143.2 ± 50	0.004[b]
TG (mg/dL)	159.7 ± 91.2	166.3 ± 97.1	165.4 ± 108.7	145.4 ± 62.7	0.085
TC (mg/dL)	171.2 ± 44.9	175.3 ± 46.7	173.1 ± 46.4	163.4 ± 40	0.046
LDL-c (mg/dL)	95 ± 35.7	98.7 ± 37.7	97.8 ± 35.1	87.1 ± 31.7	0.008

AS-CVD — atherosclerotic cardiovascular disease; BMI — body mass index; Ca-D — calcium plus vitamin D3; DFU — diabetic foot ulcer; DM — diabetes mellitus; FPG — fasting plasma glucose; HTN — hypertension; HbA1c — hemoglobin A1c; LDL-c — low-density lipoprotein-cholesterol; TC — total cholesterol; TG — triglycerides

*p-value refers to the different mean of frequency of each variable among vitamin D3 range. a refers to the analysis with Fisher's exact test. a r = –0.151 Kits' standard range: vitamin D3 (> 29 ng/mL), HbA1c (4–5.7%), FPG (70–100 MG/DL), TG (0–150 MG/DL), TC (≤ 200 MG/DL), and LDL-c (≤ 129 MG/DL). The overall coefficient variation was 7% (less than 10%) for low, medium, and high levels of vitamin D3

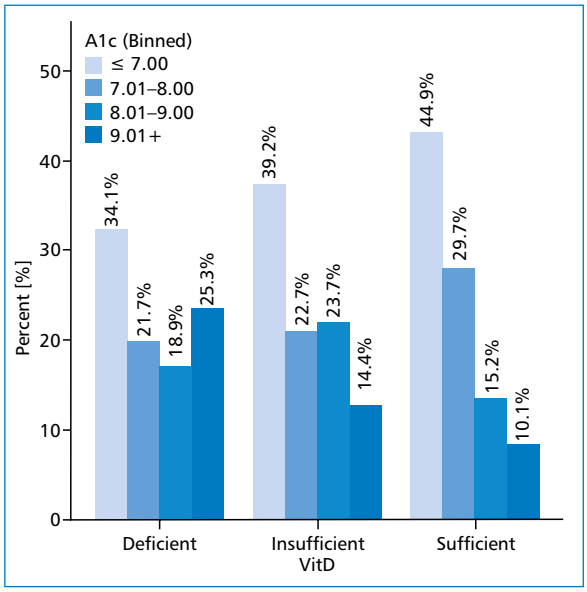

Figure 1. Distribution the Glycemic Control Status in Different Groups of Vitamin D3

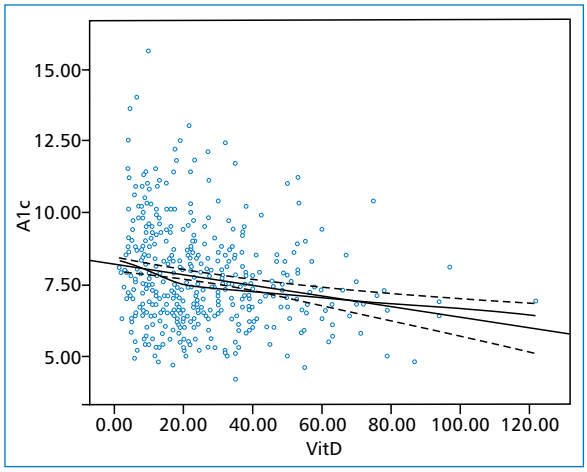

Figure 2. Scatter Dot Plot, Association between A1c (%) and Vitamin D3 Level (ng/mL)

study was performed in Tehran (36°2' N of Iran, with only eight hours of sunlight radiation). Tehran is one the most air-polluted cities in the Middle East, which is accompanied by a decrease in the cutaneous synthesis of vitamin D3 [6, 29]. Today, various studies pointed to the crucial role of 1,25(OH)2D3 receptors of beta cells, making it very important in diabetes patients. They reported a higher prevalence of vitamin D deficiency among patients with T2D compared to people without diabetes [30, 31]. Meanwhile, Anyanwu et al. conducted a study in Lagos, Nigeria. They showed that the prevalence of vitamin D deficiency was not significantly different between patients with T2D (63.2%) and people without diabetes (53.3%) [32].

Our results also showed that there was a significant association between vitamin D deficiency and bad glycemic control status. The HbA1c and vitamin D3 levels had a significant inverse association, after adjusting the confounding variables affecting the level of HbA1c.

Consistent with our results, Djalali et al. conducted a case-control study among 90 patients with T2D and 90 people without diabetes in Tehran, Iran. They showed that the prevalence of vitamin D deficiency (< 50 nmol/L) was significantly higher in the case (58.9%) than in the control groups (47%). Mean of age, BMI and vitamin D3 were lower in the case group, but not significantly [6]. Aljabri assessed the association between the level of HbA1c and vitamin D3 in 2908 females with T2D in Saudi Arabia. They showed that the level of vitamin D3 had a significant direct association with age and a significant inverse association with the level of HbA1c [28].

Contrary to our findings, Bonakdaran et al. conducted a study among 119 patients with T2D. The prevalence of vitamin D deficiency was 26.1%. There was no significant difference in age, gender, duration of DM, the serum level of TC and HbA1c between those with and without vitamin D deficiency. The prevalence of retinopathy was significantly higher in those with vitamin D deficiency [33]. The difference stems from considering a higher level of vitamin D3 as a deficiency in our study (< 16.6 ng/mL compared to < 20 ng/mL), along with the difference in the sample size. In addition, Heidari et al. assessed the level of vitamin D3 among 84 non-obese patients with T2D, in Ahvaz, Iran. The prevalence of vitamin D deficiency was 96.43%. Serum level of vitamin D3 had a significant inverse association with female gender and higher level of FPG. There was no significant correlation between serum level of vitamin D3 and waist circumstance, level of HbA1c, and insulin [34]. A higher prevalence of vitamin D deficiency might be related to the location of their study at Ahvaz (a warm and sunny climate, city with many residents with an indoor lifestyle). Small sample size and not adjusting for the associated factor for the analysis can be responsible for the lack of significant correlations in their study.

Limitations

The limitation of this study was that although it had a large sample size, chronic medical conditions such as HTN and nephropathy were highly prevalent, contributing to the abnormal serum level of vitamin D3. Fortunately, the prevalence of vitamin D deficiency was low in patients over 60 years old, based on the decision of the Centers for Disease Control and Prevention on

Table 2. Simultaneous Effect of Variables on HbA1c Level

Variable	n = 452	Regression coefficient	95% CI		P-level	P
			Lower	Upper		
Vitamin D3 range						
Deficient	217 (48)	0.442	0.072	0.811	0.019	0.063
Insufficient	97 (21.5)	0.226	–0.213	0.665	0.312	
Sufficient	138 (30.5)	Ref	–	–	–	
Type of treatment						
None	18 (4)	Ref	–	–	–	0.012
Insulin	31 (6.9)	–0.698	–1.698	0.301	0.170	
Oral medications	321 (71)	–1.094	–1.892	–0.296	0.007	
Both	82 (18.1)	–0.656	–1.527	0.216	0.140	
Age, years		–0.020	–0.039	–0.002	0.027	0.027
Duration of DM, years						
< 5	153 (33.8)	–0.852	–1.405	–0.300	0.003	< 0.001
5–10	137 (30.3)	–0.331	–0.870	0.207	0.227	
10–20	103 (22.8)	0.095	–0.456	0.647	0.734	
≥ 20	59 (13.1)	Ref	–	–	–	

CI — confidence interval; DM — diabetes mellitus; Ref — reference group
P-level refers to the comparison of the specified level with reference level. P refers to the effect of the variables

the free distribution of vitamin D supplement in these people. Therefore, it is highly recommended to give vitamin D supplements to younger people.

Conclusions

Vitamin D3 status has a vital role in the development and progression of T2D. This study showed that vitamin D deficiency and insufficiency had an alarming rate among patients with T2D. Besides, vitamin D3 and HbA1c levels had a significant direct association after adjusting for the associated factors. Therefore, the findings call for greater attention to this issue. It could be of paramount importance to prevent vitamin D deficiency and its complications, especially among patients with T2D, considering all modifiable factors associated with vitamin D deficiency.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector.

Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

None declared.

REFERENCES

1. Esteghamati A, Etemad K, Koohpayehzadeh J, et al. Trends in the prevalence of diabetes and impaired fasting glucose in association with obesity in Iran: 2005-2011. Diabetes Res Clin Pract. 2014; 103(2): 319–327, doi: 10.1016/j.diabres.2013.12.034, indexed in Pubmed: 24447808.
2. Mirzaei M, Rahmaninan M, Mirzaei M, et al. Epidemiology of diabetes mellitus, pre-diabetes, undiagnosed and uncontrolled diabetes in Central Iran: results from Yazd health study. BMC Public Health. 2020; 20(1): 166, doi: 10.1186/s12889-020-8267-y, indexed in Pubmed: 32013917.
3. Moosaie F, Davatgari RM, Firouzabadi FD, et al. Lipoprotein(a) and apolipoproteins as predictors for diabetic retinopathy and its severity in adults with type 2 diabetes: a case-cohort study. Can J Diabetes. 2020; 44(5): 414–421, doi: 10.1016/j.jcjd.2020.01.007, indexed in Pubmed: 32205075.
4. Moosaie F, Firouzabadi FD, Abouhamzeh K, et al. Lp(a) and Apolipoproteins as predictors for micro- and macrovascular complications of diabetes: A case-cohort study. Nutr Metab Cardiovasc Dis. 2020; 30(10): 1723–1731, doi: 10.1016/j.numecd.2020.05.011, indexed in Pubmed: 32636121.
5. Hashemi P, Esteghamati A, Nakhjavani M, et al. Comparative Effect of Metformin Alone or in Combination with Glibenclamide on Oxidative Stress Markers of Patients with Type 2 Diabetes: A Randomized Open Clinical Trial. Ann Clin Diabetes Endocrinol. 2018; 1(1): 1007.
6. Djalali M, Taheri E, Saedisomeolia A, et al. Vitamin D status of type 2 diabetic patients compared with healthy subjects in the Islamic Republic of Iran. Eastern Mediterranean Health Journal. 2013; 19(Supp. 3): 6–11, doi: 10.26719/2013.19.supp3.s6.
7. Jafarzadeh F, Javanbakht A, Bakhtar N, et al. Association between diabetic retinopathy and polymorphisms of cytokine genes: a systematic review and meta-analysis. Int Ophthalmol. 2022; 42(1): 349–361, doi: 10.1007/s10792-021-02011-9, indexed in Pubmed: 34432176.
8. Janbakhsh A, Abedinfam M, Sobhiyeh MR, et al. Prevalence of peripheral artery disease in patients with infectious diabetic foot ulcer in Imam Reza Hospital in Kermanshah during 2019-2020.

J Educ Health Promot. 2021; 10(1): 170, doi: 10.4103/jehp.jehp_907_20, indexed in Pubmed: 34250104.
9. Moghimi N, Faridfar A, Shahriarirad R, et al. Evaluation of the relationship between vitamin d levels and related serum markers as well as disease activity in patients with rheumatoid arthritis: a cross-sectional study in western iran. , doi: 10.21203/rs.3.rs-125995/v2.
10. Tabrizi R, Moosazadeh M, Akbari M, et al. High prevalence of vitamin D deficiency among iranian population: a systematic review and meta-analysis. Iran J Med Sci. 2018; 43(2): 125–139, indexed in Pubmed: 29749981.
11. Hashemipour S, Larijani B, Adibi H, et al. Vitamin D deficiency and causative factors in the population of Tehran. BMC Public Health. 2004; 4: 38, doi: 10.1186/1471-2458-4-38, indexed in Pubmed: 15327695.
12. Vatandost S, Jahani M, Afshari A, et al. Prevalence of vitamin D deficiency in Iran: a systematic review and meta-analysis. Nutr Health. 2018; 24(4): 269–278, doi: 10.1177/0260106018802968, indexed in Pubmed: 30296903.
13. Omranzadeh A, Baradaran A, Ghodsi A, et al. Neutrophil-to-Lymphocyte ratio as an inflammatory marker in familial mediterranean fever: a systematic review and meta-analysis. J Child Sci. 2021; 11: e100–e109, doi: 10.1055/s-0041-1728730.
14. Hajivandi S, Dachek A, Salimi A, et al. Comparison of the separate and combined effects of physiotherapy treatment and corticosteroid injection on the range of motion and pain in nontraumatic rotator cuff tear: a randomized controlled trial. Adv Orthop. 2021; 2021: 6789453, doi: 10.1155/2021/6789453, indexed in Pubmed: 34733561.
15. Mathieu C, Gysemans C, Giulietti A, et al. Vitamin D and diabetes. Diabetologia. 2005; 48(7): 1247–1257, doi: 10.1007/s00125-005-1802-7, indexed in Pubmed: 15971062.
16. Salahshour F, Mehrabinejad MM, Zare Dehnavi A, et al. Pancreatic neuroendocrine tumors (pNETs): the predictive value of MDCT characteristics in the differentiation of histopathological grades. Abdom Radiol (NY). 2020; 45(10): 3155–3162, doi: 10.1007/s00261-019-02372-x, indexed in Pubmed: 31897681.
17. Hoseini SA, Aminorroaya A, Iraj B, et al. The effects of oral vitamin D on insulin resistance in pre-diabetic patients. J Res Med Sci. 2013; 18(1): 47–51, indexed in Pubmed: 23900423.
18. Mirmiranpoor H, Hashemi P, Firouzabadi FD, et al. Effect of essential unsaturated fatty acids on structure and function of catalase at high glucose concentration. Int J Enteric Pathog. 2017; 5(3): 80–84, doi: 10.15171/ijep.2017.19.
19. Alkhatatbeh MJ, Abdul-Razzak KK. Association between serum 25-hydroxyvitamin D, hemoglobin A1c and fasting blood glucose levels in adults with diabetes mellitus. Biomed Rep. 2018; 9(6): 523–530, doi: 10.3892/br.2018.1159, indexed in Pubmed: 30546881.
20. Neyestani TR, Gharavi A, Kalayi A. Iranian diabetics may not be Vitamin D deficient more than healthy subjects. Acta Medica Iranica. 2008; 46(4): 337–341.
21. Ghavam S, Ahmadi MR, Panah AD, et al. Evaluation of HbA1C and serum levels of vitamin D in diabetic patients. J Family Med Prim Care. 2018; 7(6): 1314–1318, doi: 10.4103/jfmpc.jfmpc_73_18, indexed in Pubmed: 30613518.
22. Alhumaidi M, Agha A, Dewish M. Vitamin d deficiency in patients with type-2 diabetes mellitus in southern region of Saudi Arabia. Maedica (Bucur). 2013; 8(3): 231–236, indexed in Pubmed: 24371490.
23. Centers for Disease Control and Prevention. How much physical activity do adults need? https://www.cdc.gov/physicalactivity/basics/adults/index.htm (2.09.2020).
24. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2014; 25(10): 2359–2381, doi: 10.1007/s00198-014-2794-2, indexed in Pubmed: 25182228.
25. Oyama H, Tada M, Takagi K, et al. Long-term risk of malignancy in branch-duct intraductal papillary mucinous neoplasms . Gastroenterology. 2020; 158(1): 226–237.e5, doi: 10.1053/j.gastro.2019.08.032 , indexed in Pubmed: 31473224.
26. Heydari I, Radi V, Razmjou S, et al. Chronic complications of diabetes mellitus in newly diagnosed patients. International Journal of Diabetes Mellitus. 2010; 2(1): 61–63, doi: 10.1016/j.ijdm.2009.08.001.
27. A healthy lifestyle - WHO recommendations. Body mass index - BMI. https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi (25.08.2020).
28. Aljabri KS. Vitamin D deficiency in female Saudis with Type 2 diabetes mellitus. Trends Diabetes Metab. 2019; 1-2, doi: 10.15761/tdm.1000110.
29. Nouri-Vaskeh M, Sadeghifard S, Saleh P, et al. Vitamin D deficiency among patients with tuberculosis: a cross-sectional study in iranian-azari population. Tanaffos. 2019; 18(1): 11–17, indexed in Pubmed: 31423135.
30. Ozfirat Z, Chowdhury TA. Vitamin D deficiency and type 2 diabetes. Postgrad Med J. 2010; 86(1011): 18–25; quiz 24, doi: 10.1136/pgmj.2009.078626, indexed in Pubmed: 20065337.
31. Issa CM. Vitamin D and type 2 diabetes mellitus. Adv Exp Med Biol. 2017; 996: 193–205, doi: 10.1007/978-3-319-56017-5_16, indexed in Pubmed: 29124701.
32. Anyanwu AC, Olopade OB, Onung SI, et al. Serum vitamin D levels in persons with type 2 diabetes mellitus in Lagos, Nigeria. International Journal of Diabetes and Clinical Research. 2020; 7(4), doi: 10.23937/2377-3634/1410133.
33. Bonakdaran S, Varasteh AR, Khaajeh-Dalouie M. Serum 25 hydroxy vitamin D3 and laboratory risk markers of cardiovascular diseases in type 2 diabetic patients. IJEM. 2010; 11(5): 504–509, indexed in Pubmed: 19370277.
34. Haidari F, Zakerkish M, Karandish M, et al. Association between serum vitamin D level and glycemic and inflammatory markers in non-obese patients with type 2 diabetes. Iran J Med Sci. 2016; 41(5): 367–373, indexed in Pubmed: 27582585.