Vitamin D status in patients with type-2 diabetes mellitus in Riyadh City, Saudi Arabia

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Background
Type-2 diabetes mellitus (T2DM) is a progressive and chronic disease characterized by both β-cell dysfunction and increased insulin resistance. Vitamin D is a crucial factor in the development of T2DM because it is necessary for normal insulin secretion. Despite ample sunshine, vitamin D deficiency is common in the Middle East.
Objective
To report the vitamin D status and its impact on the people in Riyadh City, Saudi Arabia, with T2DM.
Patients and methods
The study was carried out on 100 patients of 31–79 years old with T2DM. According to their vitamin D status, they were classified into three groups: group 1 (deficient, vitamin D: <20 ng/ml), group 2 (insufficient, vitamin D: 20–30 ng/ml), and group 3 (normal, vitamin D: >30 ng/ml). All were subjected to history taking, clinical examination, and assessment of fasting blood samples of serum concentrations of 25-hydroxy vitamin D [s-25(OH)D], blood glucose, glycated hemoglobin, lipid profile, liver enzymes (alanine transaminase and aspartate transaminase), urea and creatinine.
Results
Inadequate vitamin D level was observed in 80% of the participants, with a mean s-25(OH)D of 18.3±10.9 ng/ml. S-25(OH)D correlated negatively with fasting blood sugar (FBS) (P=0.008), with cholesterol and low-density lipoprotein (P=0.012 and 0.003, respectively). The low vitamin D status was strongly associated with poor glycemic control (P=0.001) and in females (P=0.002). There was no significant association between s-25(OH)D level and different age groups.
Conclusion
There is an overwhelming prevalence of vitamin D deficiency in our sample of Saudi diabetic patients. Association of low vitamin D status with poor glycemic control and atherogenic lipid profile suggests a role of vitamin D in the control of T2DM and dyslipidemia and the importance of early detection of its deficiency and vitamin D supplementation.

Keywords:
type-2 diabetes, vitamin D, Saudi Arabia

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Introduction

Type-2 diabetes mellitus (aspartate transaminase) is a progressive and chronic disease characterized by both β-cell dysfunction and increased insulin resistance, defined as the inadequate response of skeletal muscle, liver, and adipose tissue to endogenous insulin secretions, and few drugs ameliorate increases in insulin resistance [1].

Since the discovery of oil in the Arabian Gulf area in the 1950s, there had been dramatic increase in the incidence of metabolic disorders especially diabetes, mainly due to changes in the pattern of lifestyle and food intake [2,3].

Saudi Arabia is currently at the top in the list of Middle East countries with the highest number of estimated cases of diabetes mellitus [4]. The prevalence of T2DM in Saudi Arabia is around 23.7% of the total population which is the highest by percentage in Asia [5].

Vitamin D is nature's own product; it is produced in the skin through the action of sunlight on 7-dehydrocholestrol [6]. Vitamin D has been suggested to have a great role in global health not only in the musculoskeletal system but also in cellular proliferation and differentiation, immune system modulation, inhibition of rennin synthesis and erythropoiesis [7].

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Vitamin D deficiency is a crucial factor in the development of T2DM. Vitamin D is believed to improve the body's sensitivity to insulin and thus reduce the risk of insulin resistance. It can also regulate the production of insulin in the pancreas through control of the insulin receptor gene [8]. However, the link between vitamin D status and diabetes still remains poorly understood.

In the Middle East, despite ample sunshine, vitamin D deficiency is common due to cultural practice and dark skin color [9]. Few studies from the Middle East have examined the association between vitamin D status and diabetes [10–12].

As a result, this relationship needs to be specifically explored in different populations, including the Middle East. The aim of this research, therefore, was to clarify vitamin D status in the Saudi Arabian people with T2DM.

Patients and methods

Patients

According to The American Diabetic Association (2015) [13]. Fasting glucose equal to or greater than 126 mg/dl (7.0 mmol/l) or glucose concentration 2 h after the administration of 75 g oral glucose load equal to or greater than 200 mg/dl (11.1 mmol/l). Random glucose equal to or greater than 200 mg/dl or glycated hemoglobin (HbA1c) equal to or greater than 6.5%; after taking informed consent of each participants to participate in the study we identified 100 patients of 31–79 years old with T2DM who were treated in an outpatient clinic of Endocrinology and Metabolism in Riyadh City, Saudi Arabia from January 2016 to January 2017.

According to Endocrine Society Clinical Practice Guideline of vitamin D deficiency [14]. Vitamin D deficiency was defined as 25-hydroxy vitamin D [25 (OH)D] of less than 20 ng/ml (<50 nmol/l), vitamin D insufficiency was defined as a 25(OH)D between 20 and 30 ng/ml (50–75 nmol/l). The normal serum concentration 25-hydroxy vitamin D [s-25(OH)D] was defined as at least 30 ng/ml (≥75 nmol/l); according to their vitamin D levels, the study participants were classified into three groups:

(1) Group 1: less than 20 ng/ml.
(2) Group 2: 20–30 ng/ml.
(3) Group 3: more than 30 ng/ml.

Exclusion criteria for the studied groups:

(1) Patients with type 1 diabetes.
(2) Pregnant and lactating women.
(3) Patients with hepatic or renal diseases.
(4) Patients who had received supplements containing vitamin D before testing.

Methods

Individuals of the studied groups were subjected to the following:

(1) Full history taking.
(2) Thorough clinical examination.
(3) Laboratory investigations.

The laboratory investigations included:

Sample collection

Fasting blood samples were collected in aseptic syringes and were equally aliquoted in red, gray, and lavender vacutainers. Red-capped vacutainers were used for the estimation of lipid profile, liver enzymes (alanine transaminase and aspartate transaminase), urea, creatinine and vitamin D (25 hydroxycholecalciferol); gray-capped vacutainers were used for the estimation of blood sugar and lavender vacutainers were used for the estimation of HbA1c.

Method

25(OH)D Total assay was estimated in VIDAS [BIOMRIEUX MINI Vidas (France) analyzer] by enzyme-linked fluorescent assay technique. Glucose was estimated by glucose oxidase and a modified Trineder color reaction, catalyzed by the enzyme peroxidase. Fasting lipid profile and liver enzymes were estimated by Konelab kits using Indiko fully automated analyzers. HbA1c was measured in clover A1c using the well-established method of boronate affinity.

Statistical analysis

The collected data were summarized in terms of mean± SD for quantitative data and frequency and percentage for qualitative data. Analysis was done using analysis of variance (*F*-test) using post-hoc least significant difference for multiple comparisons and Student's *t*-test for quantitative data. Fischer's exact test is used for analysis of qualitative data. A *P* value of less than 0.05 was considered statistically significant. All statistical analyses were carried out using the computerized statistical package for the social sciences (SPSS, version 20.0 for Windows; SPSS Inc., Chicago, Illinois, USA).

Results

A total of 100 diabetic patients (49% were men and 51% women) were enrolled in this study. The mean age

of the study group was 51.8±12.3 year. The mean HbA1c among diabetic patients was 9.4±1.9. The average serum 25(OH)D value was 18.3±10.9 ng/ml (Table 1).

According to the vitamin D level, the patients were classified into three groups: group 1 (deficient, <20 ng/ml), group 2 (insufficient, 20 : 30/ml) and group 3 (normal, >30 ng/ml).The results were analyzed using the *F*-test to compare data for group 1, group 2, and group 3 as shown in Table 2.

Seventy-one (71%) patients had vitamin D deficiency, only 9% had vitamin D insufficiency, and one-fifth (20%) were normal with significant statistical difference in their vitamin D level between the three groups (*P*=0.001). FBS was significantly related to the vitamin D level with *P*=0.008.The total cholesterol and low-density lipoprotein (LDL) were also significantly related to the vitamin D status with *P*=0.012 and 0.003, respectively.

As regards other biochemical parameters, there was no statistically significant difference among the study groups.

Figure 1 shows the level of HbA1c in different vitamin D groups: 1, 2, and 3, where HbA1c was significantly higher in group 1 (9.67) and group 2 (9.63) than in group 3 (8.37) with *P*=0.023.

In comparing the different levels of HbA1c among the studied groups to assess the role of vitamin D deficiency in glycemic control, it was found that the number of patients with HbA1c (>8) was highest in group 1 (vitamin D-deficient group) 54 (76.1%), which was statistically significant with Fischer's exact test=18.23 and *P*=0.001 (Table 3).

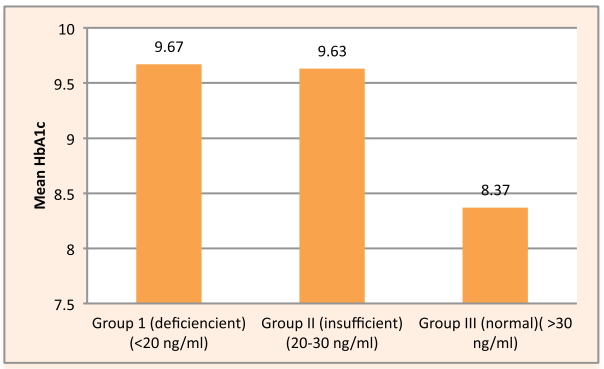
Table 4 shows the vitamin D status in different age groups; vitamin D deficiency was maximally observed

Table 1 Characteristics of the study participants

Sex [*n* (%)]	
Males	49 (49)
Females	51 (51)
Age (mean±SD)	51.8±12.3
Vitamin D (mean±SD)	18.3±10.9
FBS (mean±SD)	200±62.4
HbA1c (mean±SD)	9.4±1.9
Cholesterol (mean±SD)	196.6±41.5
HDL (mean±SD)	40.3±11.3
LDL (mean±SD)	125.7±34.2
TGS (mean±SD)	155.2±87.8
ALT (mean±SD)	24.5±14.3
AST (mean±SD)	22.7±14.4
Urea (mean±SD)	29.1±9.7
Creatinine (mean±SD)	0.81±0.3

ALT, alanine transaminase; AST, aspartate transaminase; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TGS, Triglycerides.

Figure 1



Mean glycated hemoglobin (HbA1c) among different groups of vitamin D level.

Table 2 Comparison of group 1, group 2, and group 3

	Vitamin D status			*F* test	*P* value
	Group 1 (deficient) (<20 ng/ml) (*N*=71)	Group 2 (insufficient) (20–30 ng/ml) (*N*=9)	Group 3 (normal) (>30 ng/ml) (*N*=20)		
Vitamin D	12.01±3.35	25.58±2.51[a]	37.44±4.10[a,b]	445.7	0.001**
FBS (diabetic>126 mg/dl)	209.54±59.39	210.22±80.74	161.90±51.52[a,b]	5.06	0.008**
Cholesterol (*N*<200 mg/dl)	204.39±39.19	175.78±32.42[a]	178.35±45.98[a]	4.62	0.012*
HDL (*N*>35 mg/dl)	39.21±12.35	45.0±8.92	42.10±7.24	1.37	0.26
LDL (optimal<100 mg/dl)	133.10±32.73	105.78±23.29[a]	108.6±34.87[a]	6.30	0.003**
TGS (*N*<150 mg/dl)	159.39±86.68	119.11±40.06	156.30±105.7	0.84	0.44
ALT (*N*≤52 μ/l)	25.49±15.59	18.78±8.03	23.55±10.84	0.94	0.40
AST (*N*≤52 μ/l)	23.83±16.48	18.11±4.37	20.50±6.96	0.91	0.41
Urea (*N*=10–50 mg/dl)	28.37±8.96	27.0±6.46	32.55±12.53	1.72	0.19
Creatinine (*N*=0.2–1.2 mg/dl)	0.81±0.27	0.73±0.31	0.84±0.23	0.49	0.61

Data are presented as the mean±SD; ALT, alanine transaminase; AST, aspartate transaminase; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TGS, Triglycerides; [a]Significant compared with group 1; [b]Significant compared with groups 1 and 2; **P* value for differences between groups. ***P*<0.01.

Table 3 Vitamin D status in relation to glycated hemoglobin

HbA1c%	Vitamin status			Total	Fischer's exact test	*P* value
	Group 1	Group 2	Group 3			
6.5–7	9 (12.7)	2 (22.2)	4 (20.0)	15 (15.0)	18.32	0.001**
7.1–8	8 (11.3)	0 (0.0)	10 (50.0)	18 (18.0)		
>8	54 (76.1)	7 (77.8)	6 (30.0)	67 (67.0)		
Total	71 (71.0)	9 (9.0)	20 (20.0)	100		

**$P<0.01$.

Table 4 Vitamin D status according to age and sex of the study groups

	Group 1 (deficient) (<20 ng/ml) (*N*=71)	Group 2 (insufficient) (20–30 ng/ml) (*N*=9)	Group 3 (normal) (>30 g/ml) (*N*=20)	Fischer's exact test	*P* value
Age (years)					
31–40	17 (23.9)	2 (22.2)	2 (10.0)	13.31	0.06
41–50	22 (31.0)	0 (0.0)	5 (25.0)		
51–60	15 (21.1)	2 (22.2)	8 (40.0)		
61–70	9 (12.7)	3 (33.3)	5 (25.0)		
71–80	8 (11.3)	2 (22.2)	0 (0.0)		
Sex					
Male	41 (57.7)	0 (0.0)	8 (40.0)	12.27	0.002**
Female	30 (42.3)	9 (100)	12 (60.0)		

**$P<0.01$.

in the fifth decade (41–50 years) 22 (31%) patients, while the normal vitamin D level was maximally observed in the sixth decade (51–60 years), eight (40%) patients. However, there was no statistically significant difference between different age groups (P=0.06).

As regards sex distribution, in vitamin D-deficient patients (group 1): men were more predominant, 41 (57.7%); while in group 2 and group 3, women were more predominant, nine (100%) and 12 (60%), respectively and the results were statistically significant (P=0.002) (Table 4).

Discussion

Vitamin D deficiency has strong argument in its effect on pathogenicity and development of T2DM. The diverse effect of vitamin D on glucose and calcium homeostasis has made it an ideal contender to know its role in glycemic control in T2DM. So our study was conducted to identify vitamin D status in diabetic patients and its relation to glycemic control and different biochemical parameters.

The present study shows that the prevalence of vitamin D deficiency in diabetic participants was alarmingly high, nearly more than 2/3 (71%) of the study participants had vitamin D deficiency [s-25(OH)D: <20 ng/ml] and 9% had vitamin D insufficiency [s-25 (OH)D: 20–30 ng/ml]. These together suggest that 80% of the studied diabetic patients had inadequate vitamin D level, which was in accordance with the findings of Zhang *et al.* [15], who studied the prevalence of diabetes in vitamin D-deficient Kuwaiti adults and also found that 80% of Kuwaiti adults had inadequate vitamin D level and is nearly similar to the results obtained by Sadiya *et al.* [12], who explore the vitamin D status and its relationship with metabolic markers in persons with obesity and T2DM in the UAE and reported that 83.2% of Emirati diabetic patients had vitamin D deficiency. But it was lower than the findings of Alhumaidi *et al.* [11], who study vitamin D deficiency in patients with T2DM in the southern region of Saudi Arabia and reported that the prevalence of inadequate vitamin D level was 98.5% in their studied groups which was considered the highest reported prevalence in Saudi Arabia.

The mean vitamin D level in the present study was 18.3±10.9 ng/ml. This result was higher than the finding of Zhang *et al.* [15] who reported a median vitamin D level of 13.8 ng/ml; the results obtained by Sadiya *et al.* [12] who reported a mean vitamin D level of 33.8±20.3 nmol/l=13.5±8.1 ng/ml, Alhumaidi *et al.* [11] who also found that the vitamin D level in his diabetic participants was 15.8±7.5 ng/ml, Dabbour *et al.* [16] who studied vitamin D status in T2DM patients in the Makkah region of Saudi Arabia and it was 6.17±2.47 ng/ml and Kafeshani *et al.* [17] who studied the vitamin D level in diabetic and nondiabetic patients in Isfahan, Iran and found that the mean vitamin D

among diabetic patients was 27.44±3.66 nmol/l=10.97±1.46 ng/ml. It was also nearly similar to the findings of Chaudhary *et al.* [18] who study vitamin D level in diabetic Indians and it had a mean of 19.09±5.34 ng/ml.

The low vitamin D status in our study population may result from reduced exposure to sunshine and low dietary intake of fortified products and dietary supplements. Researchers have shown that vitamin D deficiency is highly prevalent among healthy Saudi women as well as men and is largely attributed to obesity, poor exposure to sunlight, poor dietary vitamin D supplementation, sedentary lifestyle and lack of education, which in turn affects bone mineral density and bone turnover markers [19,20].

The present study demonstrated that FBS and HbA1c were significantly high in patients with low vitamin D status, which was in coincidence with the finding of Sadiya *et al.* [12], Chaudhary *et al.* [18], Swamy *et al.* [21] and Sehgal *et al.* [22], who evaluated vitamin D levels in diabetic Indians. It was also similar to the findings of Zhang *et al.* [23] who studied the vitamin D status in Chinese T2DM, Boyraz *et al.* [24] who compared the vitamin D level in Turkish diabetic patients on oral hypoglycemic agents and insulin treatment and Shenoy *et al.* [25] who studied the association between vitamin D, FBS, HbA1c, and fasting lipid profile in euglycemic Indians.

In the present study, low vitamin D status was strongly associated with poor glycemic control, where the highest level of HbA1c (>8) was present in 67.1% of group 1 (vitamin D deficient patients) which was in agreement with Chaudhary *et al.* [18] and Zhang *et al.* [23]. This was in contrary to Sadiya *et al.* [12] and Olt [26] who studied the relationship between vitamin D and glycemic control in Turkish patients with T2DM and found nonsignificant association between low vitamin D status and poor glycemic control.

Taking into consideration that all the study participants are diabetics, we should pay our attention toward the possible role of vitamin D deficiency in T2DM which is thought to have several potential mechanisms, including increasing the formation of proinflammatory cytokines and acute-phase reactants, likely to increase low-grade inflammation, as well as the well-known promotion of insulin secretion from β-cells [27–29]. The efficacy of vitamin D in stimulating insulin release can be affected by vitamin D axis gene polymorphisms, such as those for the activating enzyme (vitamin D 1α-hydroxylase; CYP27B1) and the transport protein (vitamin D binding protein), as well as for vitamin D receptors (VDR) [30–35]. In another study, variants of the VDRs in pancreatic β-cells, skeletal muscle, and adipose tissue were associated with variation in the effects of vitamin D on glucose metabolism [36]. Certain vitamin D binding proteins and allelic variations in the VDR gene might also affect insulin secretion and glucose tolerance, which, in turn, might contribute to the genetic risk of T2DM [37].

In the present study, low vitamin D status was associated with atherogenic lipid profile. The low vitamin D status in the present study was associated with a significant increase in cholesterol and LDL, but with nonsignificant increase in triglyceride levels and also had a nonsignificant effect on high-density lipoprotein level which is in accordance with many studies like the study obtained by Sadiya *et al.* [12] and the study of Saedisomeolia *et al.* [38] who study the association between the serum level of vitamin D and lipid profiles in T2DM patients in Iran.

Moreover, several previous studies support that vitamin D deficiency alone directly affect the lipid profile irrespective of the diabetic status of the patients: Alhumaidi *et al.* [11] found that the mean vitamin D level was lower in nondiabetic than in diabetic individuals which was associated with a nonsignificant increase of cholesterol in the nondiabetic group and Shenoy *et al.* [25] who found that low vitamin D status was significantly associated with atherogenic lipid profile in euglycemic Indians.

It was suggested that vitamin D can modify the lipid profile by direct and indirect mechanisms. It can directly decrease triglyceride levels by increasing the activity of lipoprotein lipase in adiposity [39]. It can also indirectly reduce the serum levels of total and LDL cholesterol as calcium interferes with fatty acid absorption through the formation of insoluble calcium–fatty complexes in the gut, resulting in increasing the conversion of cholesterol to bile acids [40] however, the relation to calcium was not included in the present study.

Regarding vitamin D status in different age groups, there was nonsignificant relation between vitamin D status and age in diabetic participants which was similar to the findings of Kafeshani *et al.* [17] and Shenoy *et al.* [25] and in contrast with many studies as those of Zhang *et al.* [15], Sadiya *et al.* [12], and

Dabbour *et al.* [16] all found significant positive relation between vitamin D status and age. In the present study, there was no particular age group associated with low vitamin D status in Saudi diabetic patients which mean that vitamin D deficiency can occur at any age as the general Saudi population are not exposed to sunlight and is characterized by lack of outdoor activities because of the hot weather most of the year, especially in Riyadh.

In the present study, female sex was significantly associated with lower vitamin D status which was in accordance with Zhang *et al.* [15] and in contrary to many previous studies who document a nonsignificant difference between men and women [11,12,16,17,23]. This can be explained by the fact that in the Arabic world, women had lower outdoor activities and the use of sunscreen before going outdoors. And specifically in Saudi Arabia all women wore their traditional black Abaya outdoors which reduced the surface area exposed to direct sunlight [41]. The black clothing blocks 100% of ultraviolet-B radiation [42].

Limitation of the study: the present study is limited by the small number of patients and lack of lifestyle data. Parathyroid hormone, calcium, and other inflammatory markers were not measured and those can affect the islet β-cell function.

Conclusion

The purpose of the current study was to clarify vitamin D status in Saudi Arabian people with T2DM. The findings of this study suggest an alarmingly high prevalence of vitamin D deficiency, and low vitamin D status in patients with T2DM in Riyadh city in Saudi Arabia. The present data indicate that the availability of adequate sunlight alone is not sufficient for the prevention of vitamin D deficiency and raises awareness of hypovitaminosis D in the diabetic population, regardless of the geographic location. Also low vitamin D status was associated with poor glycemic control and atherogenic lipid profile in diabetic patients, which mean that early detection of vitamin D deficiency and supplementation may help in the improvement of glycemic control and prevent complications of T2DM and dyslipidemia.

Meanwhile, there was no significant relation between vitamin D status and different age groups and also a low vitamin D status was highly prevalent in women, which suggest that deficiency can occur at any age specially in women, so any program directed to improve vitamin D status in diabetics should include encouraging outdoor activities, exposure to direct sunlight (may be in health clubs), early detection, and supplementation of vitamin D should be directed toward all diabetic individuals of any age specially women.

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Conflicts of interest

There are no conflicts of interest.

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