

Relationship of Vitamin-D Deficiency with Kidney Disease in Patients with Type-2 Diabetes Mellitus (T2DM) in the Makkah Region: A Cross-Sectional Study

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Aim: Vitamin D deficiency is linked with type 2 diabetes mellitus (T2DM) and the occurrence of complications in patients with type 2 diabetes mellitus. None of the studies have focused on the association between vitamin D levels in patients with type 2 diabetes mellitus and diabetic nephropathy (DN) in the Makkah region, Saudi Arabia. Hence, the purpose of this study is to investigate the relationship of vitamin D with kidney disease in patients with T2DM in the Makkah region, of Saudi Arabia.

Materials and Methods: This descriptive cross-sectional study was conducted at different hospitals in the Makkah region on T2DM patients from 2021 to 2022. In total, 328 patients with confirmed diabetes were enrolled in this study. T2DM patients over the aged >18 to 92 years were included in the study. General laboratory characteristics of the study population were measured, including fasting blood sugar, HbA1C (Glycated hemoglobin), vitamin D, kidney function (BUN-Blood urea nitrogen and creatinine), and lipid profiles (cholesterol, triglycerides, LDL-Low density lipoprotein, and HDL-High density lipoprotein).

Results: 46.6% (n=153) of participants had normal serum vitamin D levels. Insufficient and deficient serum vitamin D level were observed in 43.9% (n=144) and 9.5% (n=31) of participants, respectively. Of the participants, 25.9% (n=85) had good glycemic control (<7.0%). Moderate and poor glycemic control were observed in 39.9% (n=131) and 34.1% (n=112) of the participants, respectively. A significant negative correlation (p<0.5) was found between vitamin D levels and kidney function test results (blood urea nitrogen and serum creatinine levels). An inverse relationship was observed between HbA1c levels and vitamin D deficiency.

Conclusion: Nephropathy is more likely to develop in people with type 2 diabetes mellitus and vitamin D deficiency.

Keywords: prevalence, diabetes, type-2 diabetes mellitus, T2DM, vitamin-D, nephropathy

Introduction

Diabetes mellitus is an intricate metabolic disease that poses a global health burden because an alarming number of premature deaths and morbidities have been documented in recent years.^{1,2} Impaired insulin production and action are the manifestation of diabetes mellitus.³ Diabetes mellitus is categorized into Type-1 diabetes mellitus (T1DM) and T2DM. In recent decades, the increasing health burden of T2DM has become a major international concern. T2DM has been reported in >95% of individuals with diabetes.⁴ Globally, approximately 462 million individuals are affected by T2DM, which represents 6.28% of the world's population.⁵ The prevalence rate in the Kingdom of Saudi Arabia ranges from 9% to 22% and there are an estimated seven million patients with diabetes in the country.^{6,7} Similar patterns of T2DM prevalence have been noticed in Kuwait.^{7,8} Risk factors for the development of T2DM include obesity, sedentary lifestyle, alcohol consumption, smoking, and fatty diet.⁹ The primary organs affected with T2DM are skeletal muscles,

brain, and kidneys.¹⁰ Approximately 40% of patients with diabetes are diagnosed with DN, which is characterized by kidney dysfunction and proteinuria.¹¹ The frequency of DN increases with an increase in T2DM rises.¹² Vitamin D is a hormonal molecule that participates in the homeostasis of calcium and phosphate. Additionally, it is also involved in the genomic (expression of genes) and non-genomic functions (glucose metabolism, enhancing insulin resistance, insulin secretion, and stimulation of receptors associated with insulin).^{13,14} The metabolically active form of vitamin D is produced in the kidney.¹⁵ Several studies have reported that vitamin D deficiency contributes to the development of chronic kidney disease (CKD).^{16–20} In addition, vitamin D deficiency accelerates the development and genesis of T2DM because it is involved in insulin secretion.²¹ Many studies have revealed a link between vitamin D levels and chronic kidney disease or diabetes mellitus.^{22–24} Numerous studies conducted in humans and animals have indicated that vitamin D has reno-protective effects, such as anti-fibrosis, anti-inflammatory, and anti-proteinuria effects, and also prevents podocyte damage.^{25–28} Vitamin D supplements are beneficial in patients with CKD or diabetes mellitus.^{29,30} Most studies have focused on the relationship between vitamin D, CKD, and diabetes mellitus.^{21–24} None of the studies have investigated the relationship between vitamin D and nephropathy in T2DM patients in the Makkah region. Hence, the purpose of this study is to investigate the relationship of vitamin D with kidney disease for patients with T2DM in the Makkah region, of Saudi Arabia.

Materials and Methods

Design of the Study

The current descriptive cross-sectional study was conducted in different hospitals in the Makkah region from 2021 to 2022 on T2DM patients after obtaining permission from each hospital and informed consent from the patients. The study was conducted under the Declaration of Helsinki, and the protocol was approved by The Biomedical Research Ethics Committee at Umm Al-Qura University, Makkah, Saudi Arabia (HAPO-02-K-012-2023-03-1486). Randomly selected T2DM patients over the aged >18 to 92 years were included in the study which were sex and age matched. Patients with renal and cardiac diseases were excluded from the study. As the sun in Makkah region cities shines in both the winter and summer seasons in similar amounts, there were no major seasonal effects on the vitamin D levels in the body. Standard range for general laboratory parameters are as follows: HbA1c (normal-5.6 to 6.4, diabetes->6.4), Vitamin D (50nM), BUN (6–24mg/dL), Creatinine (for men-0.59–1.04 mg/dL and for women-0.74–1.35 mg/dL), Cholesterol (<200 mg/dL), LDL (<100 mg/dL), HDL (for men-<40 mg/dL and for women-<50 mg/dL), and HbA1c category (normal-<7.0% good glycaemic control, moderate-7-8.5% moderate glycaemic control and poor->8.5% -poor glycaemic control).

Sample Size

In total, 328 patients with confirmed diabetes were included in the study. The following parameters were collected.

1. Characteristics of the study participants, which include age and gender.
2. General laboratory characteristics of the study population were measured, including fasting blood sugar, HbA1C, Vitamin D, kidney function (BUN and creatinine), and lipid profiles (cholesterol, triglycerides, LDH, and HDL).

Statistical Analysis

General laboratory parameters were expressed as mean±SD deviation or median (interquartile range). Categorical variables, such as normal level, insufficiency, and deficiency, were analysed as proportions (%). SPSS package version 11.0 for Microsoft Windows was used to analyse the data collected. In addition, HbA1C was classified as normal, moderate, or poor glycaemic levels and analysed as proportions. The stacking bar chart was used to illustrate which categories of HbA1C were more likely to have vitamin D deficiency. Linear regression analysis was performed to determine the correlation between vitamin D levels and kidney function test results (BUN and creatinine).

Statistical Software

Data were analysed using SPSS (version 15.0; IBM Corp., Armonk, NY, USA), and graphs, tables, and other graphics were prepared using Microsoft Word and Excel.

Results

A total of 328 patients with diabetes were included in this study, 43.6% of whom were male (n=143) and 56.5% of whom were female (n=185) (Table 1). A general and laboratory profile [fasting blood sugar (FBS), HbA1C, blood urea nitrogen (BUN), creatinine, vitamin-D level, triglycerides (TAG), HDL and LDL] of the participants were collected, and creatinine levels (91.5±99.81) were higher while HDL (1.2±0.39) levels were lower (Table 2). In terms of glycaemic control, 25.9% (n=85), 39.9% (n=131), and 34.1% (n=112) of the participants had good, moderate, and poor glycaemic control, respectively (Table 3). Among the participants, 46.6% (n=153), 43.9% (n=144), and 9.5% (n=31) had normal, insufficient, and deficient serum vitamin D levels, respectively (Table 3). A significant negative correlation ($r=0.130$, $p=0.032$) was found between vitamin D and BUN levels (Figure 1). There was also a significant negative correlation ($r=0.0454$, $p=0.442$) between vitamin D and creatinine (Figure 2). According to Figure 3, patients with HbA1c (7–8.5%, $R^2=0.0012$, $p=0.5353$) were more likely to be vitamin-D deficient.

Table 1 General Characteristics of the Study Participants

Variables		N	Percentage
Gender	Male	143	43.6
	Female	185	56.4
	Total	328	100
Variables		Mean	SD
Age		51.7	± 20.35

Note: The data has been represented in Mean±SD (standard deviation).

Table 2 General Laboratory Parameters of the Study Population

Laboratory Parameters	Mean ± SD	Median, IQR
FBS	9.5 ± 13.01	8.1, 6.8–10.2
HbA1C	8.3 ± 1.90	7.9, 6.9–9.3
Vitamin D	40.7 ± 31.99	29.2, 24–47.6
BUN	5.9 ± 5.20	4.7, 3.7–6.3
Creatinine	91.5 ± 99.81	72, 56–91
Cholesterol	4.4 ± 2.70	4.3, 3.3–5
Triglycerides	1.6 ± 0.97	1.4, 1.1–1.8
HDL	1.2 ± 0.39	1.2, 0.9–1.4
LDL	2.8 ± 1.21	2.77, 2–3.5

Note: The data has been represented in Mean±SD, Median and Interquartile range.

Abbreviations: FBS, Fetal bovine serum; HbA1c, Glycated haemoglobin; BUN, Blood urea nitrogen; HDL, high density lipoprotein; LDL, Low density lipoprotein.

Table 3 Laboratory Characteristics of HbA1c & Serum Vitamin-D in the Study Population

Laboratory Characteristics	n	Percentage
HbA1c category		
< 7.0% (Good glycemic control)	85	25.9
7–8.5% (Moderate glycemic control)	131	39.9
>8.5% (Poor glycemic control)	112	34.1
Serum Vitamin D		
≥ 30ng/mL (Normal levels)	153	46.6
20.1–29.9 (Vitamin D insufficiency)	144	43.9
< 20ng/mL (Vitamin D deficiency)	31	9.5

Note: The data has been represented in N and %. HbA1c (Glycated haemoglobin).

Discussion

Makkah region cities receives a lot of sunlight (equal sunlight in both summer and winter) and is situated at a latitude of 21.3891° north, 39.8579° E, with an altitude of 277 m. However, approximately 63% of the patients had a vitamin-D deficiency (VDD) in the Makkah region.³¹ The general medical inpatient population was found to have high levels of vitamin D deficiency.³² The current study reported a 9.1% (<20ng/mL) prevalence of vitamin D deficiency in 31 T2DM patients. Several reports showed that prevalence of vitamin D deficiency ranged from 28%-75%.^{33–35} Sadat-Ali et al³⁴ reported a 37% prevalence of vitamin D deficiency in healthy men in eastern Saudi Arabia. Aljabri et al³⁶ reported a 27% prevalence of vitamin D deficiency in patients with T2DM in Saudi Arabia. The current study reported normal serum vitamin D levels and vitamin D insufficiency in 46.6% (≥30ng/mL) and 43.9% (20.1–29.9 ng/mL) of patients with T2DM, respectively. Several studies have reported a similar prevalence of normal serum vitamin D and vitamin D insufficiency in patients with T2DM in Saudi Arabia.^{34,37–39} Furthermore, our results showed that lower serum vitamin D was observed in patients with T2DM, which is consistent with previous findings.^{36,39,40} In the present study, our results showed that 25.9%, 39.9%, and 34.1% of the participants had good, moderate, and poor glycemic control, respectively. This is in agreement with several studies conducted on patients with T2DM.^{41–43} Interestingly, an inverse relationship has been found between the level of HbA1c and vitamin-D suggesting that patients with high HbA1c were more likely to have vitamin-D deficiency and this finding is correlated with several previous studies conducted

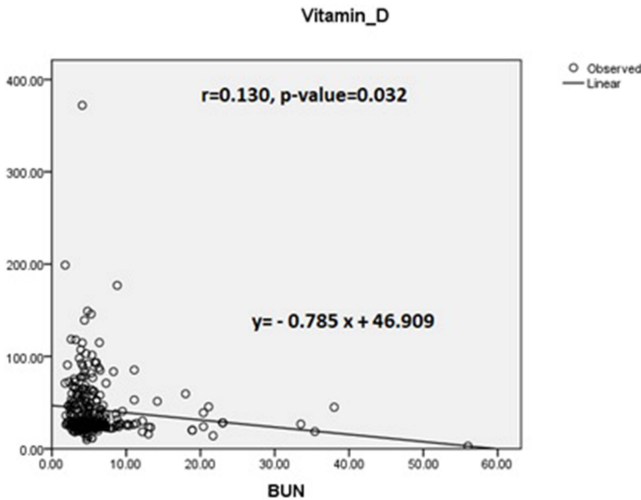


Figure 1 Scatter plot showing a significant correlation between vitamin-D level and BUN.

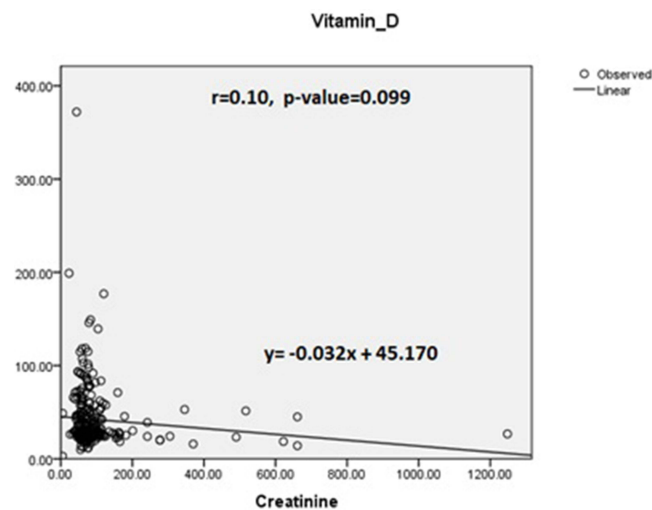


Figure 2 Scatter plot showing a significant correlation between vitamin-D levels and creatinine.

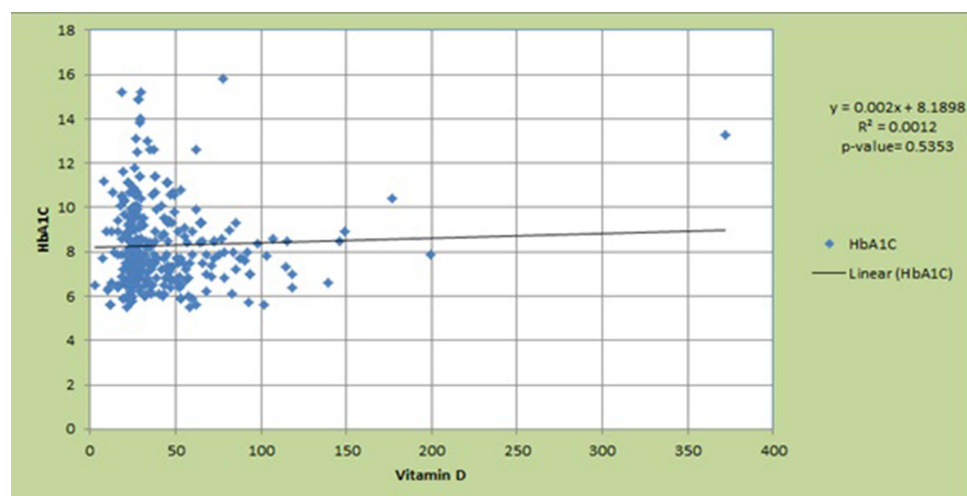


Figure 3 Stacked bar chart illustrating the relationship HbA1c and serum vitamin-D.

in Saudi Arabia.^{43–45} Numerous studies have examined the association between lower vitamin D, CKD progression, and mortality.^{46–48} One study reported that patients with DN have a higher probability of suboptimal vitamin D levels, which can lead to a faster progression of both DM and CKD.⁴⁶ A recent study showed that vitamin D deficiency is a crucial predictor of DN in T2DM.⁴⁹ Blood urea nitrogen and serum creatinine levels are used as biomarkers to evaluate kidneys.⁵⁰ In the present study, the mean BUN was 6.1 ± 5.56 in patients with T2DM. A recent study reported the mean BUN in patients with T2DM which was 6.65 ± 3.08 .^{51,52} Numerous studies reported the relationship between low BUN with DN.^{53–55} In the current study, a significant negative correlation was also observed between serum creatinine and vitamin D levels, which correlates with several lines of evidence.^{56–58} The current study has many limitations associated with cross-sectional studies; in particular, the temporal link cannot be assessed between exposure and outcome because both are determined at the same time and (ii) subjects were chosen on the basis of clinical data available in previous studies.

Conclusion

In conclusion, Vitamin D and kidney function tests (BUN and serum creatinine levels) also showed a negative correlation, suggesting that this could coincide with the development of different stages of kidney disease. Additionally, the study indicated that low vitamin D levels are associated with both T2DM and DN and those patients

with T2DM are more likely to develop kidney disease. Vitamin D must be supplemented in individuals with pre-diabetes to reduce the incidence of diabetes. However, multi-center studies are needed to validate the correlation between vitamin D supplementation in individuals with pre-diabetes and the incidence of diabetes.

Disclosure

The authors report no conflicts of interest in this work.

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