ORIGINAL RESEARCH [Darraj, H] et al

**Title: Vitamin D Deficiency and Glycaemic Control among Patients with Type 2 Diabetes Mellitus in Jazan City, Saudi Arabia.**

Hussain Darraj1; Mohammed Badedi1; Kirsten Poore2; Abdulrahman Hummadi1; Abdullah Khawaji1; Yahia Solan3; Ibrahim Zakry1; Abdullah Sabai1; Majid Darraj3; Dhayf Alrahman Mutawwam1; Mohammed Daghreeri1; Safaa Sayed1; Wael Alaallah1; Abdulaziz Alfadhly4; Abdullah Alsabaani5

1Ministry of Health, Jazan, Saudi Arabia; 2University of Southampton, Southampton, United Kingdom; 3Jazan University, Jazan, Saudi Arabia; 4Prince Mansour Military Hospital for Family and Community Medicine, Taif city, Saudi Arabia; 5King Khalid University, Abha, Saudi Arabia.

Correspondence: Hussain Darraj, Jazan Health Affairs, Ministry of Health, PO 1075, Abu Arish 45911, Saudi Arabia. Email: dr.h.d@hotmail.com; Tel [+966567171984]

**Abstract**

***Background***: The prevalence of vitamin D deficiency (VDD) is predicted to be high in patients with type 2 diabetes mellitus (T2DM), but the exact figure is not known in Jazan, Saudi Arabia. Emerging data suggests that VDD plays a role in glycaemic control. The aim of this study was to measure the prevalence of VDD among T2DM patients and to investigate its association with patients’ characteristics and glycaemic control in Jazan. ***Methods***: This is an analytical cross-sectional study which recruited 309 patients with T2DM randomly from the Jazan diabetes registry. Logistic regression analysis was conducted to determine the VDD predictors and to examine the association of VDD in predicting glycaemic control adjusting for other covariates. ***Results*:** The VDD prevalence was found to be 60.8% in patients with T2DM. Age, gender, diabetic retinopathy (DR), dyslipidaemia, glycaemic control and obesity were significantly associated with VDD, and all except obesity were independent predictors of VDD. There was a significant negative correlation between 25-hydroxyvitamin D and glycosylated haemoglobin (HbA1c). VDD was a significant independent predictor of poor glycaemic control after adjustment for hypertension, DR, diabetic neuropathy (DN), type of diabetes medication, diabetes duration, and education level. ***Conclusion***: In this Saudi Arabian population, VDD is highly prevalent in people with T2DM and is associated with poor glycaemic control. Health education targeting patients with T2DM and national strategies regarding vitamin D fortification are needed to prevent VDD in Saudi Arabia. Earlier VDD diagnosis by healthcare providers may help to improve the outcome for patients with T2DM. Establishing the causal association between VDD and glycaemic control and clarifying the biological role of vitamin D in T2DM are important aims for future studies.

**Keywords:** [diabetes mellitus, T2DM, vitamin D deficiency, VDD, glycaemic control, diabetes complication]

**Introduction**

Globally, diabetes mellitus (DM) is a highly prevalent chronic disease that places a significant burden on the patient’s life and healthcare costs.1 “Diabetes mellitus is a heterogeneous metabolic disorder characterized by the presence of hyperglycaemia due to impairment of insulin secretion, defective insulin action or both”.2 T2DM is the most common type of DM, affecting 90–95% of all patients with DM.3 In the United Kingdom (UK), the reported prevalence of T2DM is 5.26%.4 In Saudi Arabia, a recent review study reported that the prevalence of T2DM is much higher, around 33%, and it is expected to increase to 45.8% by 2030.5 Therefore, it is important to investigate factors that might affect T2DM, such as VDD, to help provide information to improve the quality of T2DM care.

Vitamin D (cholecalciferol) is acquired through irradiation of the skin and vitamin D intake via dietary sources.6 Serum 25-hydroxyvitamin D level is the main circulatory indicator of vitamin D status,7 and VDD is defined as a serum level of 25-hydroxyvitamin D lower than 20 ng/ml.8 High prevalence of VDD has been reported worldwide,9 including Saudi Arabia, where it was recently estimated to affect approximately 60% of the general population.10 VDD plays a central role in several non-skeletal diseases, such as DM and cardiovascular disease.11

The co-occurrence of VDD and T2DM has been reported in several studies. For instance, in the UK, a cross-sectional study found that the prevalence of VDD tended to be higher in patients with diabetes than in healthy individuals (83% versus 70%).12 In Saudi Arabia, a case control study found that that 76.6% of the patients with T2DM had VDD and 58.1% of the healthy participants had VDD.13 Overall, VDD in patients with T2DM was found to range from 30% to 91.4% across the literature.12-17 To our knowledge, no study has been conducted to measure the prevalence of VDD among patients with T2DM in Jazan. Therefore, a suitably designed cross-sectional study in Jazan is needed to determine the prevalence of VDD in patients with T2DM.

Despite the growing evidence which suggests that there is a link between VDD and high prevalence of T2DM, few research studies have investigated the possible connection between VDD and microvascular complications.18 For instance, some studies have suggested that DR,19,20 DN 19,21 and diabetic nephropathy (DNP) 18,21 are significantly associated with VDD. Conversely, other studies showed that there was no significant association between VDD and DR,18,21 DN 18 and DNP.19 Overall, there are conflicting findings in the current literature regarding the association between VDD and microvascular complications in T2DM.

Good glycaemic control is important in diabetes management as it reduces the risk of diabetes complications.22 According to the American Diabetic Association, HbA1c <7% is the optimal glycaemic control.22 It has been suggested that VDD is associated with glycaemic control in T2DM.23 However, the role of VDD in glycaemic control is not yet fully understood. Only a few research studies have investigated the link between VDD and glycaemic control.24 A negative relationship between serum 25-hydroxyvitamin D levels and HbA1c in patients with T2DM has been observed in several populations, including patients in Saudi Arabia.24,25 Moreover, a low serum 25-hydroxyvitamin D level has been shown to be an independent predictor for HbA1c in patients with T2DM.18 In contrast, a cross-sectional study conducted in western India failed to show a significant association between serum 25-hydroxyvitamin D and HbA1c in patients with T2DM.14 To our knowledge, no study has investigated the association between VDD and glycaemic control in patients with T2DM in Jazan.

Although the role of VDD in T2DM is not fully understood, there are a number of potential mechanisms that have been suggested to describe the role of vitamin D in DM, such as systemic inflammation via the formation and the effects of modulating cytokines, which lead to enhanced insulin sensitivity and promote beta-cell survival, and insulin resistance via inducing insulin receptor expression, thus increasing insulin sensitivity during glucose transportation, and pancreatic beta cell malfunction via a change of calcium flux, which can adversely affect beta cell function.26 Moreover, obesity could be a confounder as VDD is typically associated with obesity due to 25-hydroxyvitamin D storage in fat tissue, which leads to low serum 25-hydroxyvitamin D leading to both insulin resistance and insulin sensitivity in T2DM.26

This study aimed to study the prevalence of VDD and its association with microvascular complications and glycaemic control in patients with T2DM in Jazan.

**Material and Methods**

**Study Design, Area and Target Population**

An anaytical cross-sectional design was applied in this study, which was conducted in Jazan, southwestern Saudi Arabia.27 The population of Jazan is relatively homogeneous, with inhabitants sharing the same language, ethnicity and religion.27 Every patient with T2DM in Jazan is registered in a Primary Healthcare Centre (PHC). Therfore, the study sample was recruited from the PHCs registry in Jazan.

**Sample Size and Sampling Technique**

The total calculated sample size was 380 participants. The sample size calculation was conducted using Epi-Info software (version 7.2.2.6 for Windows, Centres for Disease Control and Prevention (CDC), Atlanta, GA, USA) using the following parameters: confidence interval (CI), 95%; Alpha, 0.5; 76.6% expected frequency of VDD in cases of T2DM, which was obtained from a study carried out in southern Saudi Arabia.13 The computed sample size was 266, then the rate of 30% was used to adjust for the expected non-response rate. The current study successfully recruited 309 out of the 380 participants using random sampling technique (Figure 1).

****

**Figure 1:** Participant enrolment and the sampling technique used in the current study

**Inclusion and Exclusion Criteria**

Patients with T2DM who were older than 18 years of age and those who signed Informed Consent were included. Individuals on vitamin D supplements and pregnant women were excluded.

**Ethical Considerations**

Ethical approval for the current study was granted by the local ethics committee in Jazan (reference number: 1836). Informed consent was obtained by all participants.

**Data Collection**

The data were gathered using structured face-to-face interviews with patients by a trained physician. During the interview, the physician will take sociodemographic and clinical data including: age, gender, education level, work status, marital status, smoking status, height, weight, diabetes duration, type of diabetes medication, diabetes microvascular complications and comorbidity). Blood samples were subsequently obtained from the participants to measure serum 25-hydroxyvitamin D and HbA1c levels.

**Data Processing and Analysis**

The data were coded with anonymous identification numbers in order to guarantee the privacy of the participants. A single data entry method was conducted by the principal investigator using the Statistical Package for the Social Sciences (version 24 for Windows, IBM Corp., Armonk, NY, USA). BMI was categorized as underweight, normal, overweight and obese according to BMI scores <18.5kg/m2, from 18.50 to <24.9kg/m2, from 25 to 29.9kg/m2, and ≥30kg/m2, respectively, Vitamin D status as deficient when serum 25-hydroxyvitamin is <20 ng/ml or non-deficient when serum 25-hydroxyvitamin is ≥20 ng/ml, glycemic control status as good glycaemic control when HbA1c level is <7% or poor glycaemic control when HbA1c level is ≥ 7%. The continuous variables were described by mean and  SD and the categorical variables by percentages and frequencies. Binary logistic regression analyses were used to assess the predictors of VDD and the predictors of glycemic control. A *P* value of <0.05 was set for the statistical significance level.

**Results**

**Population characteristics**

**Table 1:** Sociodemographic and clinical characteristics of all participants, participants with VDD and participants without VDD

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Overall (n=309)** | **VDD****N(%)=188 (60.8%)** | **95% CI****55.3-66.1%** | **No-VDD****N(%)=121 (39.2%)** | **95% CI****33.9-44.7%** | ***P*** |
| Age, years mean±SD | 58.9 ± 12 | 54.2 ± 11.8 | 52.9-55.4 | 58.4 ± 12 | 57.1-59.7 | *0.003* |
| Gender  |  |  |  |  |  |  |
| Male | 130 (42.1%) | 64 (49.2%) | 40.8-57.7% | 66 (50.8%) | 42.3-59.2% |  |
| Female | 179 (57.9%) | 124 (69.3%) | 62.2-75.6% | 55 (30.7%) | 24.4-37.8% | *<0.001* |
| Education |  |  |  |  |  |  |
| Educated | 174 (56.3%) | 106 (60.9%) | 53.5-67.9% | 68 (39.1%) | 32.1-46.5% |  |
| Illiterate | 135 (43.7%) | 82 (60.7%) | 52.3-68.6% | 53 (39.3%) | 31.4-47.7% | 0.975 |
| Smoking status |  |  |  |  |  |  |
| Nonsmoker | 264 (85.4%) | 156 (59.1%) | 53.1-64.9% | 108 (40.9%) | 35.2-46.9% |  |
| Smokers | 45 (14.6%) | 32 (71.1%) | 56.6-82.3% | 13 (28.9%) | 17.7-43.4% | 0.127 |
| HbA1c  |  |  |  |  |  |  |
| DM controlled | 68 (22.0%) | 25 (36.8%) | 26.3-48.6% | 43 (63.2%) | 51.1-73.7% |  |
| DM uncontrolled | 241 (78.0%) | 163 (67.6%) | 61.5-73.2% | 78 (32.4%) | 26.8-38.5% | *<0.001* |
| Diabetes duration  |  |  |  |  |  |  |
| ≤10 | 159 (51.5%) | 105 (66.0%) | 58.4-72.9% | 54 (34.0%) | 27.1-41.6% |  |
| >10 | 150 (48.5%) | 83 (55.3%) | 47.34-63.1% | 67 (44.7%) | 36.9-52.7% | 0.054 |
| DR |  |  |  |  |  |  |
| Absent | 200 (64.7%) | 112 (56.0%) | 49.1-62.7% | 88 (44.0%) | 37.3-50.9% |  |
| Present | 109 (35.3%) | 76 (69.7%) | 60.6-77.6% | 33 (30.3%) | 22.4-39.5% | *0.018* |
| DN |  |  |  |  |  |  |
| Absent | 278 (90.0%) | 174 (62.6%) | 56.8-68.1% | 104 (37.4%) | 31.9-43.2% |  |
| Present | 31 (10.0%) | 14 (45.2%) | 29.2-62.2% | 17 (54.8%) | 37.8-70.9% | 0.059 |
| DNP  |  |  |  |  |  |  |
| Absent | 294 (95.1%) | 180 (61.2%) | 55.5-66.6% | 114 (38.8%) | 33.4-44.5% |  |
| Present | 15 (4.9%) | 8 (53.3%) | 30.1-75.2% | 7 (46.7%) | 24.8-69.9% | 0.541 |
| HTN |  |  |  |  |  |  |
| Absent | 103 (33.3%) | 58 (56.3%) | 46.7-65.5% | 45 (43.7%) | 34.5-53.3% |  |
| Present | 206 (66.7%) | 130 (63.1%) | 56.3-69.4% | 76 (36.9%) | 30.6-43.7% | 0.249 |
| DLP |  |  |  |  |  |  |
| Absent | 208 (67.3%) | 118 (56.7%) | 49.9-63.3% | 90 (43.3%) | 36.7-50.1% |  |
| Present | 101 (32.7%) | 70 (69.3%) | 59.7-77.5% | 31 (30.7%) | 22.5-40.3% | *0.034* |
| BMI |  |  |  |  |  |  |
| Non-obese | 176 (57%) | 98 (55.7%) | 48.3-62.8% | 78 (44.3%) | 37.2-51.7% |  |
| Obese | 133 (43.0%) | 90 (67.7%) | 59.3-75.0% | 43 (32.3%) | 25.0-40.7% | 0.033 |

VDD: vitamin D deficiency (serum 25-hydroxyvitamin D <20ng/ml), HbA1c: glycosylated haemoglobin, BMI: body mass index, DR: diabetic retinopathy, DNP: diabetic nephropathy, DN: diabetic neuropathy, HTN: hypertension, DLP: dyslipidaemia, SD: standard deviation, N: sample size, CI: confidence interval, *P*: *P*-value <0.05 is the significance level, as tested by t test, Chi-Square and Fisher’s Exact, where appropriate.

Table 1 presents the participants’ characteristics and their association with VDD. The results showed that the mean level of 25-hydroxyvitamin D was 19.4±6.7 ng/ml and the mean level of HbA1c was 8.7±1.8%. Furthermore, around half of participants had had T2DM for more than ten years. Regarding microvascular complications amongst participants, DR, DNP and DN were evident, with 35.3%, 4.9% and 10% respectively. Oral antidiabetic medications were used in 46.6% of the participants, while 53.4% were being treated with oral antidiabetic agents plus insulin. The percentage of participants of normal, overweight or obese was 18.5%, 38.5% and 43%,respectively, with a higher obesity rate in females relative to males (69.2% versus 30.8%).

**Prevalence of Vitamin D Deficiency and Its Association with the Participants’ Characteristics**

The prevalence of VDD in patients with T2DM was 60.8% (95% CI 55.3-66.1%), whereas for non-VDD patients with T2DM it was 39.2% (95% CI 33.9-44.7%). Younger age was more significantly associated with VDD (54.2±11.8 years) than older age (58.4±12 years) (*t*(307)=3.03, *P*=0.003). Additionally, the number of females with VDD was significantly higher than the number of males (69.3 versus 49.2, *X2*(1)=12.70, *P*=<0.001). There was significant higher proportions of VDD in patients with DR (69.7%) than in patients without DR (56%) (*X2*(1)= 5.58, *P*=0.018). Patients with uncontrolled diabetes have significantly higher VDD rate (67.6%) than the patients with controlled diabetes (36.8%) (*X2*(1)=21.21, *P*<0,001). Patients with dyslipidaemia was also associated with significantly higher VDD compared to those without dyslipidaemia (69.3% and 56.7% respectively, *X2*(1)=4.51, *P*=0.34). There was a significant difference in the proportion of VDD between obese (67.7%) compared with non-obese (55.7%) participants (*X2*(1)=4.57, *P*=0.033).

**Table 2:** Logistic regression analysis of association between patient characteristics and VDD

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Univariateanalysis | Multivariateanalysis |  |
| **OR****(CI 95%)** | ***P*** | **OR****(CI 95%)** | ***P*** |  |
| Age  | 0.97(0.95-0.99) | *0.003* | 0.96(0.94-0.98) | *<0.001* |
| GenderMale | 1 |  | 1 |  |
| Female | 2.33(1.46-3.71) | *<0.001* | 2.34(1.38-3.94) | *0.002* |
| BMINon-obese | 1 |  | 1 |  |
| Obese | 1.67(1.04-2.66) | *0.033* | 1.32(0.78-2.22) | *0.300* |
| DRAbsent | 1 |  | 1 |  |
| Present | 1.81(1.10-2.97) | *0.019* | 1.93(1.07-3.47) | *0.028* |
| DLPAbsent | 1 |  | 1 |  |
| Present | 1.72(1.04-2.85) | *0.035* | 2.12(1.20-3.74) | *0.010* |
| HbA1cControlled | 1 |  | 1 |  |
| Uncontrolled | 3.60(2.05-6.31) | *<0.001* | 3.45(1.85-6.46) | *<0.001* |

BMI: body mass index, DR: diabetic retinopathy, DLP: dyslipidaemia, HbA1c: glycosylated haemoglobin OR: odds ratio, CI: confidence interval, *P*: *P*-value, *P* of <0.05 is the significance level. The variables with odds ratios of 1 are the reference categories.

Table 2 shows the univariate and multivariate binary logistic regression analysis in order to identify the predictors of VDD in T2DM. At the 95% CI, the univariate logistic regression analysis showed that being younger, female, having DR, dyslipidaemia and uncontrolled diabetes were found to be statistically significant predictors of VDD among patients with T2DM in the study. The multivariate logistic regression analysis revealed that poor glycaemic control was independently associated with VDD, with participants with poor glycaemic control being 3.45 times more likely to be VDD than participants with good glycaemic control. This was followed by the female gender, with females being 2.34 times more likely to be VDD than males in our sample. Dyslipidaemia, DR and age were found to be independent predictors of VDD, with age being the weakest predictor.

**The Association of Vitamin D Deficiency with Glycaemic Control**

Figure 2 shows a medium significant negative correlation between HbA1c and 25-hydroxyvitamin D levels in patients with T2DM (r=-0.41, p<0.001) i.e. The lower Vitamin D level, the higher HbA1c. Moreover, the prevalence of poor glycaemic control in patients with T2DM was 78% (95% CI: 73.1–82.3%). Table 3 shows that VDD, education (illiteracy level), a DM duration of >10 years, DR, DN, hypertension and the type of diabetic medication (both oral and insulin) were significantly associated with glycaemic control.

**r = −0.411, p < 0.001**

**Figure 2:** Correlation between vitamin D and glycaemic control in all study participants

**Table 3:** Participants’ characteristics and their association with glycaemic control (poor vs good).

|  |  |  |
| --- | --- | --- |
|  Glycaemic control  (poor) N=241 (78%)  | **95% CI****73.1-82.3%** | ***P*** |
| Age, years M ± SD | 56.5 ± 12 | 55-58 | 0.096 |
| Gender  |   |  |  |
| Male | 95 (73.1%) | 64.9-80.0% |  |
| Female | 146 (81.6%) | 75.2-86.6% | 0.075 |
| Education |  |  |  |
| Educated | 125 (71.8%) | 64.7-78.0% |  |
| Illiterate | 116 (85.9%) | 79.1-90.8% | *0.003* |
| Diabetes duration |  |  |  |
| ≤10 | 114 (71.7%) | 64.3-78.1% |  |
| >10 | 127 (84.7%) | 78.0-89.6% | *0.006* |
| DR |  |  |  |
| Absent | 139 (69.5%) | 62.8-75.5% |  |
| Present | 102 (93.6%) | 87.3-96.9% | *<0.001* |
| DN |  |  |  |
| Absent | 212 (76.3%) | 70.9-80.9% |  |
| Present | 29 (93.5%) | 79.3-98.2% | *0.028* |
| DNP  |  |  |  |
| Absent | 227 (77.2%) | 72.1-81.6% |  |
| Present | 14 (93.3%) | 70.2-98.8% | 0.142 |
| HTN |  |  |  |
| Absent | 70 (68.0%) | 58.4-76.2% |  |
| Present | 171 (83.0%) | 77.3-87.5% | *0.003* |
| DLP |  |  |  |
| Absent | 163 (78.4%) | 72.3-83.4% |  |
| Present | 78 (77.2%) | 68.1-84.3% | 0.821 |
| Diabetes medication  |  |  |  |
| Oral  | 95 (66.0%) | 57.9-73.2% |  |
| Oral + insulin | 146 (88.5%) | 82.7-92.5% | *<0.001* |
| BMI |  |  |  |
| Non-obese | 131 (74.4%) | 67.5-80.3% |  |
| Obese | 110 (82.7%) | 75.4-88.2% | 0.082 |
| Vitamin D status |  |  |  |
| Not deficient | 78 (64.5%) | 55.6-72.4% |  |
| Deficient | 163 (86.7%) | 81.1-90.8% | *<0.001* |

BMI: body mass index, DR: diabetic retinopathy, DNP: diabetic nephropathy, DN: diabetic neuropathy, DLP: dyslipidaemia, HTN: hypertension, M: mean, SD: standard deviation, N: sample size, CI: confidence interval, *P*: *P*-value, *P* of <0.05 is the significance level, as tested by t test, Chi-Square and Fisher’s Exact, where appropriate. The data for the good glycaemic control group can be calculated based on the overall values from table 1.

Table 4: Logistic regression analysis between patient characteristics and glycaemic control

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Univariateanalysis | Multivariate analysis |  |
| **OR****(CI 95%)** | ***P*** | **OR****(CI 95%)** | ***P*** |  |
| Vitamin D statusNot deficient | 1 |  | 1 |  |
| Deficient | 3.59(2.05-6.31) | *<0.001* | 3.79(2.01-7.14) | *<0.001* |
| Diabetes duration ≤10 year | 1 |  | 1 |  |
| > 10 year | 2.18 (1.24-3.83) | *0.007* | 0.93 (0.43-2.01) | 0.859 |
| DRAbsent | 1 |  | 1 |  |
| Present | 6.40(2.81-14.56) | *<0.001* | 2.12(1.097-4.11) | *0.011* |
| DNAbsent | 1 |  | 1 |  |
| Present | 4.53 (1.05-19.42) | *0.043* | 3.83 (0.79-18.48) | 0.094 |
| HTNAbsent | 1 |  | 1 |  |
| Present | 2.30 (1.33-4.00) | *0.003* | 1.58 (0.85-2.94) | 0.151 |
| Diabetes medicationOral | 1 |  | 1 |  |
| Oral & insulin | 3.96 (2.20-7.15) | *<0.001* | 2.42 (1.20-4.90) | *0.014* |
| EducationEducated | 1 |  | 1 |  |
| Illiterate | 2.39(1.33-4.30) | *0.004* | 2.12(1.10-4.11) | *0.025* |

VDD: vitamin D deficiency, DR: diabetic retinopathy, DN: diabetic neuropathy, HTN: hypertension, OR: odds ratio, CI: confidence interval, *P*: *P*-value, *P* of <0.05 is the significance level. The variables with odds ratios of 1 are the reference categories.

Table 4 illustrates the results of the univariate and multivariate binary logistic regression analyses used to examine the predictors of poor glycaemic control. The univariate logistic regression analysis revealed with a 95% CI that VDD, illiteracy level, a DM duration of >10 years, DR, DN, hypertension and taking both oral diabetic medication and insulin were significantly associated with poor glycaemic control. The results of the multivariate binary logistic regression analysis showed a significant association between VDD and glycaemic control after adjustment for the other covariates and that the odds of reporting poor glycaemic control were 3.79 times higher in patients with T2DM and VDD than in patients with T2DM without VDD.

**Discussion**

The current study included a total of 309 patients with T2DM and it found that the prevalence of VDD in patients with T2DM was 60.8% in Jazan. Moreover, the study found that younger age, female gender, DR, dyslipidaemia, poor glycaemic control and BMI (obese) were significantly associated with VDD and that all of them except BMI were independent predictors of VDD. In addition, there was a significant negative correlation between 25-hydroxyvitamin D and HbA1c. Further analysis revealed that VDD was a significant independent predictor of poor glycaemic control after adjustment with hypertension, DR, DN, type of diabetes medication, diabetes duration, and education level.

The current study found a high prevalence of VDD in patients with T2DM (60.8%). This result is slightly lower than that of a previous study conducted in southern Saudi Arabia, which found that 76.6% of patients with T2DM had VDD;13 however, there were certain limitations in this study which might have led to this higher rate, such as its case control design and that the patients were recruited from tertiary hospitals.13 In line with our finding, previous studies have reported that the prevalence of VDD among patients with T2DM was around 60%.16,18,28 Several features of the current study sample may have influenced this high VDD prevalence. Firstly, most of the study sample were females. Furthermore, the female sex was independently significantly associated with VDD in our results, as shown by some 29-32 but not all other studies.33,34 The traditional clothes might be a predisposing factor to vitamin D deficiency due to reduction of sun exposure. Secondly, the majority of the current study’s participants were overweight or obese. The rate of obesity was high in our sample and obesity was associated with VDD. Similarly, several studies have found a link between the excess weight and VDD in T2DM 30,31,35 but others have not.14,18 A possible explanation for this association is that vitamin D is sequestered in the adipose tissue,26 so patients with obesity report lower serum 25-hydroxyviatmin D levels. The current study found that there was a higher rate of obesity in females than in males, which could have led to the detected association between gender and VDD. However, when adjusted with other covariates, obesity loses its effects. It seems that obesity plays as a confounder in the relationship of VDD with T2DM. Thirdly, dyslipidaemia was associated with VDD even after adjustment with other covariates, as shown previously.30 The higher rate of VDD in patients with T2DM in the current sample could be attributed to dyslipidaemia. However, some studies have reported that there is no association between dyslipidaemia and VDD among patients with T2DM.31,33 The current study suggests that a younger age is more highly associated with VDD, which is consistent with other published research.34 This finding could be explained by dietary behaviour. A study conducted in Saudi Arabia found that the healthy diet was adopted by older individuals and that the unhealthy diet was adopted by younger individuals.36 Although this is statistically significant, it may not have any clinical relevance since the odds ratio was close to 1. However, other studies have reported that there is no significant association between VDD and age.14,18,30,31,33,35

Our results showed that there was a marginal significance level (P=0.054) of the association between VDD and diabetes duration. This result is supported by a previous study which reported a significant association between vitamin D and diabetes duration.37 Conversely, other studies have found that diabetes duration was not associated with VDD.30,33 A possible explanation for our findings is that longer duration with diabetes is associated with diabetes complications,38 which, in turn, is associated with VDD.18

The current study found that there is a significant positive association between DR and VDD in patients with T2DM. Similarly, some studies reported that serum 25-hydroxyvitamin D levels were significantly lower in participants with DR than in those without DR in patients with T2DM.18,21 Conversely, other studies have found that VDD was not associated with DR in patients with T2DM.19,20 The current study findings suggest that DN and DNP are not associated with VDD in patients with T2DM. This is consistent with other research studies, which found that DN 19,21 and DNP 18,21 were not associated with VDD. Conversely, some research studies have suggested that VDD is significantly associated with DN 18 and DNP.19

Good glycaemic control is considered as one of the most important goals of T2DM management.22 The current study found that 25-hydroxyvitamin D levels were inversely correlated with glycaemic control measured by HbA1c levels. This finding is consistent with a number of previous research studies.18,23,25 Additionally, the current study found that glycaemic control is independently associated with VDD. Similarly, a cross-sectional study reported a significant positive association between VDD and poor glycaemic control.39 Conversely, a cross-sectional study found that vitamin D is not associated with HbA1c.14 The exact mechanism by which VDD may affect glycaemic control is not fully understood; however, potential pathways have been suggested which involve pancreatic beta cell dysfunction, reduced insulin sensitivity, and inflammation.40 These proposed mechanisms are important focuses for future studies.

**Strengths and Limitations**

The strengths of the current study were that it was a population-based and the participants were selected randomly. There was an 18.3% non-response or excluded rate; however, this was mitigated when the sample size was calculated by accounting for 30% non-response rate. The limitations of the current study were that sun exposure and vitamin D dietary intake were not assessed in the current study; however, patients on a vitamin D supplement were excluded. Moreover, Jazan’s population is homogeneous 27 and it was assumed that they follow a similar pattern.

**Recommendations and Conclusion**

The current study found VDD to be highly prevalent among patients with T2DM in Jazan, which is a major health issue. It also successfully identified an association for VDD in T2DM with glycaemic control. As such, a number of measures are recommended in order to improve diabetes care. For instance, primary prevention, health education and promotional campaigns targeted at patients with T2DM should be implemented to encourage a healthier lifestyle and to promote weight reduction to reduce levels of obesity, especially in females as the current study shows that they have a higher rate of VDD. The importance of moderate sun exposure should also be emphasised and the use of appropriate clothing. Moreover, the majority of the products fortified with vitamin D in Saudi Arabia contain less than the recommended levels.41 Therefore, national policies are needed to support vitamin D fortification, as VDD is common not only in T2DM patients, but also in the general population in Saudi Arabia.10 In relation to the secondary prevention of VDD, healthcare providers should raise the suspicion of VDD in T2DM patients and give vitamin D supplements judiciously to those affected. Further observational and experimental research with an appropriate design are needed to prove the causality of VDD in association with diabetes microvascular complications and also glycaemic control and to elucidate the pathogenesis of vitamin D in T2DM.

**Acknowledgments**We would like to thank the study’s participants for their participation and cooperation and to acknowledge the effort of Jazan Diabetes Centre for providing technical support.

**Disclosure**

The author reports no conflicts of interest in this work.

**References**

1. World Health Organization. *Global Report on Diabetes*. Geneva: World Health Organization; 2016.
2. Punthakee Z, Goldenberg R, Katz P. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. *Canadian Journal of Diabetes.* 2018;42: S10-5.
3. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2018. *Diabetes Care.* 2018;41(Supplement 1): S13-27.
4. Zghebi SS, Steinke DT, Carr MJ, Rutter MK, Emsley RA, Ashcroft DM. Examining Trends in Type 2 Diabetes Incidence, Prevalence and Mortality in the UK Between 2004 and 2014. *Diabetes, Obesity and Metabolism.* 2017;19(11): 1537-45.
5. Meo SA. Prevalence and Future Prediction of Type 2 Diabetes Mellitus in the Kingdom of Saudi Arabia: A Systematic Review of Published Studies. *The Journal of the Pakistan Medical* *Association.* 2016;66(6): 722-5.
6. Borel P, Caillaud D, Cano NJ. Vitamin D Bioavailability: State of the Art. *Critical Reviews in Food Science and Nutrition.* 2015;55(9): 1193-205.
7. Deluca HF. Overview of General Physiologic Features and Functions of Vitamin D. *The American Journal of Clinical Nutrition.* 2004;80(6): 1689S-96S.
8. Simsek Y, Kucukler FK, Arduc A, Guler S. Is There an Association Between Vitamin D Level and Microvascular Complications of Type 2 Diabetes Mellitus?. *West Indian Medical Journal Open.* 2015;2(3): 138-41.
9. Griz LH, Bandeira F, Gabbay MA, Dib SA, Carvalho EF. Vitamin D and Diabetes Mellitus: An Update 2013. *Brazilian Archives of Endocrinology and Metabolism.* 2014;58(1): 1-8.
10. Al-Alyani H, Al-Turki HA, Al-Essa ON, Alani FM, Sadat-Ali M. Vitamin D Deficiency in Saudi Arabians: A Reality or Simply Hype: A Meta-analysis (2008–2015). *Journal of Family and Community Medicine.* 2018;25(1): 1.
11. Papandreou, D., and Hamid, Z.-T.-N. (2015). The Role of Vitamin D in Diabetes and Cardiovascular Disease: An Updated Review of the Literature. *Disease Markers.* *2015*;2015: 580474.
12. Tahrani AA, Ball A, Shepherd L, Rahim A, Jones AF, Bates A. The Prevalence of Vitamin D Abnormalities in South Asians with Type 2 Diabetes Mellitus in the UK. *International Journal of Clinical Practice.* 2010;64(3): 351-5.
13. Alhumaidi M, Agha A, Dewish M. Vitamin D Deficiency in Patients with Type-2 Diabetes Mellitus in Southern Region of Saudi Arabia. *Maedica.* 2013;8(3): 231-6.
14. Sheth JJ, Shah A, Sheth FJ, Trivedi S, Lele M, Shah N, Thakor P, Vaidya R. Does Vitamin D Play a Significant Role in Type 2 Diabetes?. *BioMed Central Endocrine Disorders.* 2015;15(1): 5.
15. Ozder A, Eker HH, Bilginc M. Status of Vitamin D among Turkish Adults with Type 2 Diabetes Mellitus in Primary Health Care. *Acta Medica Mediterranea.* 2015;31: 229-36.
16. Saedisomeolia A, Taheri E, Djalali M, Moghadam AM, Qorbani M. Association Between Serum Level of Vitamin D and Lipid Profiles in Type 2 Diabetic Patients in Iran. *Journal of Diabetes and Metabolic Disorders.* 2014;13(1):7.
17. Alam MS, Kamrul-Hasan M, Kalam ST, Selim S, Akter F, Saifuddin M. Vitamin D Status in Newly Diagnosed Type 2 Diabetes Patients Attending in a Tertiary Hospital of Bangladesh. *Mymensingh Medical Journal.* 2018;27(2): 362-8.
18. Ahmadieh H, Azar ST, Lakkis N, Arabi A. Hypovitaminosis D in Patients with Type 2 Diabetes Mellitus: A Relation to Disease Control and Complications*. International Scholarly Research Notices Endocrinology.* 2013; 641098.
19. Usluogullari CA, Balkan F, Caner S, Ucler R, Kaya C, Ersoy R, Cakir B. The Relationship Between Microvascular Complications and Vitamin D Deficiency in Type 2 Diabetes Mellitus. *BioMed Central Endocrine Disorders.* 2015;15(1): 33.
20. Reddy GB, Sivaprasad M, Shalini T, Satyanarayana A, Seshacharyulu M, Balakrishna N, Viswanath K, Sahay M. Plasma Vitamin D Status in Patients with Type 2 Diabetes with and without Retinopathy. *Nutrition.* 2015;31(7-8): 959-63.
21. Suzuki A, Kotake M, Ono Y, Kato T, Oda N, Hayakawa N, Hashimoto S, Itoh M. Hypovitaminosis D in Type 2 Diabetes Mellitus: Association with Microvascular Complications and Type of Treatment. *Endocrine Journal.* 2006;53(4): 503-10.
22. American Diabetes Association. 6. Glycemic Targets: Standards of Medical Care in Diabetes—2018. *Diabetes Care.* 2018;41(Supplement 1): S55-64.
23. Saif-Elnasr M, Ibrahim IM, Alkady MM. Role of Vitamin D on Glycemic Control and Oxidative Stress in Type 2 Diabetes Mellitus. *Journal of Research in Medical Sciences.* 2017;22(1): 22.
24. Almetwazi MS, Noor AO, Almasri DM, Popovici I, Alhawassi T, Alburikan KA, Harrington CA. The Association of Vitamin D Deficiency and Glucose Control among Diabetic Patients. *Saudi Pharmaceutical Journal.* 2017;25(8): 1179-83.
25. Aldossari K, Aljowair AM, Alqahtani NT, Al-shiprain MS, Al-shathri MM, Alshehri DA. Association Between Low Vitamin D Level and Glycemic Control. *Primary Care Diabetes.* 2017;11(Supplement 1): e5.
26. Mezza T, Muscogiuri G, Sorice GP, Prioletta AN, Salomone E, Pontecorvi A, Giaccari AN. Vitamin D Deficiency: A New Risk Factor for Type 2 Diabetes. *Annals of Nutrition and Metabolism.* 2012;61(4): 337-48.
27. Mahfouz MS, Rahim BE, Solan YM, Makeen AM, Alsanosy RM. Khat Chewing Habits in the Population of the Jazan Region, Saudi Arabia: Prevalence and Associated Factors. *Public Library of Science One.* 2015;10(8): e0134545.
28. Di Cesar DJ, Ploutz-Snyder R, Weinstock RS, Moses AM. Vitamin D Deficiency is More Common in Type 2 than in Type 1 Diabetes. *Diabetes Care.* 2006;29(1): 174.
29. Yu JR, Lee SA, Lee JG, Seong GM, Ko SJ, Koh G, Kong MH, Park KY, Kim BJ, Lim DM, Lee DH. Serum Vitamin D Status and Its Relationship to Metabolic Parameters in Patients with Type 2 Diabetes Mellitus. *Chonnam Medical Journal.* 2012;48(2): 108-15.
30. Rolim MC, Santos BM, Conceição G, Rocha PN. Relationship Between Vitamin D Status, Glycemic Control and Cardiovascular Risk Factors in Brazilians with Type 2 Diabetes Mellitus. *Diabetology and Metabolic Syndrome.* 2016;8(1): 77.
31. Chen Y, Zhao CT, Zhen Z, Wong A, Tse HF, Yiu KH. Association of Myocardial Dysfunction with Vitamin D Deficiency in Patients with Type 2 Diabetes Mellitus. *Journal of Diabetes and Its Complications.* 2014;28(3): 286-90.
32. Sipahi S, Acikgoz SB, Genc AB, Yildirim M, Solak Y, Tamer A. The Association of Vitamin D Status and Vitamin D Replacement Therapy with Glycemic Control, Serum Uric Acid Levels, and Microalbuminuria in Patients with Type 2 Diabetes and Chronic Kidney Disease. *Medical Principles and Practice.* 2017;26(2): 146-51.
33. Alcubierre N, Castelblanco E, Martínez-Alonso M, Granado-Casas M, Esquerda A, Traveset A, Martinez-Gonzalez D, Franch-Nadal J, Mauricio D. Vitamin D Deficiency is Associated with Poorer Satisfaction with Diabetes-related Treatment and Quality of Life in Patients with Type 2 Diabetes: A Cross-sectional Study. *Health and Quality of Life Outcomes.* 2018;16(1): 44.
34. Zoppini G, Galletti A, Targher G, Brangani C, Pichiri I, Trombetta M, Negri C, De Santi F, Stoico V, Cacciatori V, Bonora E. Lower Levels of 25-hydroxyvitamin D3 are Associated with a Higher Prevalence of Microvascular Complications in Patients with Type 2 Diabetes. *BMJ Open Diabetes Research and Care.* 2015;3(1): e000058.
35. Caretta N, de Kreutzenberg SV, Valente U, Guarneri G, Ferlin A, Avogaro A, Foresta C. Hypovitaminosis D is Associated with Erectile Dysfunction in Type 2 Diabetes. *Endocrine.* 2016;53(3): 831-8.
36. Moradi-Lakeh M, El Bcheraoui C, Afshin A, Daoud F, AlMazroa MA, Al Saeedi M, Basulaiman M, Memish ZA, Al Rabeeah AA, Mokdad AH. Diet in Saudi Arabia: Findings from a Nationally Representative Survey. *Public Health Nutrition.* 2017;20(6): 1075-81.
37. Aksoy H, Akçay F, Kurtul N, Baykal O, Avci B. Serum 1,25 Dihydroxy Vitamin D (1,25(OH)2D3), 25 Hydroxy Vitamin D (25(OH)D) and Parathormone Levels in Diabetic Retinopathy. *Clinical biochemistry.* 2000;33(1): 47-51.
38. Nanayakkara N, Ranasinha S, Gadowski A, Heritier S, Flack JR, Wischer N, Wong J, Zoungas S. Age, Age at Diagnosis and Diabetes Duration are All Associated with Vascular Complications in Type 2 Diabetes. *Journal of Diabetes and Its Complications.* 2018;32(3):279-90.
39. Iqbal K, Islam N, Mehboobali N, Asghar A, Iqbal MP. Association of Vitamin D Deficiency with Poor Glycaemic Control in Diabetic Patients. *Journal of the Pakistan Medical Association.* 2016;66(12): 1562-5.
40. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The Role of Vitamin D and Calcium in Type 2 Diabetes. A Systematic Review and Meta-analysis. *The Journal of Clinical Endocrinology and Metabolism.* 2007;92(6): 2017-29.
41. Sadat-Ali M, Al Elq A, Al-Farhan M, Sadat NA. Fortification with Vitamin D: Comparative Study in the Saudi Arabian and US Markets. *Journal of Family and Community Medicine.* 2013;20(1): 49.