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Association of Vitamin D Serum Levels With Glycemic, Lipid Profiles, and Diabetic Complications in Saudi Type II Diabetes Patients

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Abstract

Background: Vitamin D is essential for calcium regulation and immune function. Its deficiency is linked to various diseases. In Saudi Arabia, the prevalence of vitamin D deficiency is high, but its association with type II diabetes mellitus (DM) complications is not well understood. This study aimed to investigate the association between serum vitamin D levels and glycemic control, lipid profiles, and major DM complications among type II DM patients in Riyadh, Saudi Arabia.

Methods: A cross-sectional study was conducted on 500 type II DM patients. Serum vitamin D levels were measured and correlated with anthropometric data, glycemic (fasting blood glucose and hemoglobin A1c (HbA1c)) and lipid (high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides) profiles, and DM complications (neuropathy, nephropathy, and retinopathy). Statistical analysis was performed to determine significant associations.

Results: Vitamin D levels were significantly correlated with age, gender, HDL levels, and neuropathy. Females exhibited higher vitamin D levels than males ($P < 0.05$). HDL levels were significantly associated with vitamin D levels ($P < 0.001$), but no significant correlation was found with fasting blood glucose or HbA1c. Vitamin D-deficient patients were more likely to develop neuropathy ($P < 0.05$).

Conclusion: Vitamin D deficiency is associated with neuropathy and lower HDL levels in type II DM patients. These findings suggest the potential role of vitamin D in managing DM complications. Further research with larger samples is needed to confirm these results.

Keywords: Diabetes; HDL; Saudi Arabia; Neuropathy; Vitamin D

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Introduction

Vitamin D is a lipid-soluble vitamin that plays a major role in human homeostasis [1]. It regulates the level of calcium in the blood through enhancing its absorption and decreasing its elimination [2].

The normal range of total vitamin D, which refers to the sum of both vitamin D forms in adult human serum, is between 50 and 125 nmol/L. A deficiency in vitamin D is considered when its serum level is below 50 nmol/L [3]. It was reported that deficiency in vitamin D has been associated with some human diseases, such as cancers and autoimmune diseases [4], and with the severity of coronavirus disease 2019 (COVID-19) disease symptoms [5]. In addition, genetic variants in *vitamin D receptor (VDR)* gene were associated with type I diabetes mellitus (DM) [6] and the complications of type II DM [7].

The prevalence of vitamin D deficiency is high in Saudi Arabia. A meta-analysis study reported that the overall vitamin D deficiency in the healthy Saudi Arabian population is 60% [8]. However, it was shown by Al-Humaidi et al that there is no difference in the frequency of vitamin D-deficient individuals among type II diabetic and non-diabetic among Saudi volunteers [9].

Diabetes is an increase of blood glucose level. It is classified into type I, type II, and gestational diabetes. The prevalence of type II DM is high among the developing countries particularly in Saudi Arabia [10].

It was found that vitamin D increases the ability of beta pancreatic cells to produce insulin and increases the insulin sensitivity in the peripheral tissues [11]. In addition, it is reported that vitamin D has an anti-inflammatory and anti-oxidant activity, therefore it may protect the body organs from the oxidative stress and inflammation induced by high glucose levels [12]. Accordingly, vitamin D deficiency can exacerbate the DM complications, such as neuropathy, retinopathy, and nephropathy.

To the best of our knowledge, there is lack of information regarding the influence of vitamin D level deficiency on the type II DM complications among Saudi patients. Therefore, this study aimed to find out the association of total serum vitamin D levels with the glycemic and lipid profiles and with the major type II DM complications among Saudi patients living in the capital city, Ar-Ryiadh.

Materials and Methods

Study design

This retrospective, cross-sectional study was conducted at a network of tertiary private hospitals in Saudi Arabia. The study period spanned from January 2019 to June 2023, aiming to assess the association of serum vitamin D levels with glycemic control, lipid profiles, and DM complications among type II DM patients.

Data collection

Data were collected from the electronic medical records (EMR) of 500 type II DM patients. Patient information was sourced from clinical records, laboratory results, nursing notes, and documented clinical outcomes. To ensure accuracy and uniformity in data gathering, a standardized data collection form was utilized, designed to capture relevant clinical and laboratory parameters comprehensively.

The collected data included demographic details (age and gender), clinical measurements (weight and blood pressure), and biochemical markers such as fasting blood glucose, HbA1c, lipid profiles (HDL, LDL, and triglycerides), and serum vitamin D levels. Additionally, DM complications, including neuropathy, nephropathy, and retinopathy, were documented based on clinical diagnoses by specialists in the hospital.

The thresholds that define vitamin D status are typically based on serum concentrations of 25-hydroxyvitamin D (25(OH)D), according to the guideline of the Endocrine Society and the Institute of Medicine that sufficient vitamin D level is ≥ 30 ng/mL (or ≥ 75 nmol/L), while deficient vitamin D level is less than 20 ng/mL [13]. This is also the protocol of classification of vitamin D deficiency used by Dr. Sulaiman Al-Habib Medical Group, Riyadh, Saudi Arabia.

Data management and confidentiality

Patient data were retrieved through the VIDA System, a secure healthcare platform widely implemented across both public and private healthcare sectors in Saudi Arabia. All data were de-identified prior to retrieval to ensure confidentiality and privacy, adhering to stringent data protection standards. After extraction, data were organized and stored in Microsoft Excel for cleaning, processing, and subsequent statistical analysis.

Ethical considerations

Approval for this study was obtained from the Institutional Review Board at Al Habib Research Center, Dr. Sulaiman Al-Habib Medical Group, Riyadh, Saudi Arabia (IRB Log No: RC22.10.03). The study adhered to ethical guidelines for research involving human subjects, with all procedures conforming to the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study, and all data were anonymized to protect patient identities.

Statistical analysis

Data were analyzed to identify the associations between serum vitamin D levels and various biochemical and clinical parameters. The normality of continuous variables was assessed using Shapiro-Wilk test. All P-values were greater than 0.05. These indicate that continuous data collected from the participants are normally distributed, justifying the use of parametric tests. Pearson correlation analysis was used to assess the linear relationship between continuous variables and serum vitamin D levels. The Student's *t*-test was used to compare the mean of two groups. Additionally, Chi-square tests (χ^2) were used to examine the association between categorical variables. All analyses were performed using SPSS software (version 26, USA), with a significance level set at $P < 0.05$.

The sample size was calculated using MedCalc® Statistical Software version 22.018 (MedCalc Software Ltd, 2024), based on an assumed statistical power of 80%, a 5% margin of error, and a population size of more than 10,000 DM patients in Saudi Arabia. The minimum required sample size was determined to be 382 participants. Our study included a total of 500 patients, exceeding this requirement and thereby enhancing the statistical robustness and generalizability of the findings.

Results

Patients' parameters

The study included a total of 500 participants, comprising 259 females and 241 males. The average age of the participants was 61.17 ± 11.35 years.

Regarding biochemical markers, the overall mean HbA1c level was 7.09 ± 1.63. The average body mass index (BMI) and systolic blood pressure were 30 ± 8.5 kg/m^2 and 123 ± 18 mm Hg, respectively. The mean vitamin D level for all participants was 46.13 ± 28.74 nmol/L, and 410 (82%) participants were classified as vitamin D deficient.

The average values of the lipid profile parameters LDL, HDL, and total cholesterol of the participants were 2.73 ± 1, 1.2 ± 0.4, and 4.5 ± 1.7 mmol/L, respectively.

The average values of the biochemical profile parameters uric acid, blood urea nitrogen, and blood creatinine among the participants were 318 ± 90 µmol/L, 5.5 ± 2.1 mmol/L, and 72 ± 21 µmol/L, respectively.

Association of anthropometric data of the patients with vitamin D levels

Regarding the association of vitamin D levels with the anthro-

Table 1. Association of Vitamin D Levels With Anthropometric Parameters

Parameter	Pearson correlation	P value
Age	0.175**	< 0.001
Weight	-0.094*	0.045
BMI	-0.053	0.292

Significant correlations: *P < 0.05, **P < 0.001. BMI: body mass index.

pometric parameters of the patients, it was found that total vitamin D levels were significantly (P < 0.05) correlated and inversely with the weight of the patients and directly with the age of the patients (Table 1).

The Chi-square test between the gender of the DM patients and vitamin D levels showed that female DM patients had significantly (χ^2 = 19.6, P < 0.001) more vitamin D levels in comparison with male patients (Table 2). Additionally, the mean HDL level among patients with low vitamin D levels was significantly lower (*t*-test, P < 0.001) than that in patients with normal vitamin D levels (Table 2). In addition, the average age of vitamin D-deficient patients (56.4 ± 11.5 years) was significantly lower (P = 0.02) than that of the patients with normal levels (61.2 ± 8 years). The mean values of other lipid biomarkers, HbA1c, creatinine, uric acid, blood urea nitrogen, and BMI were not statistically (*t*-test, P < 0.001) different between the two groups: deficient and normal vitamin D levels.

Correlation of vitamin D level with glycemic and lipid profiles

Table 3 shows the correlation of vitamin D levels with the glycemic and lipid profiles of the DM patients. It was shown that only HDL was significantly (P < 0.001) correlated with the level of total serum vitamin D among the patients.

Table 3. Correlation of Vitamin D Levels With Glycemic and Lipid Profiles

Parameter	Pearson correlation	P value
HbA1c	-0.084	0.074
Glucose	-0.088	0.099
Uric acid	-0.004	0.950
Blood urea nitrogen	-0.039	0.492
Serum creatinine	-0.062	0.191
LDL-cholesterol	-0.064	0.206
HDL-cholesterol	0.186**	< 0.001

Significant correlation: **P < 0.001. HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Correlation of vitamin D level with other serum biochemical parameters

There was no significant correlation (P > 0.05) between the level of total vitamin D with uric acid, blood urea nitrogen, and serum creatinine, as represented in Table 3.

Binary regression between vitamin D level and DM complications

Table 4 shows that only the DM complication neuropathy was significantly (P < 0.05) associated with the vitamin D levels,

Table 2. Baseline Characteristics by Vitamin D Status Among Diabetic Patients

Variable	Low vitamin D (n = 410)	High vitamin D (n = 90)	P value
Gender			< 0.001**
Male	224 (92.6%)	18 (7.4%)	
Female	186 (72.0%)	72 (28.0%)	
Age (years)	56.4 ± 11.5	61.2 ± 8	0.02
BMI (kg/m^2)	30.4 ± 8	30 ± 6	0.76
Systolic BP (mm Hg)	123 ± 18	119 ± 12	0.62
HbA1c (%)	7.21 ± 1.9	6.83 ± 1.5	0.29
Uric acid (µmol/L)	327 ± 91	314 ± 88	0.62
BUN (mmol/L)	5.16 ± 2.7	5.01 ± 2.4	0.73
Creatinine (µmol/L)	75 ± 21	71 ± 19	0.68
Total cholesterol (mmol/L)	4.53 ± 1.8	4.37 ± 2.5	0.59
LDL (mmol/L)	2.92 ± 1.1	2.69 ± 0.99	0.13
HDL (mmol/L)	1.16 ± 0.40	1.38 ± 0.25	< 0.001**

Vitamin D is defined as levels below 20 ng/mL (50 nmol/L). Continuous variables analyzed using *t*-test; categorical variables using Chi-square test. Statistically significant: **P value < 0.01. BMI: body mass index; BP: blood pressure; BUN: blood urea nitrogen; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Table 4. Binary Regression Between Vitamin D Levels and Diabetic Complications

Diabetic complication	Vitamin D deficient (n, %)	Normal vitamin D (n, %)	Total (n)	P-value
Retinopathy	30 (75%)	10 (25%)	40	0.121
Neuropathy	7 (77.8%)	2 (22.2%)	9	0.032*
Nephropathy	5 (71.4%)	2 (28.6%)	7	0.447
Peripheral artery disease	4 (80%)	1 (20%)	5	0.065
Coronary artery disease	18 (72%)	7 (28%)	25	0.199
Stroke	9 (75%)	3 (25%)	12	0.371
Total	73 (73.7%)	25 (26.3%)	98	-

Significant association: *P < 0.05. Vitamin D is defined as levels below 20 ng/mL (50 nmol/L).

where patients with vitamin D deficiency were more likely to develop neuropathy than patients with normal vitamin D levels.

Discussion

The deficiency in vitamin D levels in human is associated with many diseases. However, little is known about the association of vitamin D levels with the DM complications among Saudi population. In this study, we investigated the association of vitamin D with the anthropometric, glycemic, and lipid profiles, in addition to the major DM complications. We found that increased levels of vitamin D are significantly associated with the female gender, increased patient's age, increased HDL level, and a lower prevalence of neuropathy among the DM volunteers. These results can increase our understanding of the role of vitamin D in the pathophysiology of DM.

Some studies reported that deficiency in vitamin D is more frequent among Arab females than males [14]. In contrast, we found in this study that female DM patients have higher levels of vitamin D than male patients. Interestingly, we found in this study that the level of vitamin D is directly correlated with the patients' age. These results may suggest that older women use oral vitamin D supplements as a prophylactic and therapeutic measure against menopause-induced osteoporosis [15].

We found in the current study that the level of vitamin D is inversely correlated with the patients' body weight. It was reported previously that obese people have a significant lower levels of vitamin D in comparison with non-obese individuals [16]. This might indicate that vitamin D regulates the lipid metabolism. Yang et al showed that vitamin D increases the lipid metabolism through inhibiting parathyroid hormone secretion [17].

Several studies showed that vitamin D increases the level of HDL and decreases the levels of LDL and triglycerides [1, 18]. In the current study, we did not find a significant correlation between the level of vitamin D and LDL; however, there is a positive correlation between serum vitamin D and HDL level. This finding is in contrast with what was reported previously by Alkhatatbeh et al [19]. This may indicate the importance of confirming these findings using a larger sample size. Al-Hawari et al reported that the promoter region of *Apolipoprotein A* gene that expresses the protein component of HDL has multiple binding sites of vitamin D receptor.

We did not find in this study any significant correlation between the level of vitamin D and DM biomarkers. This finding agrees with what was reported previously that vitamin D deficiency was not associated with type II DM among Saudi patients [10].

The results of this study showed that decreased levels of vitamin D are significantly associated with a higher prevalence of neuropathy among the DM patients. It was reported that vitamin D reduces the oxidative stress, the major cause of hypertension and neuro-damage which could explain its potential protective association with DM complications. Al-Hawari et al reported that *VDR* genetic variants were associated with the retinopathy complication among Arabic DM patients in Jordan [7].

Although a statistically significant association was found between vitamin D deficiency and the presence of neuropathy, the small number of cases in this subgroup may reduce the strength of this finding. Therefore, further studies with larger sample size of DM neuropathy complication are needed to confirm this association.

There are some limitations in this study. First, because it is a retrospective and cross-sectional study, we cannot confirm a cause-and-effect relationship. Second, the design of this study did not include data about the type of diet, medications administrated by the participant patients, and the exposure to sun light. The diet and medication can affect the lipid, glycemic, and vitamin D levels [20]. In addition, this study included only patients from the capital city in the center region of Saudi Arabia and did not include other parts in Saudi Arabia. Finally, even though we adjusted for some important factors, there may still be other hidden factors that might influence the results.

Conclusions

In conclusion, this study found the significant association between vitamin D levels and various clinical parameters in type II DM patients in Saudi Arabia. Vitamin D levels were linked to age, gender, HDL levels, and higher prevalence of neuropathy. Despite no significant correlation with glycemic markers, the protective role of vitamin D against DM complications was found. However, the study's limitations warrant further research with a larger, more diverse population to confirm these findings.

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Conflict of Interest

Authors declare that there is no conflict of interest.

Informed Consent

Informed consent was obtained from all participants in this study.

Author Contributions

Study conception and design: YFJ and YJ; data collection: JA; analysis and interpretation of results: YFJ and YJ; draft manuscript: YFJ, YJ, and JA. All authors reviewed the results and approved the final version of the manuscript.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Abbreviations

25(OH)D: 25-hydroxyvitamin D; BMI: body mass index; DM: diabetes mellitus; EMR: electronic medical records; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; IRB: Institutional Review Board; LDL: low-density lipoprotein; SPSS: Statistical Package for the Social Sciences; VDR: vitamin D receptor

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