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Original Research Article

Evaluation of Vitamin D in Patients with Type 2 Diabetes Mellites

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Abstract: ***Background*:** Type 2 diabetes mellitus is a chronic metabolic condition caused by either a reduction in insulin secretion and/or effect. It affects more than 90% of all diabetic patients. Diabetes is a complex illness that is brought on by a number of genetic and environmental (diet and lifestyle) risk factors working together. On average, one person dies from diabetes-related complications every eight seconds throughout the world. Also, according to a recent International Diabetic Federation (IDF) survey, 537 million persons aged 20-79 years are now living with diabetes worldwide. It is expected to increase to 783 million (12.2%) by 2045. Furthermore, 240 million individuals globally have undiagnosed diabetes. Therefore, there is a rising interest in studying the possible therapeutic value of fat-soluble micronutrients like vitamin D for preventing or controlling type 2 diabetes mellitus. ***Aim of Study*:** The present study was designed to evaluate levels of vitamin D in patients with type 2 diabetes mellitus. ***Patients and Methods*:** To achieve this aim, in a case-control study conducted in Diyala governorate at Baqubah Teaching Hospital and Balad Ruz General Hospital from first of January to the end of March 2023, the study included 60 patients with type 2 diabetes mellitus (30 males and 30 females). On the other hand, 30 people as a control group of both sexes (15 males and 15 females) were taken, and the ages of the two groups ranged between 30 and 65 years. The information about patients in this study was retrieved from the patients themselves through a direct interview with them, according to a prepared questionnaire. In the present study, blood samples were collected from each participant for estimation of vitamin D by (ELISA), HbA1c by (Cobas), lipid profile by (colorimetric methods) and calculated BMI. ***Results*:** The mean ± Standard Deviation (SD) of vitamin D levels for the type 2 diabetes group were (11.16± 2.18) ng /ml, with a highly significant decrease ($p < 0.001$) when compared with control group (20.73± 3.64) ng /ml. The mean ± SD of HbA1c level for the type 2 diabetes group was (8.88± 1.86) %, with a highly significant increase ($p < 0.001$) when compared with control (5.59 0.45) %. The mean ± SD of cholesterol, TG, and LDL-C levels for the type 2 diabetes group were (161.48± 21.70) mg/dl, (203.40± 8.16) mg/dl and (81.15± 21.62) mg/dl, respectively, with a highly significant increase ($p < 0.001$) when compared with the control group (105.77± 12.50) mg/dl, (191.73± 8.70) mg/dl, and (22.96± 13.38) mg/dl, respectively. The mean ± SD of HDL-C levels for the type 2 diabetes group was (39.66± 2.52) mg/dl and control (44.46± 4.82) mg/dl, with a highly significant decrease when compared with the control group. The mean ± SD of BMI for the type 2 diabetes group was (27.20± 4.25) and control (26.66± 2.30), respectively, with no significant difference ($p > 0.05$) when comparing the two groups. ***Conclusion*:** The current study concluded that Vitamin D levels showed a highly significant decrease in patients with uncontrolled type 2 diabetes mellitus when compared with those in the control group.

Keywords: International Diabetic Federation (IDF) survey, therapeutic value of fat-soluble, vitamin D.

INTRODUCTION

The pancreas is a vital endocrine-exocrine organ that produces several hormones and enzymes. Its enzymes help in the digestion of carbohydrates, fats, and proteins whereas its hormones such as insulin control blood glucose levels [1]. Diabetes mellitus is a disorder of carbohydrate metabolism, characterized by persistent hyperglycemia, glucosuria and polyuria. Diabetes mellitus (DM), an endocrinemetabolic disorder of multiple etiologies manifested by consistent

elevated levels of glucose in the blood. It occurs either due to the destruction of beta-cells of pancreas or due to the development of resistance towards insulin and leads to various metabolic dysfunctions in the body which critically affect numerous regions of the body, secondarily. Vitamin D (calcitriol) is a fat-soluble vitamin that is required for bone mineral metabolism as it is involved in calcium and phosphorus metabolism and skeletal homeostasis, as well as a wide range of non-skeletal actions. It is classed as a pro-hormone rather than a real vitamin since it exhibits hormone-like effects. The primary source of vitamin D is cholecalciferol, or vitamin D3 [25(OH)D3], which is generated by sunlight (specifically UVB radiation) on the skin from the cholesterol precursor 7-dehydrocholesterol. Vitamin D is also found in animal foods (cholecalciferol) and in vegetable foods (ergocalciferol, or vitamin D2).

There are two successive hydroxylations that happen to vitamin D precursors (vit D2 and D3), regardless of their source. Initially, in the liver, vitamins D2 and D3 are converted to 25(OH)D2 and 25(OH)D3, respectively, by the action of 25-hydroxylase. These are converted to the biologically active form of vitamin D (1,25(OH)2D) in the kidneys by the action of 1-α-hydroxlyases. Vitamin D, like other steroid hormones, is transported through the bloodstream linked to vitamin D-binding protein (DBP), a specific protein that belongs to the albuminoid family and has binding sites for all vitamin D metabolites and a high affinity for 25OHD and 1,25(OH)2D, thereby creating a large pool of circulating 25OHD, which prevents rapid vitamin D deficiency. Also, it is bound to albumin and lipoproteins in smaller quintities. Aim of the Study to evaluate levels of vitamin D and HbA1c in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

Study Design

This study is a case-control study conducted in Diyala governorate at Baqubah Teaching Hospital and Balad Ruz General Hospital from first of January to end of February 2023, the study included 60 patients with type 2 diabetes mellitus (30 males and 30 females). On the other hand, 30 people as a control group of both sexes (15 males and 15 females) were taken. The ages of the two groups were ranged between (30-65) years. All the following tests were conducted on all members of both groups to determine the level of vitamin D, glycated haemoglobin (HbA1c), lipid profile, and BMI. Through a direct interview with them, all participants provided their informed consent to take part in the study, data collection, and analysis for research motives. The information about the patients group and control group in this study was retrieved from the patients themselves, according to a prepared questionnaire (including their demographic characteristics, age, weight, length, etc.).

Sample Collection and Preparation

All participants' samples were collected by using a disposable syringe to extract approximately five milliliters of blood from the antecubital vein. The obtained blood was divided into two portions; the first portion, 3 ml, was put in a separation gel tube, which facilitates serum separation by centrifugation at 3000 rpm for 10–15 minutes. The clear serum was pipetted into clear, dry Eppendorf tubes and stored at -20 °C for the subsequent measurement of vitamin D, and lipid profile. The second part, consisting of 2 mL of blood, was put in a blood collection tube containing ethylene diamine tetra acetic acid (EDTA) as an anticoagulant for immediate measurement of glycated haemoglobin (HbA1c).

Materials

Apparatuses and Equipment's

All the apparatus and equipment that are used in this study, along with with their sources, are mentioned in Table 1.

Table 1: Apparatuses and Equipment used in the study

Instruments	Source
Human reader HS	Human/Germany
Centrifuge	Kuksan/Japan
Cobas C 111 analyzer	Roche/Germany
Spectrophotometer	Cecil/England
Incubator	Pasteur/France
Deep freeze	Sanyo/Japan

Table 2: List of Chemical (kits) Used in the Study.

Kits	Source	No. of kits
Human Vitamin D ELISA kit	Sunlong /china	1
Glycated haemoglobin (HbA1c) Kit	Roche /Germany	1
Cholesterol Kit	Linear/ Spain	1
Triglycerides Kit	Linear/ Spain	1
HDL Kit	Linear/ Spain	1

RESULTS

The control group included 15 females and 15 males, totaling 30 participants. This accounts for 33.3% of the total sample, while in the T2DM group, there were 30 females and 30 males, totaling 60 participants. This accounts for 66.7% of the total sample. Overall, there were an equal number of females (45) and males (45) in the present study, making a total of 90 participants. There was no difference in sex between the two groups (p = 1.00). Additionally, the other descriptive statistics and statistical analysis results for the demographic parameters measured in this study with their p-values for both the control and type 2 diabetic patient groups are shown in Table 3 below.

Table 3: Clinical Characteristics of the Study Subjects by Group

Parameters	Subjects	Mean ± SD*	P-value
Age (year)	DM	50.93± 8.84	**0.46**
	Control	49.47± 9.11	
Weight (Kg)	DM	81.27± 11.18	**0.8**
	Control	81.97± 12.76	
Height (m)	DM	1.73± 0.08	**0.39**
	Control	1.75± 0.09	
BMI (Kg/m^2)	DM	27.20± 4.25	**0.52**
	Control	26.66± 2.30	

*__SD__: Standard Deviation.

These results show that there is no statistically significant difference (p > 0.05) in the age, weight, and height of type 2 diabetic patients when compared to those of the control group. The table 4 below provides statistical analysis results for the levels of vitamin D, and HbA1c and their comparison in both the T2D patients and the control group, along with their associated p-values.

Table 4: Vitamin D and HbA1c Comparison Between the Studied Groups

Parameters (unit)	Subjects	Mean ± SD	P-value
Vitamin D (ng/ml)	DM	11.16 ± 2.18	< **0.001**
	Control	20.73 ± 3.64	
HbA1c (%)	DM	8.88 ± 1.86	< **0.001**
	Control	5.59 ± 0.45	

The current study conducted vitamin D (calcitriol) analysis in the studied groups; the mean vitamin D level for the T2DM group was 11.16 ng/mL (SD = 2.18), whereas the control group had a mean vitamin D level of 20.73 ng/mL (SD = 3.64).

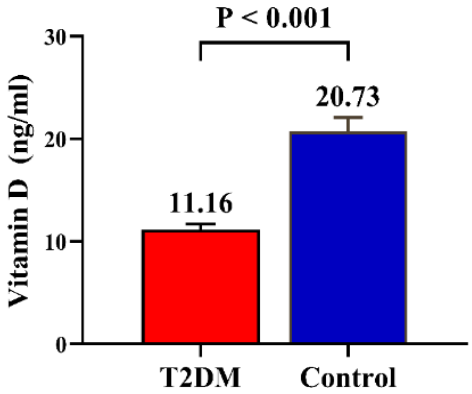

Figure 1: The mean of Vitamin D (ng/ml) levels in patients and control group

Additionally, the current study conducted an analysis of HbA1c in the studied population, which is a widely used measure of glucose control and serves as an important indicator for long-term monitoring and diagnosis of diabetes. In this study, the mean HbA1c level for the T2DM group was 8.88% (SD = 1.86), while the control group had a mean HbA1c level of 5.59% (SD = 0.45). The difference in HbA1c levels between the two groups was statistically highly significant (p < 0.001); see figure 1.

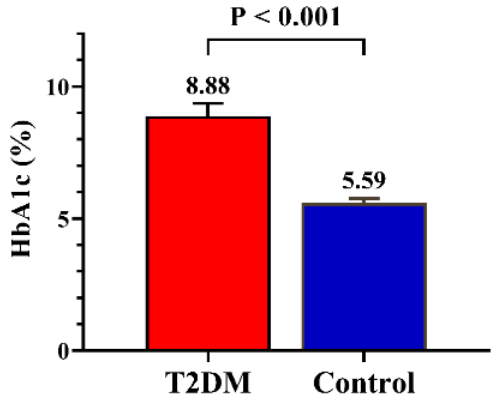

Figure 2: The mean of HbA1c% levels in patients and control group

The table 5 below provides statistical analysis results for the levels of serum lipid profile concentrations and their comparison in both the T2D patients and the control group, along with their associated p-values.

Table 5: Lipid Profile Descriptive Statistics and Comparison by Groups

Parameters (mg/dl)	Subjects	M± SD	P-value
Cholesterol	DM	161.48± 21.70	**< 0.001**
	Control	105.77± 12.50	
TGs	DM	203.40± 8.16	**< 0.001**
	Control	191.73± 8.70	
HDL	DM	39.66± 2.52	**< 0.001**
	Control	44.46± 4.82	
LDL	DM	81.15± 21.62	**< 0.001**
	Control	22.96± 13.38	
VLDL	DM	40.68± 1.63	**< 0.001**
	Control	38.35± 1.74	

The results of the present study show a highly significant increase ($p < 0.001$) in total cholesterol (figure 3), TG level (figure 4), LDL-C (figure 5), and VLDL-C (figure 6) in T2DM as compared with the control group. Whereas there was a highly significant decrease ($p < 0.001$) in HDL-C in the sera of T2D patients when compared to those of the control group, see figures 7.

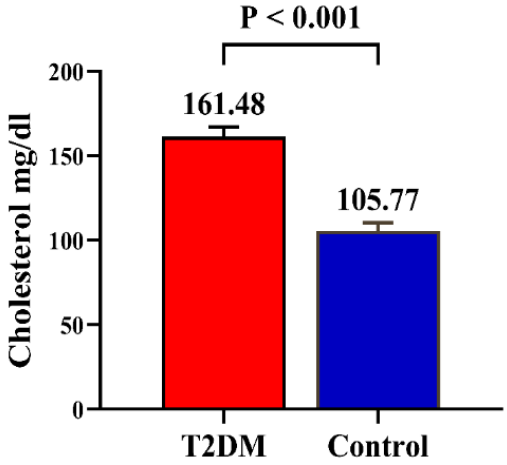

Figure 3: The mean of Cholesterol (mg/dl) levels in patients and control group

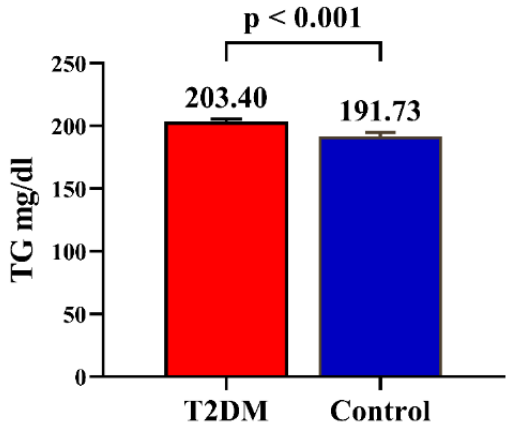

Figure 4: The mean of TG (mg/dl) levels in patients and control group

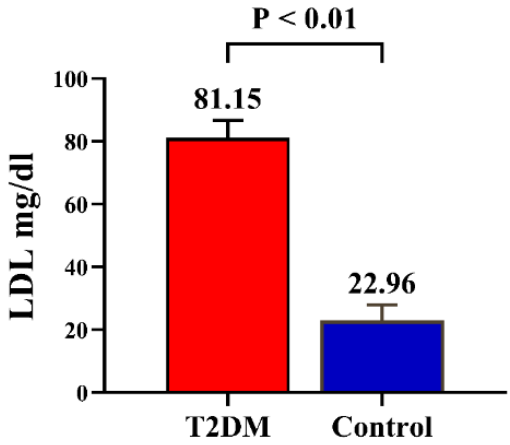

Figure 5: The mean of LDL-C (mg/dl) levels in patients and control group

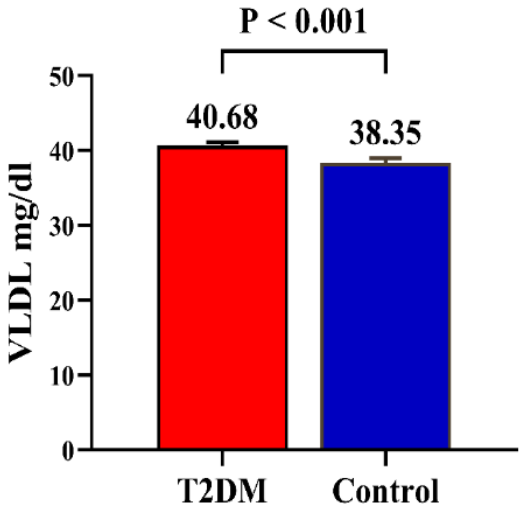

Figure 6: The mean of VLDL-C (mg/dl) levels in patients and control group

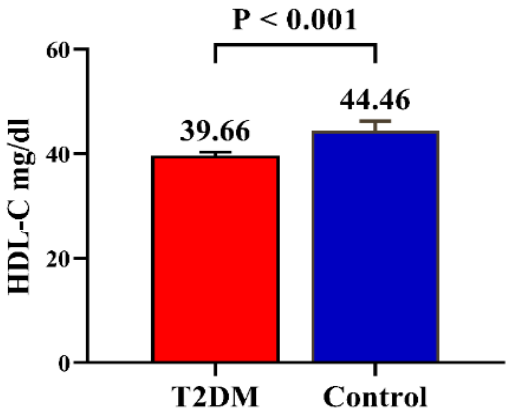

Figure 7: The mean of HDL-C (mg/dl) levels in patients and control group

A correlational analysis was also conducted to explore the relationships between vitamin D and different variables within the T2DM group. The table 6 below provides information on the correlation coefficient and the p-value associated with each correlation.

Table 6: Pearson Correlation Results between Vitamin D with Age, BMI, HbA1c, and Lipid Profile

Combination n = 60	*r*	P-value
Vitamin D - Age	0.33	**0.009**
Vitamin D - BMI	0.08	0.551
Vitamin D - HbA1c	- 0.05	0.683
Vitamin D - Cholesterol	- 0.14	0.298
Vitamin D - TG	- 0.32	**0.013**
Vitamin D - HDL_C	0.11	0.402
Vitamin D - LDL_C	- 0.13	0.338
Vitamin D - VLDL_C	- 0.32	**0.013**

DISCUSSION

It was also noted that there is no statistically significant difference (p = 0.524) in the BMI of type 2 diabetic patients when compared to those of the control group. These results indicate that BMI may not be a distinguishing factor between individuals with type 2 diabetes and those without it, and these results agree with Malone *et al.* [9]. Who found in his study that obesity is not the cause of T2DM and that the insulin resistance of T2DM occurs primarily in the muscles of lean individuals predisposed to diabetes before they become obese. However, the results of the present study disagree with Yaturu *et al.* [10] who found that elevated BMI and waist circumference (WC) were significantly associated with T2DM because most obese individuals have elevated plasma levels of free fatty acids (FFA), which are known to cause peripheral (muscle) insulin resistance. This disagreement may be due to the small sample size of the control group. These findings suggest that patients with type 2 diabetes in the studied population had highly significant (p < 0.001) lower vitamin D levels compared to the control group. This finding supports the potential role of vitamin D in the pathophysiology of T2DM, and these results agree with Darraj *et al.* [11], Fondjo *et al*. [12], Parveen *et al.* [13], Dhas *et al.* [13]. Said *et al.* [14]. In their studies, they reported that patients with T2DM may have an increased risk of vitamin D deficiency compared to those without it, which may be attributed to several factors such as limited sun exposure, obesity, and impaired absorption of vitamin D in the intestine. As well as Vitamin D deficiency, it may be associated with poor glycemic control and increased insulin resistance in patients with type 2 diabetes.

Additionally, Many previous studies have reported that low levels of vitamin D have been associated with an increased risk of developing type 2 diabetes as well as complications related to diabetes. Upreti *et al.* [15] and Hu *et al.* [16] reported in their studies that oral vitamin D supplementation was associated with improved glycemic control and other metabolic parameters and complications of type 2 diabetes by improving peripheral insulin receptor sensitivity, releasing insulin from the pancreas, and reducing or eliminating insulin resistance. Although the relationship between vitamin D deficiency and T2DM is not completely understood, there are several mechanisms through which vitamin D exerts its effects: Pancreatic beta-cells have VD receptors; beta-cells of the pancreas express the vitamin D activating 1-α-hydroxylase enzyme; the insulin gene has a vitamin D response element; skeletal muscle contains a vitamin D receptor; 1,25(OH)D enhances insulin receptor gene transcription; as well as the fact that it inhibits the renin gene, resulting in the suppression of renin production. Increased activity of the renin-angiotensin system (RAS) damages the islets, which

leads to less insulin being made, so a new target for the therapy of diabetes has been suggested: blocking renin-angiotensin activity [17].

In our study, in general, the prevalence of vitamin D deficiency (VDD) or insufficiency was found in both groups of diabetic patients and control subjects, although Iraq is one of the most sunny countries in the Middle East. This finding may be due to limited exposure to direct sunlight due to cultural practices and a very hot climate in Iraq, along with the clothing style that may have affected sun exposure, prolonged breastfeeding without taking vitamin D supplements, decreased outdoor physical activity, Our study was conducted during the winter season, and the lack of government oversight on a food's vitamin D content in many, if not all, countries. The results of the present study show a highly significant increase ($p < 0.001$) in total cholesterol, TG level, LDL-C, and VLDL-C in T2DM as compared with the control group. Whereas there was a highly significant decrease ($p < 0.001$) in HDL-C in the sera of T2D patients when compared to those of the control group. These results indicate that lipid abnormalities are common in T2D patients in the studied population. These results are in good agreement with Thapa *et al.* [18], Feingold *et al.* [19] and Athyros *et al.* [20], who found in their studies that hyperlipidemia is the commonest complication of T2DM and predisposes them to premature atherosclerosis and macrovascular complications, and that most lipid abnormalities in T2D are elevated serum total cholesterol, triglycerides, LDL-C, and low serum HDL-C.

In diabetes, many factors may affect serum lipid levels because of the interrelationship between carbohydrates and lipid metabolism. The defect in insulin action and/or secretion and elevated plasma levels of the counter regulatory hormones, which are responsible for accelerated lipolysis and impaired lipid synthesis, result in an increased plasma concentration of cholesterol, TGs, and FFAs. Insulin resistance in T2DM leads to increased peripheral lipolysis and the release of FAs for energy purposes, and excesses of these FAs are accumulated in the liver and then converted to TGs. Also, increased hepatic VLDL production occurs due to increased substrate availability via FFAs, decreased apolipoprotein B100 degradation, and increased lipogenesis [21]. Also, patients with uncontrolled T2D have frequent mild to moderate hyper triglyceridemia (HTG) because uncontrolled diabetes often has low insulin levels, so TGs don't get moved into fat cells to be turned into energy later. Also, insulin critically regulates serum VLDL concentrations by suppressing hepatic VLDL production and stimulating VLDL removal by activating lipoprotein lipase (LPL). These patients also have decreased HDL cholesterol levels associated with defective LPL catabolism of TG-rich lipoproteins [22]. The higher level of small, dense LDL cholesterol (sdLDL-C) particles is the most frequent type of dyslipidemia linked with insulin resistance. These particles are more susceptible to arterial entrance and retention, oxidation, have a lower affinity for the LDL receptor, and are more likely to cause atherosclerosis [23]. Managing lipid levels is an important aspect of diabetes care to reduce the risk of cardiovascular complications. This may involve lifestyle modifications, such as adopting a healthy diet, engaging in regular physical activity, weight reduction, and other factors that affect lipids, as well as micronutrient supplementation and medication interventions, if necessary, to optimize lipid profiles [24].

CONCLUSIONS

The current study concluded that:

Vitamin D levels showed a highly significant decrease in patients with T2DM when compared with those in the control group. This finding supports their potential role in the pathophysiology of T2DM.There was a negative correlation among levels of vitamin D with glycated hemoglobin (HbA1c), and this finding implies that his levels have improved glycemic control in type 2 diabetes.

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