

Effect of Vitamin D Supplementation on Blood Glucose Homeostasis, BMI and Lipid Profile in Diabetic Patients with Vitamin D Deficiency

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ABSTRACT

Background: Vitamin D deficiency seems to be frequent and involved in pathogenesis of numerous diseases, including metabolic abnormalities and glucose homeostasis. The aim of study was to investigate the effect of vitamin D supplementation on FBS, glycemic control, lipid profile and BMI in diabetic patients with vitamin D deficiency. **Methods:** A case control study conducted on diabetic and non-diabetic patients include 50 health and 150 diabetic patients. Diabetic patients have no or vitamin D deficiency and health control as well. Both were thereafter FBS, HbA1c measured first time on supplemented vitamin D either 50, 000 UI orally or 200,000 IU IM. After three months all blood parameters were measured include FBS, HbA1C, lipid profile and BMI. T test was used for determination of statistical significant between groups. **Results:** Vitamin D supplementation had profound effect and control FBS, HbA1C, lipid profile and BMI $P < 0.05$ on both Types 1 and types 2 diabetes mellitus. However, such effect has not been found in counterpart healthy control with vitamin D deficiency. The regular weekly dose of 50,000 IU were found more promising values on FBS, HbA1C, lipid profile and BMI $P < 0.05$ than the monthly does. Physical activities of cases and control did not shown to have any cofound factors on FBS, HbA1C, lipid profile and BMI. **Conclusion:** Vitamin D can be considered as a therapeutic agent along with the other treatments for both types of Diabetes mellitus in which could be deemed to use for routine treatment due to vitamin D deficiency is worldwide problem.

Keywords: Glucose, BMI, Vitamin D, Diabetes mellitus, Supplementation, Lipid profile.

Introduction

Vitamin D deficiency seems to be frequent and linked to pathogenesis of numerous diseases, including metabolic abnormalities (1). The connotation between vitamin D deficiency and insulin resistance has been suggested (2). A numbers of clinical studies showed that vitamin D supplementation reduces risk of some metabolic parameters such as BMI, total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG), glycated hemoglobin (HbA1c), as well as decreases insulin resistance in T2DM patients (3–5). However, the action vitamin D for reducing risk of metabolic disorders development proposed through vitamin D receptor (VDR) and vitamin D-metabolizing enzymes were detected in various cell types, including pancreatic beta cells and insulin-responsive cells such as adipocytes (6,7). Some evidences suggest that vitamin D control the numerous sequential events that are responsible for enabling the pancreatic beta cells to secrete insulin, and thereby to control of blood glucose level (8-10). Low vitamin D may diminish calcium's ability to affect insulin secretion. (11,12). In addition, the evidence indicates that vitamin D treatment improves glucose tolerance and insulin resistance (13). However vitamin D deficiency leads to reduced insulin secretion (14). This article investigates the effect of vitamin D supplementation on FBS, glycemic control, lipid profile and BMI in diabetic patients with vitamin D deficiency (15-20).

Material and Methods

Study Population

A case control study carried out from beginning of January to the Beginning of April on diabetes and non-diabetes subjects. Diabetes subjects include T1DM and T2DM from diabetes center. Non-diabetes volunteer matching to

diabetes patients were selected from general population and/ or for diabetes center. The total samples size (case and control) were 200 subjects (81 male and 119 female) diabetes and non-diabetes with ages ranging between 18-70 years old.

The case and control were categorized as following

The patients in this study were diabetes and non-diabetes and the sample was categorized as following:

- 100 patients with DM and have vitamin D deficiency.
- 50 patients with DM and have no vitamin D deficiency.
- 25 Healthy with vitamin D deficiency (Control 1) and on vitamin D supplementation.
- 25 Healthy no vitamin D deficiency (Control 2).

Protocol for the study include

- Measurement of FBS and HbA1C before vitamin D supplementation started and after.
- For lipid profile and BMI measured only once after taken vitamin D for at least 3 months.

All the subjects were followed by doctor in diabetic center in which doctor prescribed vitamin D to the patients.

- On vitamin D weekly dose of 50, 000 IU oral supplementation or injectable monthly dose ranging from 200, 000 IU to 600, 00. The dose common reported in this study was 200,000 IU.
- BMI was measured through weighing weight with minimum clothing and height with bare foot by using SECA balance machine finally BMI was calculated by using $\text{weight}/\text{Ht (M)}^2$.

Questionnaire

The questionnaire for this study based on 20 items divided into four sections. It contained questions about personal information, demographic and socioeconomic characteristics, biochemical investigations, and anthropometric data.

Ethical statement

This study was granted approval by the local Ethics Committee of the Benghazi province. Informed written consent was obtained through a consent form that was given to the participants along with the questionnaire.

Statistical analysis

The data from the questionnaires was entered using Excel. Data set was exported to SPSS v.22 and Epi-info for complete analysis. Statistical analysis was carried out for the complete samples which were created according to measurements in which frequencies and percentages were used. To determine the differences regarding each categorical variable in the groups, T test was performed to compare the mean of FBS, HbA1C and lipid profile within and between groups. $P \leq 0.05$ was considered to be statistically significant.

Result

The data collected on 200 subjects were shown that the average ages of subjects were 40 ± 6 years old in which about 50% of patients fall in the age groups between 31-45 years old, followed by those with age groups between

46-60 years old (30.5%), whereas the age groups 18-30 and more than 60 years old present by 12.5% and 7.5% respectively (Table 1). Regarding gender distribution, it has been found that, approximately 60% of the subjects female and the rest (40%) male (Table 1).

Table 1. Age and gender distribution

		N	N %
Patient Age	18_30	25	12.5%
	31_45	99	49.5%
	46_60	61	30.5%
	> 60	15	7.5%
	Total	200	100.0%
Gender	male	81	40.5%
	female	119	59.5%
	Total	200	100.0%

In the next family history of Diabetes mellitus has been investigated, and found that approximately 64.5% did not have family history of DM, mother and father side present by 18.5% and 10.5% respectively and those who has parent with DM being least (4.5%) (Table 2).

Table 2. Family history of diabetes mellitus

	N	N %
Mother Yes	37	18.5%
Father Yes	21	10.5%
both mother and father	9	4.5%
No	133	64.5%
Total	200	100.0%

In table 3, 50 (25%) were healthy control, and about 52 (26%) of patients were on insulin therapy while 88 (44%) of patients were on oral hypoglycemic agents. There were about 28% of patients reported as T1DM and 47% T2DM (Table 3).

Table 3. Types of hypoglycemic agents and diabetes

		N	N %
Types of hypoglycemic agents	Healthy control	50	25.0%
	DM insulin	56	28.0 %
	DM Tablet	88	44.0%
	DM both	6	3.0%
	Total	200	100.0%
Types of diabetes	Healthy control	50	25.0%
	T1DM	56	28.0%
	T2DM	94	47.0%
	Total	200	100.0%

Glycemic control, fasting blood glucose lipid profile and body weight status have been investigated among case and control as shown in table (4). The mean blood glucose was higher in both DM patients with and without vitamin D deficiency 180 Vs 171 mg/dl. After diabetic patients received vitamin D, blood glucose has dropped from 180 mg/dl to 151 mg/dl. Furthermore, HbA1C also lowered from 8.8% to 7.5% while improved lipid profile and BMI (Table 4).

Table 4. Fasting blood glucose, glycemic control and lipid profile among control and cases

	Case and control groups			
	DM patients have vitamin D deficiency	DM patients have no vitamin D deficiency	Health have vitamin D deficiency	Healthy no vitamin D deficiency (Control)
	Mean± SD	Mean± SD	Mean± SD	Mean± SD
FBS before taken vitamin D	180± 24	171± 21	78±11	80±12
FBS after treatment with vitamin D	151±22	171±22	85±12	80±20
HbA1c before treatment with vitamin D treatment	8.8±1	8.3±1	4.3±0.6	4.0±0.7
HbA1c after taken vitamin D	7.5±1	8.3±1.2	4.3±0.6	4.5±0.8
TG	109±10	124±3	65±7	94±8
S. cholesterol	113±12	175±16	72±10	93±11
LDL	65±6	122±14	77±6	70±8
HDL	45±5	33±2	52±6	55±4
VLDL	22±1	24±3	13±1	19±2.4
weight	76±4	81±12	76±10	81±11
BMI	26.5±4	27.5±2	26.9±4	23.9±3

In regard FBS in both type 1 and 2 diabetes mellitus have found dropped significant after vitamin D treatment from 187mg/dl to 166 mg/dl in T1DM and 171 mg/dl to 153 mg/dl in T2DM (P < 0.05). These values also found dropped in HbA1c in both types of diabetes (table 5).

Table 5. Fasting blood glucose, glycemic control and lipid profile among types of diabetes

	Types of diabetes					
	Health control 2	T1DM		T2DM		P values (T1DM/T2DM)
	Mean± SD	Mean± SD	P values	Mean± SD	P values	
FBS before taken vitamin D	79±9	*187±27		#171±21		
FBS after treatment with vitamin D	85±7	*166±19	0.001	#153±13	0.005	

HbA1c before vitamin D treatment	4.6±0.5	**8.8±0.8		##8.5±0.5	
HbA1c after taken vitamin D	4.3±0.2	**7.9±0.4	0.01	##8.0±0.45	0.04
TG	80±6.8	127±15		105±12	0.002
S. cholesterol	82±9	133±12		112±11	
LDL	40±5	90±6		110±9	
HDL	45±5	43±4		43±3	
VLDL	16±3	25.4±4		21±5	
BMI	28.4±20	25.9±4		26.9±7	

The comparison has been made between FBS and HbA1C within groups of T1DM and T2DM and between T1DM and T2DM. Student T test was performed at $\alpha < 0.05$ which considered significant. The effect of types of vitamin D treatment on glycemic control, FBS and lipid profile has been investigated and found that both types of vitamin D treatment reduced FBS, HbA1C but profound and significant effect found on those used vitamin D tablet ($P < 0.05$). Both treatments found to have improved lipid profile (Table 6).

Table 6. Relation amid types of vitamin D supplement and fasting blood glucose, glycemic control and lipid profile

	Types of vitamin D supplement among diabetic patients					
	no treatment	injection		orally		P values
	Mean± SD	Mean± SD	p values	Mean± SD	P values	
FBS before taken vitamin D	91±11	150±13		167±23		
FBS after treatment with vitamin D	91±14	142± 15	0.000	143±12	0.0001	
HbA1c before vitamin D treatment	5.4±2	7.4± 0.8		7.6±0.9		
HbA1c after taken vitamin D	5.3±9	6.9±0.4	0.01	6.9±0.7	0.02	
TG	111±14	131±21		95±11		0.000
S. cholesterol	117±13	129±24		102±8		0.000
LDL	34±7	57±8		35±6		0.001
HDL	44±6	42±8		45±9		0.06
VLDL	22±5	26±4		20±4		0.00
BMI	27.6±3	27.7±2		26.3±5		0.04

The comparison has been made between FBS and HbA1C within groups vitamin supplement and between orally and injectable vitamin D. Student T test was performed at $\alpha < 0.05$ which considered significant.

In compared to monthly vitamin D supplement, the weekly dose of vitamin D (50, 000 IU) was show has more significant effect on reducing FBS , HbA1C , lipid profile and BMI as shown in Table 7.

Table 7. Relation between vitamin D doses, fasting blood glucose, glyceemic control and lipid profile

	Dose of vitamin D					P values
	No dose	Weekly (50, 000 IU)		Monthly (variable)		
	Mean± SD	Mean± SD	P values	Mean± SD	P values	
FBS before taken vitamin D	137±17	176±22		157±16		
FBS after treatment with vitamin D	139±18	149±17	0.000	141±25	0.04	
HbA1c before vitamin D treatment	6.4±1	8.4±1		8.5±1.5		
HbA1c after taken vitamin D	6.4±0.8	7.8±1	0.02	8.2±0.99		
TG	111±11	99±13		130±15		0.000
S. cholesterol	117±22	107±18		126±21		0.000
LDL	34±4	60±7		100±17		0.000
HDL	47±5	43±3		40±6		
VLDL	22±4	20±3		26±5		0.02
BMI	27.6±3	26.7±6		27.5±2		0.03

The comparison has been made between FBS and HbA1C within groups and between weekly and monthly vitamin D doses. Student T test was performed at $\alpha < 0.05$ which considered significant.

In the next, further investigate one of confound factors such as physical activities on glyceemic and lipid profile, The result in Table 8 shown that no active and low active patients have much better improved FBS, glyceemic control, lipid profile but worse BMI than moderate and high physical activities (Table 8).

Table 8. Effect of physical activities on fasting blood glucose, glyceemic control and lipid profile

	Types of physical activities			
	no active	Low	Moderate	high
	Mean± SD	Mean± SD	Mean± SD	Mean± SD
FBS before taken vitamin D	150±14	164±16	186±23	76±12
FBS after treatment with vitamin D	138±12	141±15	180±21	80±11
HbA1c before vitamin D treatment	6.9±1	8.0±1.6	9.1±1.9	9±2.1

HbA1c after taken vitamin D	6.6±1.1	7.3±1.6	8.7±1.5	8.9±2
TG	105±21	109±11	186±16	129±24
S. cholesterol	108±12	129±23	88±9	150±17
LDL	37±2	45±7	19±3	78±8
HDL	44±7	39±6	48±8	41±5
VLDL	21±2	22±7	37±7	26±5
BMI	27.3±4	26.4±8	26.7±3	22.6±6

The comparison has been made between FBS and HbA1C within same groups physical activities and Student T test was performed at $\alpha < 0.05$ which considered significant.

Discussions

The present study revealed that, Vitamin D supplementation in diabetic patients has vitamin D deficiency found to have improved roles in FBS and HbA1C. These found have been demonstrated in several studies carried by Hu, et al., (21), Kostoglou et al (22) and Li et al (23). In the most studies conducts in field of vitamin D and diabetes in which Vitamin D has linked to improved FBS and HbA1C in type 2 diabetes mellitus.

According to our knowledge no study highlighted the role of vitamin D in lowered both FBS and HbA1C. Our study considered first study highlighted role of vitamin D in lowering of glycemic control and FBS in Type1 diabetes mellitus. In the present study there also found that vitamin D supplementation improve lipid profile in diabetes patients. In compared to health control subjects, vitamin D lowered serum triglycerides, cholesterol, LDL. In fact majorities of studies were investigated role of vitamin D in control lipid profile in type 2 diabetes mellitus (24, 25, 26). Overall this study demonstrated that vitamin D improved serum levels of TC, TG, and LDL in patients with T2D but changes of serum HDL was not satisfactory. Similarly, has been found in studies of effect of vitamin D on lipid profile in Iran (27), and USA (28). However some researches have been studies such effect on types 1 diabetes mellitus but the studies were found no relation between vitamin D and lipid profile (29,30).

The current study further investigated the form and dose of vitamin D that have effect in an improved of FBS, glycemic control, lipid profile and found that weekly oral dose in concentration of 50, 000 IU have much improver of serum glucose, HbA1C, lipid profile and BMI than injectable one. However, there were different doses have been found to have significant effect on lowering FBS, HbA1C , lipid profile ranging accordingly from 1000 to 50, 000 IU (31-36). Furthermore cofound factor such as physical activities and types of food intake were also investigated and found that physical activities did not mimic vitamin D effect.

The withdrawal of patients from the study was the major limitation of the study. According the result of this study vitamin D is considered crucial for improved FBS, HbA1C, lipid profile, therefore should be one of the routine supplement to all diabetes patients. Overall, vitamin D supplementation in diabetic patients improved BFS, HbA1C, lipid profile and the suitable dose and form made such affect were weekly orally 50.000 IU. This study was highlighted such effect in both types of diabetes.

Conclusion

Vitamin D supplementation for diabetic patients with vitamin D deficiency has been found reduced FBS, HbA1c and improved lipid profile. These lowered and improved values found in both types of DM. Oral supplementation of vitamin D given much better reduction values in FBS, HbA1C, lipid profile and BMI than injectable form of vitamin D. Furthermore the weekly dose of vitamin D has significant impact on FBS, HbA1C, lipid profile and BMI than other times.

Although these effect of vitamin D supplementation was independent factors other than physical activities. Therefore, vitamin D can be considered as a therapeutic agent along with the other treatments for both types of Diabetes mellitus. In addition, the deficiency of vitamin D is associated with an increased level of BMI in the studies of both diabetic and non-diabetic subjects.

Declarations

Source of Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests Statement

The authors declare no competing financial, professional and personal interests.

Consent for publication

We declare that we consented for the publication of this research work.

Ethical Approval

This study was granted approval by the local Ethics Committee of the Benghazi province. Informed written consent was obtained through a consent form that was given to the participants along with the questionnaire.

Availability of data and material

Authors are willing to share data and material according to the relevant needs.

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