

Correlation of serum vitamin D3 with diabetes mellitus type 2: A single centre cross sectional study

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Abstract

Introduction: Vitamin D deficiency is one of the prevalent nutritional deficiency worldwide and studies reveal an association between vitamin D deficiency and type 2 diabetes mellitus. This study aims to determine the levels of serum vitamin D3 in type 2 diabetics and non-diabetic patients.

Materials and Methods: A cross-sectional study was conducted from April 2017 to March 2018 on patients diagnosed with type 2 diabetes mellitus (T2DM) taking regular anti-diabetic treatment were considered as case group and those with corresponding variables like age and sex with case group except T2DM considered as control group. The enrolled patients were investigated for fasting blood sugar (FBS), post prandial blood sugar (PPBS), HbA1c, serum creatinine and vitamin D level. Anthropometric and blood pressure measurements were conducted twice taking an average of both the measurements.

Results: Among the total of 100 patients enrolled, 80% were in case group and 20% were in control group. The mean ages were 55.09 years and 55.5 years in case and control group respectively. Blood pressure were comparable between the two groups. Mean HbA1c level was also high in case group (7.42%) compared to control group (5.17%) ($p < 0.001$). Mean FBS level (142.41 mg/dL vs. 93 mg/dL) and PPBS (170.51 mg/dL vs 31.73 mg/dL, $p < 0.001$) were significantly increased in case group compared to control group. Serum creatinine and vitamin D levels were comparable among case and control group.

Conclusion: There was no definite co-relation between vitamin D level and type 2 diabetes mellitus. The relationship between HbA1c and vitamin D was found to be insignificant.

Keywords: Anthropometric, Blood sugar, Creatinine, Diabetic, Hb1Ac, Vitamin D.

Introduction

Vitamin D, the sunshine vitamin is more obtained from sunlight that comes in contact with the skin and less from the diet. However, vitamin D deficiency or hypovitaminosis D is increasing in people with progression in years and is widely observed in diabetics. Vitamin D receptors occur in many organs including pancreatic beta cells causing their growth and differentiation and further regulation of insulin secretion. Hence its deficiency is known to cause hyperparathyroidism leading to glucose intolerance.¹ Along with the maintenance of skeletal system it is responsible in protecting the human body from cancers, autoimmune, cardiovascular disease, type II diabetes mellitus (T2DM) and infectious diseases.²

There are several studies reporting the role of vitamin D in maintaining normal glucose metabolism as well as T2DM.³ Vitamin D deficiency is one of the prevalent nutritional deficiency worldwide especially in younger and women population.^{4,5} Literature reveals that vitamin D deficiency causes glucose intolerance and altered insulin secretion⁶ and also exert a negative effect on beta cell function., nevertheless its restoration regulates the glucose metabolism.^{7,8} Clinical studies reported previously have demonstrated an inverse association between baseline serum vitamin D and incident diabetes that persisted after adjustment for T2DM risk factors such as obesity, fasting glucose, and hypertension. In non-diabetics, lower serum vitamin D was associated with higher fasting glucose especially when the level was < 40 mmol/L. A study reported

that vitamin D concentration in enrolled patients was inversely related with glucose status, insulin resistance and metabolic syndrome risk at 10-year follow-up.^{9,10}

An increased prevalence of T2DM has been described in vitamin D deficient individuals and insulin synthesis and secretion have been shown to be impaired.¹¹ However, few studies have shown inconsistent results of vitamin D effect on extra skeletal system and chronic diseases.^{12,13} An extensive debate exists on the influence of vitamin D on diabetes risk after the effects of insulin secretion, sensitivity, and overall adiposity.¹⁴

The present study mainly aims to determine the levels of serum vitamin D3 in patients of diabetes mellitus type 2 and non-diabetes patients. Further vitamin D3 levels were correlated with glycaemic control of enrolled patients.

Material and Methods

The present cross-sectional study was conducted at the Department of Medicine, Saraswati Institute of Medical Sciences Anwarpur, Hapur during a period from April 2017 to March 2018. Patients having type 2 diabetes mellitus (T2DM) taking regular treatment (either oral hypoglycemic agents or insulin or a combination of both) were considered as case group and patients who have age and sex matched with case group in all variables except T2DM considered as control group. Patients presenting with diabetic ketoacidosis/ hyperosmolar coma, who were already taking vitamin D supplementation, pregnant women, patients

suffering from chronic kidney disease/chronic liver disease or hypertension were excluded from the study.

A detailed information regarding age, clinical history, and anthropometric measurements like height and weight were collected to calculate body mass index (BMI). Blood samples (10 mL) were collected, serum was separated and stored at 20°C. Assessment of glycemic control was done by estimation of fasting blood sugar (FBS), post prandial blood sugar (PPBS), HbA1c. Serum creatinine and vitamin D level were also assessed. Anthropometric and blood pressure measurements were conducted twice and the average of the two measurements were used.

Statistical analysis

Statistical analysis was done using statistical package for social sciences (SPSS) version 21.0. Categorical variables were presented in number and percentage and correlated using Chi-Square test/Fisher's Exact test. Continuous variables were presented as mean \pm SD and median and compared using Independent T test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups. A p value of <0.05 was considered statistically significant.

Results

A total of 100 patients included in this study were divided into two groups; case group (n=80) and control group (n=20). The mean age was 55.09 years and 55.5 years in case and control group with BMI index 26.26kg/m² and 23.4 kg/m², respectively. A significant mean difference in BMI was observed among case and control group (p=0.014). Mean HbA1c level was also high in case group (7.42%) compared to control group (5.17%) (p<0.001). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were comparable between the two groups. Mean FBS level was significantly increased in case group (142.41 mg/dL) compared to control group (93 mg/dL), p<0.001. Similarly, PPBS was significantly increased in case group compared to control group (170.51 mg/dL vs 31.73 mg/dL, p<0.001). Mean serum creatinine was 1.11 and 1.06 mg/dL in case and control group, respectively. Mean vitamin D was comparable between case and control group (21.75 and 27.65 ng/dL). No significant difference was observed in blood pressure, serum creatinine and vitamin D level among case and control groups (p>0.05) as shown in Table 1.

In case group, 32.5% patients had normal FBS level (<126mg/dL), 57.5% patients showed FBS level between 126-180 mg/dL while 8 patients had FBS >180 mg/dL. All the patients from control group had normal FBS level. Significant difference was observed in FBS level between case and control groups (p<0.001). Further, 21.3% patients had normal HbA1c (<6.5%), 60% patients had HbA1c level 6.5-8.5% and 18.8% patients had found >8.5% HbA1c level in case group. Normal HbA1c level was seen in control group (p<0.001). 61.3% patients had vitamin D deficiency and 35% patients had vitamin D between 20-50 ug/dL in case group, whereas, 45% patients had vitamin D deficiency and eight patients had vitamin D level between 20-50 ug/dL

in control group. There was no significant difference between both the groups with respect to SBP, DBP, PPBS, and serum vitamin D level (Table 2).

Spearman correlation showed a negative negligible correlation between vitamin D levels and HbA1c, which was not statistically significant in case as well as control group. Correlation coefficient was found to be -0.00446 and -0.313 in case and control group (p=0.9678 and p=0.313), respectively. Fig. 1 and Fig. 2 showed correlations between vitamin D and HbA1c in case and control group, respectively.

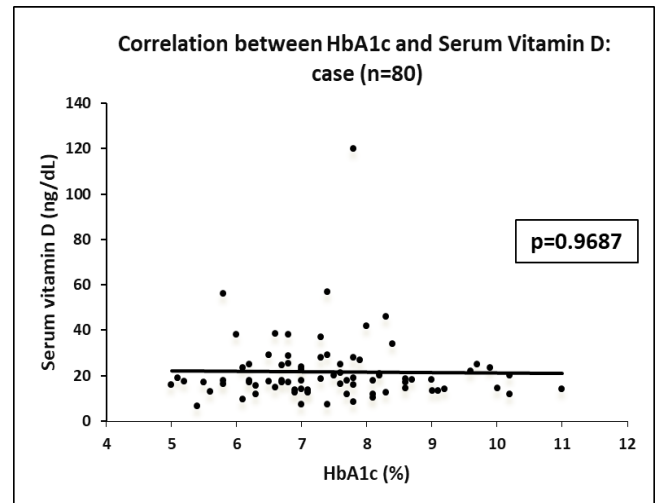


Fig. 1: Correlation between HbA1c and serum vitamin D in case group (n=80)

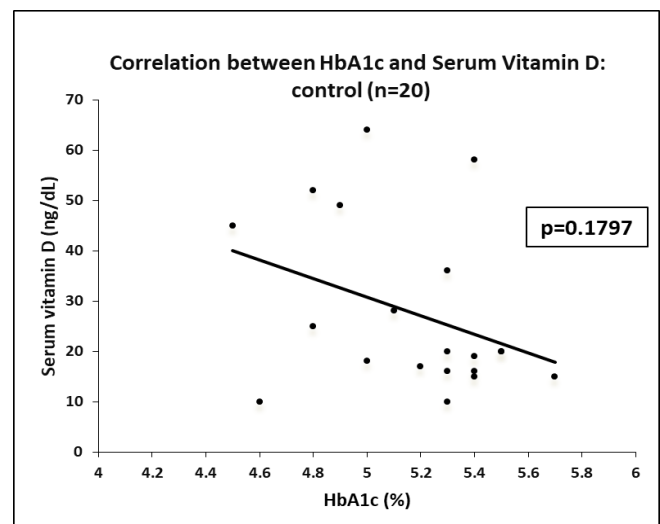


Fig. 2: Correlation between HbA1c and serum vitamin D in control group (n=20)

Table 1: Demographic characteristics

Parameters	Case group (n=80)	Control group (n=20)	P value
Age (years)	55.09 (11.02)	55.5 (11.07)	0.881
Height (cm)	164.12 (5.26)	167.8 (9.04)	0.094
Weight (kg)	70.71 (11.27)	65.55 (12.09)	0.033
BMI (kg/m ²)	26.26 (4.56)	23.4 (4.49)	0.014
HbA1c (%)	7.42 (1.28)	5.17 (0.32)	<0.001
DBP (mm Hg)	83.82 (10.03)	84.4 (9.79)	0.745
SBP (mm Hg)	132.52 (18.84)	133.1 (16.1)	0.573
FBS (mg/dL)	142.41 (27.41)	93 (9.6)	<0.001
PPBS (mg/dL)	170.51 (31.73)	116.6 (11.43)	<0.001
Serum creatinine (mg/dL)	1.11 (0.23)	1.06 (0.17)	0.357
Serum vitamin D (ng/mL)	21.75 (14.9)	27.65 (16.77)	0.133
Data shown as mean (SD). BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; HbA1c, Hemoglobin A1c; PPBS, post prandial blood sugar; SBP, systolic blood sugar.			

Table 2: Distribution of patients according to Blood pressure, Hb1Ac and serum vitamin D level

Parameters	Range	Case group (n=80)	Control group (n=20)	P value
SBP (mmHg)	<140	58 (72.5)	15 (75.0)	0.840
	140-160	16 (20.0)	3 (15.0)	
	>160	6 (7.5)	2 (10.0)	
DBP (mmHg)	<90	62 (77.5)	15 (75.0)	0.841
	90-110	16 (20.0)	4 (20.0)	
	>110	2 (2.5)	1 (5.0)	
FBS (mg/dL)	<126	26 (32.5)	20 (100.0)	<0.001
	126-180	46 (57.5)	0 (0)	
	>180	8 (10.0)	0 (0)	
PPBS (mg/dL)	<200	69 (86.3)	20 (100.0)	0.114
	200-280	11 (13.8)	0 (0)	
HbA1c (%)	<6.5	17 (21.3)	20 (100.0)	<0.001
	6.5-8.5	48 (60.0)	0 (0)	
	>8.5	15 (18.8)	0 (0)	
Serum vitamin D (ng/dL)	<20	49 (61.3)	9 (45.0)	0.122
	20-50	28 (35.0)	8 (40.0)	
	>50	3 (3.8)	3 (15.0)	
Data shown as n (%). DBP, diastolic blood pressure; FBS, fasting blood sugar; PPBS, post prandial blood sugar; SBP, systolic blood sugar.				

Discussion

Vitamin D is a multifaceted hormone playing a key role in different biological functions, hence alteration in its levels affect various processes at cellular, molecular and genetic levels causing extra skeletal complications.

T2DM is another toll taking health issue affecting a huge population in India and globally. Studies have shown an association between T2DM and low concentrations of vitamin D wherein an impaired glucose metabolism was observed.^{15,16}

Among the enrolled patients in this study 80% had T2DM and 20% were non-diabetics. The present study has demonstrated a higher incidence of vitamin D deficiency in overall recruited patients indicating that both T2DM and non-diabetic control patients were equally deficient. Lim et al.¹⁴ conducted a similar study with vitamin D deficient

patients of age 49.2 ± 13.0 , BMI 25.0 ± 3.7 and with Kaplan-Meier analysis showed a higher probability of developing T2DM in patients of vitamin D deficient group than those in the insufficient or sufficient group.

Previous studies by Grimnes et al. and Mattila et al. have shown an inverse co-relation between vitamin D level and T2DM risk.^{17,18} Pittas et al. studied a co-relation between vitamin D concentration and risk of incident type 2 diabetes in middle aged women and found to be inversely associated.¹⁹ A study in Asian population at high risk of T2DM, by Lim et al. showed that the participants with vitamin D deficiency had 3.4 times the risk of T2DM development than in those with sufficient levels, even after adjustment for obesity, insulin resistance and pancreatic β cell function with other known risk factors for T2DM. Nonetheless, vitamin-D supplementation was not found to

be effective in reducing HbA1c as revealed by Poel et al. and Randhawa et al.^{20,21} The findings from present study reveals absence of significant association of hemoglobin glycation with vitamin D and further questions its definitive role in T2DM except for poor lifestyle in the overall population. Luo et al. showed that within T2DM patients, regardless of vitamin D deficiency, its low level is associated neither with increased prevalence of the metabolic syndrome nor with glycemic control. Several *in vitro* studies indicate that vitamin D plays a vital role in insulin secretion and sensitivity, however, literature reveals inconsistencies among these results in humans.^{22,23} Likewise, a number of studies have shown a consistent inverse association between vitamin D level or its intake on the occurrence of T2DM, but this study could not demonstrate such relationship.

Elkassaby et al.²⁴ observed a momentary improvement in glycemia in T2DM with oral D3 supplementation without affecting HbA1c or beta cell function and concluded minimal or absence of therapeutic efficacy of high dose of vitamin D. A similar study by Sadiya et al. reported insignificant change in HbA1c levels after six months of supplementation in vitamin D-deficient obese T2DM patients.²⁵ The present study showed 60% patients with HbA1c level 6.5-8.5% and 18.8% patients with >8.5% HbA1c whereas 21.3% patients had normal HbA1c. However, another study conducted in South Asian patients with T2DM showed a significant decrease in both HbA1c and weight with vitamin D and calcium replacement therapy.

Furthermore, a systematic review by Mitriet al. it was revealed that out of 11, eight trials did not show improvement in glycemic control with vitamin D supplementation.²⁶ In the present study 57.5% patients showed higher FBS level and more than 60% patients with higher Hb1Ac level that was in concordance with the results of fifteen trials systematically reviewed by George et al. that showed no significant improvement was observed in fasting glucose, HbA1c or insulin resistance in those treated with vitamin D compared with placebo.

In a placebo-controlled trial by Kampmann et al. it was observed that there was no advancement in insulin resistance, blood pressure, inflammation or HbA1c with optimum vitamin D levels. This is in concordance with the present findings that vitamin D levels did not show any significant linear association with Hb1Ac in T2DM cases as well as control group patients.²⁷ The present study did not investigate any relationship between insulin resistance and markers of glucose homeostasis with altered vitamin D levels in patients with type 2 diabetes that was in accordance with the study reported by Shoumer et al.²⁸

Vitamin D supplementation can delay the onset of diabetes or improve the glycemic control in diabetics is yet to be recognized. These inconsistencies may be due to the variation in patients, their age, BMI and method of measurement. Therefore, future studies to clarify the efficacy of vitamin D supplementation in preventing

diabetes and pre-diabetes are warranted, especially in the urban population of Hapur.

Though vitamin D deficiency is prevalent in T2DM and non-diabetic control subjects, its relationship in glycation control or insulin resistance in T2DM subjects could not be confirmed in our population. This is potentially an important finding for public health, demonstrating that improvement in vitamin D status is not the only factor responsible for better health of the individuals but lifestyle and dietary changes seem to play a role which will improve the overall health including hemoglobin glycation and insulin resistance along with vitamin D levels.

Limitation

This study was a cross sectional study, carried out on urban patients where rural patients were not included. Moreover, the method used to measure vitamin D levels was ELISA method which is less sensitive to LCMS/MS method.

Conclusions

The present study did not demonstrate any association between vitamin D level and T2DM. The patients showed an insignificant relationship between HbA1c and vitamin D levels and warrants further investigation.

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Conflict of interest

None.

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