Original Article

Study on the association of Vitamin D with glycaemic control in patients with type 2 diabetes mellitus

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Abstract

Background: Type 2 diabetes mellitus (DM) is associated with increased morbidity and mortality due to the development of complications, especially due to poor glycaemic control. Besides its role in calcium homeostasis, Vitamin D is involved in the pathophysiology as well as glycaemic control of type 2 DM.

Methods: Eighty patients diagnosed with type 2 DM were included. Vitamin D levels along with fasting blood sugar, post-prandial blood sugar, glycosylated haemoglobin and insulin were measured in all the individuals. Insulin resistance was calculated as homeostasis model for assessment of insulin resistance.

Results: Vitamin D deficiency was observed in 52.5% of the patients. Vitamin D levels were not associated with markers of glycaemic control or insulin resistance.

Conclusions: Hypovitaminosis D was observed in more than half of the patients with type 2 diabetes. suggesting a potential for vitamin D supplementation in type 2 DM patients.

Keywords: Diabetes mellitus, glycated haemoglobin, glycaemic control, Vitamin D

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INTRODUCTION

Type 2 diabetes mellitus (DM) or adult-onset diabetes or noninsulin-dependent DM is the most common type of diabetes accounting for a prevalence >85% among all diabetic population.[1] Type 2 DM is associated with several complications including macrovascular and microvascular complications. Achieving good glycaemic control helps in reducing the complications associated with DM. To achieve good glycaemic control and to decrease the complications of DM, diabetes patients should follow strict dietary control, regular exercise, adherence to medication and regular monitoring of glucose levels.[2] Traditional markers of glycaemic control which are frequently used for monitoring diabetes patients include fasting blood sugar (FBS), post-prandial blood sugar (PPBS), glycosylated haemoglobin (HbA_{1c}). In addition to these markers, fructosamine, glycated albumin and 1,5-anhydroglucitol are also used as markers of glycaemic control.[3]

Vitamin D is a fat soluble vitamin that is synthesised from 7-dehydrocholesterol in the skin upon exposure to ultraviolet B rays of sunlight. 1,25-dihydroxycholecalciferol which is the active form of Vitamin D plays an important

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role in the maintenance of calcium homeostasis by binding to its receptors on its target tissues which include bone, kidney and intestine. In addition to its role in maintaining bone health, Vitamin D has several important extra skeletal biochemical functions in the body, including its role in type 1 and type 2 DM.[4] Vitamin D was shown to be associated with type 2 DM through its effects on insulin secretion, insulin sensitivity and systemic inflammation, which are the three major mechanisms underlying the development of type 2 DM.[5] Data from cross-sectional as well as longitudinal studies suggest that Vitamin D deficiency has a causal role in type 2 DM.[6,7] Moreover, a high prevalence of Vitamin D deficiency in diabetes patients has also been reported earlier.[8-10] Owing to its effects on insulin sensitivity, Vitamin D is suggested to have a presumptive role in glycaemic control. However, studies exploring the relationship between Vitamin D levels and glycaemic control in type 2 diabetes patients reported varied findings.[11-13] In this background, the present study was taken up to evaluate the association between serum Vitamin D levels and markers of glycaemic control in patients with type 2 DM.

MATERIAL AND METHODS

Subjects

The study was conducted during the period from June 2016 to June 2017 and included 80 patients attending Endocrinology and Metabolism outpatient department of Sri Venkateswara Institute of Medical Sciences, Tirupati and diagnosed with type 2 DM as per the American Diabetes Association criteria.[14] The duration of diabetes ranged from 1 to 5 years, and all the patients were on stable treatment with metformin. Patients with other forms of DM, history of smoking, alcoholism, thyroid disorders, cardiovascular disease, cerebrovascular disease, chronic kidney disease, malignancy, acute and chronic inflammatory diseases, patients who are on insulin, corticosteroids and Vitamin D or calcium supplementation, pregnant and lactating women and those not willing to participate were excluded from the study. Vitamin D deficiency is defined as 25-hydroxyvitamin D levels <20 ng/mL, levels between 21 and 29 ng/mL are considered insufficiency of Vitamin D and if 30-100 ng/mL, it is considered as sufficient Vitamin D.[15] The patients were further classified based on their Vitamin D levels using a cutoff value 20 ng/mL[15] into two groups: patients with Vitamin D >20 ng/mL (Vitamin D non-deficient) (n = 38) and patients with Vitamin D ≤20 ng/mL (Vitamin D deficient) (n = 42). Sample size was calculated based on the data obtained from previous studies using n- Master software version developed by the department of Biostatistics, Christian Medical College, Vellore. The study was approved by institutional Ethics Committee.

Sample collection

Five mL of fasting venous blood sample and a 2-h post-prandial blood sample were collected from all the individuals after an informed consent. The samples were separated and stored at–80°C until further analysis. Glucose was measured by glucose oxidase method on Beckman synchron DxC 600 auto analyser; HbA_{1c} levels were assayed on Bio-Rad D10 system by high performance liquid chromatography-based ion exchange chromatography as per the National Glycohemoglobin Standardization Program standardised to the Diabetes Control and Complications Trial;[16] serum insulin and Vitamin D were analysed by chemiluminescence immunoassay using Beckman coulter access 2 auto analyser. Insulin resistance was calculated as homeostasis model for assessment of insulin resistance (HOMA-IR) using the equation: FBS (mg/dL) × fasting insulin (μIU/mL)/405.[17] Vitamin D levels were measured on the same day of sample collection.

Statistical analysis

Distribution of the data was checked using Kolmogorov–Smirnov test. Data were expressed as mean ± standard deviation or median (interquartile range). The association between the variables studied was analysed using Pearson or Spearman correlation analysis depending on the distribution of data. $P < 0.05$ was considered as statistically significant. All statistical analyses were performed using Microsoft Excel spreadsheets and Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) for windows version 16.0.

RESULTS

The demographic and biochemical characteristics of the study population are shown in Table 1. The mean age of the patients was 46.6 years; 41 (51.2%) patients were males. The mean body mass index of the individuals was 27.2 kg/m^2; HbA_{1c} and Vitamin D levels were 7.8% and 22.7 ng/mL, respectively. With 20 ng/mL as cut-off, 52.5% of type 2 DM patients were Vitamin D deficient. Table 2 shows the comparison of parameters studied between the two groups of patients. The patients were matched with respect to age and BMI. Both groups were similar. The correlation between Vitamin D levels and markers of glycaemic control as well as insulin and insulin resistance in presented in Table 3 (all patients with type 2 DM), Table 4 (Type 2 DM patients without vitamin D deficiency) and Table 5 (Type 2 DM patients with vitamin D deficiency). Vitamin D did not show significant association with any of the markers studied.

Table 1: Demographic and biochemical characteristics of type 2 diabetes mellitus patients (*n*=80)

Parameters	Mean±SD
Age (years)	46.63±6.95
Male:female	41:39
BMI (kg/m²)	27.19±3.35
Plasma FBS (mg/dL)	136.51±27.88
Plasma PPBS (mg/dL)	190.28±47.51
HbA_{1c} (%)	7.78±1.28
Insulin (μIU/mL)	12.23±6.61
IR	4.13±2.32
Vitamin D (ng/mL)	22.68±8.99

Data expressed as mean±SD. SD=Standard deviation; BMI=Body mass index; FBS=Fasting blood sugar; PPBS=Post-prandial blood sugar; HbA_{1c}=Glycated haemoglobin, IR=Insulin resistance

Table 2: Comparison of study parameters between diabetes patients with Vitamin D >20 ng/mL and ≤20 ng/mL

Parameters	Vitamin D >20 (*n*=38)	Vitamin D ≤20 (*n*=42)	*P*
Age (years)	47.18±6.42	46.12±7.44	0.497
BMI (kg/m²)	26.58±2.29	27.74±3.65	0.124
Plasma FBS (mg/dL)	139.00±26.27	134.26±29.40	0.451
Plasma PPBS (mg/dL)	187.68±40.04	192.62±53.77	0.646
HbA_{1c} (%)	7.75±1.15	7.81±1.40	0.836
Insulin (μIU/mL)	12.99±3.85	11.54±8.36	0.331
IR	4.49±1.73	3.81±2.72	0.193

Data expressed as mean±SD. *P*<0.05 is considered statistically significant. SD=Standard deviation; BMI=Body mass index; FBS=Fasting blood sugar; PPBS=Post-prandial blood sugar; HbA_{1c}=Glycosylated haemoglobin; IR=Insulin resistance

Table 3: Correlation of Vitamin D with markers of glycaemic control in patients with type 2 diabetes mellitus (*n*=80)

	FBS	PPBS	HbA_{1c}	Insulin	Vitamin D	IR
FBS						
r	1.000	0.746	0.446	0.032	0.174	0.424
P - value		<0.001	<0.001	0.777	0.123	<0.001
PPBS						
r		1.000	0.407	0.025	−0.013	0.322
P - value			<0.001	0.826	0.912	0.004
HbA_{1c}						
r			1.000	0.087	0.046	0.249
P - value				0.440	0.685	0.026
Insulin						
r				1.000	0.123	0.902
P - value					0.278	<0.001
Vitamin D						
r					1.000	0.191
P - value						0.089
IR						
r						1.000
P - value						

P<0.05 is considered statistically significant. *r*=Correlation coefficient; FBS=Fasting blood sugar; PPBS=Post-prandial blood sugar; HbA_{1c}=Glycosylated haemoglobin; IR=Insulin resistance

Table 4: Correlation of Vitamin D with markers of glycaemic control in patients with type 2 diabetes mellitus without Vitamin D deficiency (*n*=38)

	FBS	PPBS	HbA_{1c}	Insulin	Vitamin D	IR
FBS						
r	1.000	0.817	0.488	0.150	0.247	0.629
P - value		<0.001	0.002	0.369	0.135	<0.001
PPBS						
r		1.000	0.494	0.187	0.190	0.580
P - value			0.002	0.261	0.252	<0.001
HbA_{1c}						
r			1.000	0.074	0.058	0.291
P - value				0.660	0.732	0.077
Insulin						
r				1.000	0.164	0.852
P - value					0.325	<0.001
Vitamin D						
r					1.000	0.272
P - value						0.098
IR						
r						1.000
P - value						

r=Correlation coefficient; FBS=Fasting blood sugar; PPBS=Post-prandial blood sugar; HbA_{1c}=Glycosylated haemoglobin; IR=Insulin resistance

Table 5: Correlation of Vitamin D with markers of glycaemic control in patients with type 2 diabetes mellitus with Vitamin D deficiency (*n*=42)

	FBS	PPBS	HbA_{1c}	Insulin	Vitamin D	IR
FBS						
r	1.000	0.721	0.425	−0.023	0.122	0.317
P - value		<0.001	0.005	0.887	0.440	0.041
PPBS						
r		1.000	0.360	−0.016	−0.076	0.230
P - value			0.019	0.918	0.631	0.143
HbA_{1c}						
r			1.000	0.100	0.195	0.241
P - value				0.527	0.217	0.125
Insulin						
r				1.000	0.005	0.924
P - value					0.974	<0.001
Vitamin D						
r					1.000	0.020
P - value						0.899
IR						
r						1.000
P - value						

r=Correlation coefficient; FBS=Fasting blood sugar; PPBS=Post-prandial blood sugar; HbA_{1c}=Glycosylated haemoglobin; IR=Insulin resistance

DISCUSSION

Achieving good glycaemic control is one of the important factors that helps in reducing the complications associated with DM. In addition to its role in calcium homeostasis, Vitamin D has several extra skeletal functions including its role in type 2 diabetes. Hypovitaminosis D is considered as a potential risk factor for the development of type 2 DM.

In the present study, serum Vitamin D levels were measured in 80 patients diagnosed with type 2 DM. It was found that 52.5% of the patients are Vitamin D deficient.

Hypovitaminosis D at varying prevalence rates has been reported in earlier studies in diabetic patients.[8,9,18,19] The main source of Vitamin D is through exposure to sunlight and from foods that are good sources of Vitamin D such as eggs, sea fish and foods fortified with Vitamin D such as milk and other dairy foods. Although the exact cause for Vitamin D deficiency in DM is not known, various factors including lack of exposure to sun, dietary habits such as poor intake of Vitamin D rich foods, volumetric dilution and sequestration of Vitamin D in fat depots in obese individuals may increase the susceptibility of an individual to deficiency of Vitamin D.[8]

The association of Vitamin D levels with insulin sensitivity and glucose metabolism including glycaemic control has gained considerable interest since recent times. In the present study, correlation analysis revealed that Vitamin D is not significantly associated with markers of glycaemic control or with insulin resistance [Table 3]. Similar findings were reported in earlier studies.[19,20] In contrary, other studies have reported that Vitamin D showed an inverse association with HbA_{1c} and PPBS,[21] and insulin.[22] Although it has been well demonstrated that Vitamin D has an influence on insulin sensitivity through direct as well as indirect effects, studies evaluating the same reported varied findings.

It was observed that there was no significant difference in the age, BMI, FBS, PPBS, HbA_{1c}, insulin and insulin resistance between both groups of the patients [Table 2]. Similar to the refidings no significant difference for age, BMI, FBS and HbA_{1c} in Vitamin D-deficient and non-deficient groups of patients with type 2 DM was reported in another study.[23] When the association of Vitamin D with the indicators of glycaemic control and insulin resistance was analysed in the present study, no significant association was found in both groups of patients [Tables 4 and 5]. Similarly, Sheth *et al*. also could not find any association of Vitamin D levels with HbA_{1c} and HOMA-IR.[23]

Thus, findings of the present study show that although deficient Vitamin D levels were observed in 52.5% of the patients, the relationship of Vitamin D with measures of glycaemic control such as FBS, PPBS and HbA_{1c} as well as insulin resistance could not be confirmed in the population studied. Vitamin D was shown to be associated with beta cell function and insulin sensitivity in individuals at risk for DM and thus might play a role in the pathogenesis of type 2 DM.[24] However, in a recent multi-centre, randomised control trial[25] it was reported that supplementation with 4000 IU/day of Vitamin D3 increased Vitamin D levels but did not lower the risk of DM compared to placebo after a median follow-up of 2.5 years. Since the physiological role of Vitamin D in pancreatic beta cell function and insulin sensitivity is well appreciated, and considering that almost 53% of the diabetes patients in the present study are Vitamin D deficient, it is suggested that Vitamin D levels are measured in these patients to identify hypovitaminosis D. Although it is not clear whether Vitamin D supplementation improves glycaemic status, improvement in Vitamin D levels in diabetes patients might help in improving the overall health of the individuals along with increase in Vitamin D levels. Simple measures such as dietary changes and life style modifications along with Vitamin D supplementation may help in achieving normal Vitamin D levels in DM patients. All the measurements in the diabetes patients in the present study were done at a single time point which forms a limitation of the present study. Considering the beneficial role played by Vitamin D on glucose homeostasis, the relationship between Vitamin D levels and glycaemic control needs to be explored in further large, well-controlled studies.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine 2010;38:602-6.
2. Ahmad NS, Islahudin F, Paraidathathu T. Factors associated with good glycemic control among patients with type 2 diabetes mellitus. J Diabetes Investig 2014;5:563-9.
3. Lee JE. Alternative biomarkers for assessing glycemic control in diabetes: Fructosamine, glycated albumin, and 1, 5-anhydroglucitol. Ann Pediatr Endocrinol Metab 2015;20:74-8.
4. Griz LH, Bandeira F, Gabbay MA, Dib SA, Carvalho EF. Vitamin D and diabetes mellitus: An update 2013. Arq Bras Endocrinol Metabol 2014;58:1-8.
5. Harinarayan CV. Vitamin D and diabetes mellitus. Hormones (Athens) 2014;13:163-81.
6. Scragg R, Sowers M, Bell C; Third National Health and Nutrition Examination Survey. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the third national health and nutrition examination survey. Diabetes Care 2004;27:2813-8.
7. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, *et al.* Vitamin D and calcium intake in relation to type 2 diabetes in women. Diabetes Care 2006;29:650-6.
8. Nwosu BU, Maranda L. The effects of vitamin D supplementation on hepatic dysfunction, Vitamin D status, and glycemic control in children and adolescents with Vitamin D deficiency and either type 1 or type 2 diabetes mellitus. PLoS One 2014;9:e99646.
9. 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. Diabetol Metab Syndr 2016;8:77.
10. Bayani MA, Akbari R, Banasaz B, Saeedi F. Status of Vitamin-D in diabetic patients. Caspian J Intern Med 2014;5:40-2.
11. Kostoglou-Athanassiou I, Athanassiou P, Gkountouvas A,

Kaldrymides P. Vitamin D and glycemic control in diabetes mellitus type 2. Ther Adv Endocrinol Metab 2013;4:122-8.
12. Olt S. Relationship between Vitamin D and glycemic control in patients with type 2 diabetes mellitus. Int J Clin Exp Med 2015;8:19180-3.
13. Perez-Diaz I, Sebastian-Barajas G, Hernandez-Flores ZG, Rivera-Moscoso R, Osorio-Landa HK, Flores-Rebollar A. The impact of Vitamin D levels on glycemic control and bone mineral density in postmenopausal women with type 2 diabetes. J Endocrinol Invest 2015;38:1365-72.
14. American Diabetes Association. Classification and diagnosis of diabetes. Diabetes Care 2016;39 Suppl 1:S13-22.
15. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, *et al.* Evaluation, treatment, and prevention of Vitamin D deficiency: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2011;96:1911-30.
16. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. Diabetes 1995;44:968-83.
17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-9.
18. Buhary BM, Almohareb O, Aljohani N, Alrajhi S, Elkaissi S, Sherbeeni S, *et al.* Association of glycosylated hemoglobin levels with Vitamin D status. J Clin Med Res 2017;9:1013-8.
19. Akshay Kumar SV, Kumar S, Bharathy N, Dinakaran A, Ray L. Evaluation of vitamin D status and its correlation with glycated haemoglobin in type 2 diabetes mellitus. Biomed Res 2017;28:66-70.
20. Al-Shoumer KA, Al-Asoosi AA, Ali AH, Nair VS. Does insulin resistance in type 2 diabetes alter Vitamin D status? Prim Care Diabetes 2013;7:283-7.
21. Saif-Elnasr M, Ibrahim IM, Alkady MM. Role of Vitamin D on glycemic control and oxidative stress in type 2 diabetes mellitus. J Res Med Sci 2017;22:22.
22. Hurskainen AR, Virtanen JK, Tuomainen TP, Nurmi T, Voutilainen S. Association of serum 25-hydroxyvitamin D with type 2 diabetes and markers of insulin resistance in a general older population in Finland. Diabetes Metab Res Rev 2012;28:418-23.
23. Sheth JJ, Shah A, Sheth FJ, Trivedi S, Lele M, Shah N, *et al.* Does Vitamin D play a significant role in type 2 diabetes? BMC Endocr Disord 2015;15:5.
24. Kayaniyil S, Vieth R, Retnakaran R, Knight JA, Qi Y, Gerstein HC, *et al.* Association of Vitamin D with insulin resistance and beta-cell dysfunction in subjects at risk for type 2 diabetes. Diabetes Care 2010;33:1379-81.
25. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, *et al.* Vitamin D supplementation and prevention of type 2 diabetes. N Engl J Med 2019;381:520-30.