ORIGINAL ARTICLE

CORRELATION BETWEEN VITAMIN D DEFICIENCY AND GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS. A CLINICAL STUDY

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ABSTRACT

Background: Vitamin D has significance in the glucose metabolism, its effects involve secretion and insulin sensitivity, and involvement in the regulation of inflammation. Deficiency of vitamin D has increasingly become the cause of poor glycemic control of patients with type 2 diabetes mellitus (T2DM). The authors of this paper sought to establish the relationship between the glycemic control, in the form of glycated hemoglobin (HbA1C), measured by T2DM patients and serum 25-hydroxyvitamin D [25(OH)D].

Methods: A cross-sectional clinical study was performed in one of the tertiary care hospitals with 100 adult patients with diagnosed T2DM (30-70 years). Serum 25(OH)D and HbA1c were sampled through a chemiluminescent immunoassay and high-performance liquid chromatography by respectively measuring blood samples by fasting and estimations respectively. Demographic variables, Body mass index, blood pressure and length of diabetes were inputted. The correlation analysis and multivariate regression were also conducted to establish the relationship between the level of vitamin D and the level of glycemic indices.

Results: The mean age of the subjects of a study was 52.8 + 9.6 and 54 percent of the research participants were males. Mean serum vitamin D amounted to 18.7 ± 7.8 ng/mL and mean HbA1c was 8.2 ± 1.4%. Sixty-four percent of patients had been identified to be short of vitamin D (<20 ng/mL). The correlation between serum vitamin D and HbA1c was established to be negative (r = -0.42, p = 0.001). The logistic regression analysis revealed that a 5-ng/ml increase in the vitamin D was associated to a reduced risk of poor glycemic control by 28 percent (aOR = 0.72, p = 0.004).

Conclusion: Vitamin D deficiency is highly prevalent in the T2DM patients and there is a steep connection between improper glycemic control and vitamin D deficiency. The screening and remedies towards vitamin D deficiency may serve as a supplemental ingredient to metabolic performance and it ought to be considered as part of the normal diabetes management.

Keywords: Type 2 diabetes mellitus, Vitamin D deficiency, HbA1c, Glycemic control, 25-hydroxyvitamin D, Insulin resistance

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INTRODUCTION

In the world, T2DM is a significant cause of CVD, nephropathy, neuropathy and retinopathy. Recurrent high blood glucose levels measured using glycated hemoglobin (HbA1c) predict microvascular and macrovascular complications[1,2]. Besides the classical risk factors (obesity, sedentary lifestyle and genetic predisposition), there is increasing evidence that the state of the micronutrients, particularly the vitamin D may also be a modifier of glucose homeostasis. Enzymes and vitamin D receptors are activated in pancreatic 8-cells, skeletal muscular, adipose tissue, and immune cells. Theorized mechanisms of the associations between 25-hydroxyvitamin D [25(OH)D] low and poor glycemic regulation: (i) regulation of insulin release by 25(OH)D effect on Calcium flux in 25 (OH) D-depleted 25 (OH) D-sufficiency cells; (ii) facilitation of insulin sensitivity to the action of 25 (OH)[3,4].

Though biologic plausible, the clinical findings are intermittent and context-dependent and fluctuation of sunlight exposure, pigmentation, foods consumption, obesity levels, and duration of diabetes could confound correlation[5,6]. Due to the lack of outdoor activities in the environment, fitting cultural attire, air pollution, and dieting, the lack of vitamin D is widespread even in sunny South Asian locations. It would be informative to establish the association between decreased 25(OH)D concentrations and elevated levels of HbA1c in local T2DM groups to the questions of the simple and cost-effective adjuncts to the current diabetes management. To have the association of serum 25(OH)D and glycemic control (HbA1c) in patients with T2DM and test the association after the control of the key confounders (age, sex, BMI, diabetes duration, medications, season, sun exposure, and physical activity)[7,8].

MATERIALS AND METHODS

The research design was a cross-sectional analytical study, in the form of a 6-month-long clinical trial, in the endocrinology and diabetic outpatient clinics of a 3-rd tier teaching hospital. A sample consisting of 100 adult patients diagnosed with type 2 diabetes mellitus was recruited to the study by the non-probability consecutive sampling technique. The participants who were qualified were between 30-70 years and had a known case of type 2 diabetes with a stable antidiabetic regimen of at least eight weeks prior to enrolment. Type 1 diabetes, gestational diabetes, chronic renal or hepatic disorder, endocrine disorder, or high doses of vitamin D, steroids or anticonvulsants were used as the exclusion criteria to eliminate confounding factors.

The interviewees and the subjects were interviewed and assessed physically after presenting written informed consent. The demographic data, history of past medical conditions, and duration of diabetes were taken, and medications under use. The anthropometric measurements including height, weight, body-mass index (BMI) and waist circumference were measured using calibrated tools. Measured blood pressure was done in sitting position after half an hour after a five-minute rest. The information on sunlight coverage, nutrition patterns, and physical exercise were provided with the help of a short food-frequency questionnaire and the International Physical activity Questionnaire (IPAQ).

The venous blood was subjected to overnight fasting of 812 hours in order to be analyzed in the laboratory. Glycated hemoglobin (HbA1c) was measured in 2ml of blood in an EDTA tube using a high-performance liquid chromatography (HPLC), and serum 25-hydroxy-vitamin D [25(OH)D] serum fasting plasma glucose and lipid profile and renal functioning were measured in 5ml of blood in a serum-separation tube. The results on serum 25(OH)D levels were measured by means of an automated chemiluminescent immunoassay (CLIA) system. The levels of vitamin D were categorized as deficiency (lower than 20 ng/mL), insufficiency (20- 29 ng/mL) and adequacy (30 or above ng/mL). All the samples were handled within 1 hour of collection and centrifuged at 3000 rpm of 10 minutes followed by the storage of serum aliquots at -20 C until analysis in a batch.

In an attempt to balance the quality of data, the instruments were calibrated, 10 percent of the samples were rerun and unaware poor blinded lab staff were not aware of clinical data. There were in-house and out-of-house quality-control practices in all their tests. The SPSS version used was 26, by which the information was compiled and analyzed. Continuous variables were displayed in the form of mean SD or median (IQR) and categorical variables were displayed in the form of frequency and percentages. The character of data dictated the use of Pearson correlation coefficient or Spearman correlation coefficient to determine the level of the correlation between serum 25(OH)D and the HbA1c levels. The relationship between vitamin D deficiency and inadequate glycemic control (HbA1c ≥ 7%) was investigated based on logistic and linear regression models, and the effect on age, sex, BMI, diabetes predisposition, physical activity, and sun exposure as confounding variables were adjusted. The accepted level of significance was considered p <.05.

RESULTS

The study has recruited 100 patients who have type 2 diabetes mellitus (T2DM). They consisted of 54 males and 46 females, the average age of which was 52.8 years old, and the standard deviation was 9.6 years (35-70 years). Diabetes period was 1 to 15 years with a mean of 7.3-3.5 years. The average serum vitamin D level was 18.7 / + 7.8 ma/L which is a good concentration of deficiency. Table 1 reveals general demographic and clinical data of the research population. Glycated hemoglobin (HbA1c) stood at 8.2 + 1.4 which means that there was poor glycemic regulation among the majority of the subjects. The majority of them were adult middle aged with obese-overweight body mass index. The diastolic and systolic blood pressures averages are indicative of mild hypertension. HbA1c of 8.2 indicates that most patients were not under good control in terms of glycemic control and vitamin D of less than 20 ng/mL shows that most of the patients are deficient.

According to Table 2, 64 percent of the patients were vitamin D deficient, 24 percent were not sufficient and only 12 percent were sufficient. This proves that almost 9 in ten diabetic patients possessed inappropriate levels of vitamin D even though they were residing in an area that is rich in sunlight. The result highlights a high level of micronutrient deficiency in this group.

Table 3 represents the comparison of the mean HbA1c by the various vitamin D status groups. HbA1c was also found to be much higher in the case of the vitamin D-deficient patients (8.7% versus 7.1%). The p-value of 0.002 is statistically significant, implying that the poorer the glycemic control is the lower the level of vitamin D is.

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 100)

Variable	Mean ± SD / n (%)
Age (years)	52.8 ± 9.6
Gender	Male: 54 (54%) / Female: 46 (46%)
Duration of diabetes (years)	7.3 ± 3.5
BMI (kg/m²)	27.6 ± 4.1
Systolic BP (mmHg)	134.5 ± 12.8
Diastolic BP (mmHg)	83.7 ± 8.6
Fasting plasma glucose (mg/dL)	159.4 ± 36.2
HbA1c (%)	8.2 ± 1.4
Serum 25(OH)D (ng/mL)	18.7 ± 7.8

Table 2: Distribution of Vitamin D Status Among Study Participants

Vitamin D Status	25(OH)D Range (ng/mL)	Frequency (n)	Percentage (%)
Deficient	< 20	64	64%
Insufficient	20–29	24	24%
Sufficient	≥ 30	12	12%
Total	—	**100**	**100%**

Table 3: Comparison of Glycemic Control (HbA1c) Across Vitamin D Status Categories

Vitamin D Status	Mean HbA1c (%) ± SD	p-value
Deficient (<20 ng/mL)	8.7 ± 1.3	
Insufficient (20–29 ng/mL)	7.9 ± 1.2	
Sufficient (≥30 ng/mL)	7.1 ± 1.1	**0.002**

Table 4 shows the correlation analysis of serum vitamin D levels and glycemic parameters. There was also a strong negative relationship ($r = -0.42$, $p < 0.001$) between serum vitamin D and HbA1c levels, such that, the lower the levels of vitamin D, the higher the levels of HbA1c. The same was the same case with fasting glucose ($r = -0.36$, $p = 0.001$). The correlation with the time of diabetes was however, low and statistically negligible.

Table 4: Correlation Between Serum Vitamin D and Glycemic Parameters

Parameter	Correlation Coefficient (r)	p-value	Direction
HbA1c (%)	–0.42	**<0.001**	Negative
Fasting Plasma Glucose (mg/dL)	–0.36	**0.001**	Negative
Duration of Diabetes (years)	–0.18	0.07	Not significant

Multivariate regression of logistic (Table 5) showed that after accounting the age, BMI and years of diabetes, an increase in serum vitamin D by 5 ng/mL was correlated with a 28 percent decrease in the odds of poor glycemic control (aOR = -0.72, p = 0.004). This means that there is an inverse relationship that is independent and negative between the levels of vitamin D and hyperglycemia in diabetics.

Table 5: Logistic Regression Analysis for Poor Glycemic Control (HbA1c ≥ 7%)

Predictor Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval	p-value
Age (years)	1.02	0.97 – 1.08	0.32
BMI (kg/m²)	1.05	0.94 – 1.18	0.36
Duration of diabetes (years)	1.11	1.01 – 1.23	0.03
Serum 25(OH)D (per 5 ng/mL increase)	**0.72**	**0.58 – 0.89**	**0.004**

All these findings are indicative of the fact that low serum levels of vitamin D are closely related with poor glycemic control in patients with type 2 diabetes mellitus. Vitamin D screening and supplementation approaches can be potentially helpful in managing diabetes.

DISCUSSION

The ongoing study examined the relationship between glycemic management and the serum vitamin D condition in individuals with type 2 diabetes mellitus (T2DM)[8]. The findings revealed that the prevalence rate of vitamin D deficiency (64) and the considerable negative relationship between the serum 25(OH)D and the blood glucose contents (HbA1c) level. The average HbA1c of the patients who had deficient vitamin D levels was much higher than the average levels of HbA1c of the patients who had sufficient levels of vitamin D showing that vitamin D inadequacy can be a contributor towards poor levels of glycemic control[9,10].

These results are consistent with the past ones, which have been conducted both at the local scale and abroad. Authors such as Al-Shoumer (2015) and Kaur (2019) also discovered a negative relationship between HbA1c and vitamin D among T2DM patients and this study proved that the hypothesis that vitamin D is an important factor of glucose metabolism is supported[11-14]. The proposed mechanisms include improving the functionality of the pancreatic 8-cells through the activation of vitamin D receptor (VDR), the sensitivity of the insulin by the changes of the expression of the insulin receptors, and the reduction of the systemic inflammation by inhibiting a pro-inflammatory cytokine, TNF-a and IL-6. In addition, vitamin D is capable of regulating the calcium homeostasis in intracellular location that is essential in the exocytosis and the signal transduction of insulin[15,16].

The given deficiency in the majority of the patients studied in the given study is in conformity to the heightened awareness that the problem of vitamin D deficiency occurs on a large scale even in sun-covered regions such as South Asia[17]. Part of the reasons behind this paradox are darker pigmentation of the skin, culture of clothing, absence of outdoor physical activity, deficiency in the diet and environmental pollution that reduces the exposure of ultraviolet B. The findings underscore the necessity to measure the degree of vitamin D as an ingredient in metabolic health check of diabetic individuals, particularly in the group that does not have access to sunlight[18].

The logistic regression analysis of the study showed that the increase of serum vitamin D by 5 ng/mL led to the reduction of the likelihood of poor glycemic control by 28-percent despite considering the confounding factors such as age, BMI, and length of diabetes[19]. This implies that vitamin D deficiency is not only that makes one signify impoverished wellbeing but it may be engaged in a process of glucose regulation. There are interventional studies that have addressed the question of whether the addition of vitamin D can result in a decrease of glycemic indices; some studies have shown a substantial decrease in the HbA1C and Fasting glucose, other studies have shown no effect, perhaps due to heterogeneous dose and baseline vitamin D and time of treatment. However, the inadequate patients can be corrected through being supplemented to complement the regular method of diabetes therapy; this is physiologically feasible, and without any risk[20].

The links between vitamin D and glycemic control may also occur mediated by insulin resistance, adiposity and inflammatory pathways. Obese people experience a decrease in the circulating concentration of 25(OH)D due to sequestration of the 25 (OH)D in the adipose tissue[7]. This study also elevated mean BMI and hence, obesity can aggravate vitamin D deficiency as well as impaired glucose metabolism. More so, the insulin-sensitizing action of vitamin D might be impaired by chronic inflammation associated with obesity which worsens the metabolic states[8].

Admitted limitations should be made even in instances of good performance. The cross-sectional design and the serum vitamin D was only measured in one point which is not always a long-term status[20]. Such problems as nutrition, VDR gene genetic difference and parathyroid homone level were not quantified that can influence the outcome. It may be also possible that the seasonal difference that was observed could still have affected the distribution of serum vitamin D, but to ascertain cause and effect relationship as well as the optimal dose of vitamin D that produces desired effects on glycemia, longitudinal as well as interventional studies on the impact of standardized regime of vitamin D supplementations are advisable[18].

Overall, this paper establishes the truth of the fact that vitamin D deficiency prevalence among T2DM patients is extremely high and that it has close associations with poor glycemic control. Examples of prevention measures that may support the metabolic health of diabetic groups are vitamin D screening and remediation through safe sun exposure, diet or supplement, which could be a cost-effective and preventive intervention. Implementation of micronutrient management in the protocols of managing diabetes would therefore contribute towards the management of the glycemic outcomes and the reduction of the long terms complications[11-20].

CONCLUSION

In this paper, it was demonstrated that the relationship between the levels of serum vitamin D and glycemic control among type 2 diabetes mellitus patients was negative and significant. The degree of vitamin D deficiency was extremely high and associated with the raise of the degree of HbA1c and non-meal glucose level. The results show that when the right levels of vitamin D are taken the vitamin D may be of assistance in controlling the metabolism and may be a viable substitute to use when treating diabetes. To improve the long-term outcomes screening and additional supplementation with vitamin D should also be taken as a unit within the entire diabetes care.

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