

Status and Effect of Vitamin D on Microvascular Complication in Type II Diabetes Mellitus Patients

¹P Krushna Kishore, ²Ipsita Choudhary

ABSTRACT

Introduction: Vitamin D has a great impact on human health and disease. Recent studies proved that hypovitaminosis D is a possible risk factor for the pathogenesis of diabetes and its complications. In the present study, we evaluated vitamin D levels and its correlation with the duration of diabetes, sex, glycosylated hemoglobin (HbA1C), and microvascular complications in type II diabetes mellitus (T2DM) patients with and without microvascular complications.

Objectives: To study and correlate vitamin D levels and its relation with duration of diabetes, sex, glycemic control, and microvascular complication in T2DM patients with and without microvascular complications.

Materials and methods: Cross-sectional case–control study of 200 patients (35–70 years) suffering from T2DM was included. The T2DM patients without microvascular complications served as control group. Enrolled subjects underwent complete physical examination to detect the presence of microvascular complications, which includes microfilament tests, detailed fundus examination, urinary microalbumin/creatinine ratio. Fasting blood sugar, HbA1C, and serum vitamin D were also measured by using serum sample.

Results: Prevalence of vitamin D deficiency and insufficiency was found to be significantly higher in T2DM patients with microvascular complications (19.54 ± 2.56 vs 28.57 ± 2.93) as compared with T2DM patients without microvascular complications ($p < 0.001$). Hypovitaminosis D was found to be significantly more in females (60.75%) compared with males (39.96%) in both the study groups ($p < 0.0001$). Hypovitaminosis D was correlated with glycemic control and prevalence of microvascular complications.

Conclusion: Vitamin D is correlated with glycemic status and sex difference and has a role in pathogenesis of T2DM and its complications.

Keywords: Glycemic control, Microvascular complications, Type II diabetes mellitus, Vitamin D.

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¹PhD Student, ²Associate Professor

^{1,2}Department of Biochemistry, Rama Medical College & Hospital Rama University, Kanpur, Uttar Pradesh, India

Corresponding Author: P Krushna Kishore, PhD Student Department of Biochemistry Rama Medical College & Hospital Rama University, Kanpur, Uttar Pradesh, India, Phone: +918264570799, e-mail: kishorepadal@yahoo.com

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INTRODUCTION

Diabetes mellitus is a common metabolic disorder characterized by hyperglycemia, effecting more than 420 million population worldwide.¹ Diabetes mellitus is a major health problem, predisposing to markedly increased cardiovascular mortality and serious morbidity related to development of microvascular complications.² Vitamin D has traditionally been associated with calcium and phosphorus homeostasis and bone metabolism. However, recent studies suggested nontraditional roles of vitamin D in human health including cardiovascular diseases, autoimmune diseases, cancer, etc.³⁻⁵ Studies also have shown low vitamin D status to be associated with the development of type II diabetes mellitus (T2DM) as well as metabolic syndrome.⁶ It has led to the hypothesis that vitamin D insufficiency correlates positively with insulin resistance and cardiovascular and microvascular risk.⁷ Up until recently, vitamin D deficiency was considered rare in those parts of the world that had plenty of sunshine all year round, but the World Health Organization now estimates that globally one billion people have vitamin D deficiency or insufficiency.^{8,9} The purpose of the present study is to determine the status of vitamin D and its relation with glycemic control, sex, duration, and its role in microvascular complication in T2DM with and without microvascular complications.

MATERIALS AND METHODS

The present study was conducted in the Biochemistry Department on 200 clinically diagnosed T2DM subjects, with the age group of 35 to 70 years, attending the medicine outpatient department at Rama Medical Hospital, Kanpur, Uttar Pradesh. The study was approved by the institute's ethical clearance committee. Consent letter was taken from all the enrolled subjects. The 200 patients were divided into control group (group I) containing 100 T2DM patients without microvascular complications and case group (group II) containing 100 T2DM patients with microvascular complications.

Exclusion Criteria

Lactating and pregnant women were excluded. Subjects suffering from type I diabetes, myocardial infarction, liver and renal diseases, and individuals taking calcium or vitamin D supplementation were also exempted.

Each patient underwent complete history taking, complete physical examination for the detection of microvascular complications which includes microfilament tests, detailed fundus examination, and urinary microalbumin/creatinine ratio.

Biochemical Analysis

About 3 mL of venous blood was collected from the antecubital vein in fasting condition. Samples were centrifuged after 30 minutes, serum was isolated and used for the measurement of following parameters:

- Fasting blood glucose was measured by glucose oxidase–peroxidase method. (Kits were supplied by Erba Diagnostics, using ERBA CHEM 5 semi autoanalyzer).
- Glycosylated hemoglobin (HbA1C) was estimated by ion-exchange high-performance liquid chromatography method by using ERBA EM 360.
- 25-Hydroxy vitamin D (25-OHD) was measured by chemiluminescence immunoassay method (by COBAS E411 analyzer).

Statistical Analysis

Statistical Package for the Social Sciences version 19 software was used for statistical analysis. Values of continuous variables were expressed as mean \pm standard deviation (SD); p -value < 0.05 was considered significant. Student's t -test was used to assess the relationship between continuous variables, such as 25-OHD, age, HbA1C, and diabetes duration.

RESULTS

The present cross-sectional case–control study was conducted on 200 clinically diagnosed T2DM subjects in the age group of 35 to 70 years. These 200 patients were divided into control group (group I) containing 100 T2DM patients without microvascular complications and case group (group II) containing 100 T2DM patients with microvascular complications. Serum vitamin D was measured and correlated with glycemic control (HbA1C), duration of diabetes, and gender differences to find the role in pathogenesis of microvascular complications of T2DM patients.

Values are mean SD or percentages, as appropriate, \square p value for difference between groups by t -test or chi-square, as appropriate; FBS: Fasting blood sugar

Table 1 displays the baseline characters: The mean age of case group was 61.39 ± 7.56 years and that of controls was 51.74 ± 6.43 years and was significantly higher (p -value < 0.001); 66.28% males and 33.72% females were enrolled in case group, 68.54% males and 31.46% females were included in control group.

The mean serum 25-OHD level (ng/mL) in controls was 28.57 ± 2.93 ng/mL while in cases it was 19.54 ± 2.56 ng/mL. Highly significant correlation was found between the two groups ($p < 0.0001$).

Table 1 also displays the mean HbA1C level between the control group (6.95 ± 1.03) and study group (7.28 ± 1.21); significant difference was found ($p < 0.05$) between the two groups.

From Table 2 it is clear that serum concentration of 25-OHD in men was significantly higher compared with women in both study groups. A highly significant correlation was found ($p < 0.001$) between men and women.

The association between serum vitamin D and HbA1C of both groups was done using Pearson's correlation coefficient. The "r" value between vitamin D and HbA1C was -0.8205 , which suggested that there was an inverse correlation between the two parameters (Table 3).

Table 1: Baseline characteristics with mean value and SD

Parameters	T2DM with microvascular complication mean \pm SD n = 100	T2DM without microvascular complication mean \pm SD n = 100	*p-value
Vitamin D	28.57 \pm 2.93	19.54 \pm 2.56	<0.0001
HbA1C	6.95 \pm 1.03	7.28 \pm 1.21	0.039
Age	51.74 \pm 6.43	61.39 \pm 7.56	<0.0001
Male, %	66.28	68.54	<0.001
Female, %	33.72	31.46	<0.001
Duration of diabetes	2.09 \pm 0.34	6.54 \pm 0.54	<0.001
FBS	134.87 \pm 20.15	188.03 \pm 16.44	<0.0001

Values are mean (SD) or percentages, as appropriate, \square p -value for difference between groups by t -test or chi-square, as appropriate; FBS: Fasting blood sugar

Table 2: Mean vitamin D values in males and females

Mean vitamin D	Men	Women	p-value
T2DM without complication	29.81 (36.27%)	25.35 (56.84%)	<0.0001*
T2DM with complication	20.68 (43.65%)	17.22 (64.67%)	<0.0001*

*Values are mean or percentages, as appropriate to calculate p -value, t -test used

Table 3: Association of serum 25-OHD with HbA1C

HbA1C	Total subjects (n = 200) (groups I + II)	Mean serum 25-OHD
Less than 6	13 + 5	38.43
Between 6 and 7	56 + 38	26.84
More than 7	31 + 57	14.38

DISCUSSION

Traditionally, vitamin D has been associated with calcium and phosphate metabolism and bone homeostasis. But recent studies proved the extraskeletal effects of vitamin D. Animal studies and lab experiments proved the role of vitamin D in insulin secretion and insulin sensitivity.^{10,11}

The present study has shown decreased level of vitamin D was severe in case group compared with control group and an inverse relation was observed between glycosylated hemoglobin levels with serum 25-OHD levels in the whole population studied, implying that vitamin D levels may affect glucose control in T2DM. Pittas and Dawson-Hughes¹² in their early study found an inverse association between serum vitamin D and prevalence of diabetic complications.

Previous studies by Mattila et al¹³ and Kayaniyil et al¹⁴ also found a negative correlation between serum vitamin D levels and impaired glucose tolerance. Vitamin D receptors distributed on pancreatic b cells, adipose tissue, and skeletal muscle are the factors through which vitamin D regulates glucose homeostasis,¹⁵ which additionally has been found to express the enzyme 1-alpha-hydroxylase (Bland et al¹⁶). Vitamin D promotes insulin secretion from beta cells of pancreas, thus appearing to regulate insulin secretion. Therefore, vitamin D insufficiency may be related to impaired synthesis in diabetes.

Previous studies¹⁷⁻¹⁹ showed that microvascular complications and progress of diabetic microvascular complications are associated with decreased 25-OHD concentrations in T2DM patients. In the present study also, similar results were found, T2DM patients with microvascular complications were having lower vitamin D levels compared with T2DM patients without microvascular complications.

Scragg et al²⁰ in their observational study in T2DM subjects concluded that mean vitamin D concentration in men were significantly higher than that for women. Our study also proved mean vitamin D level concentrations in women were significantly lower than those for men. But a cross-sectional study conducted by Alhumaidia et al²¹ found a contrasting result.

Vitamin D status is known to be lower in the elderly compared with the young as the subcutaneous synthesis of vitamin D decreases with increasing age, due to a reduced concentration of 7-dehydrocholesterol in the skin²² and reduced absorption of oral vitamin D.²³ Even though our study found an inverse association between duration and mean Vitamin D levels, the age difference between study groups must be taken into account.

CONCLUSION

- We conclude that vitamin D is correlated with glycaemic control and sex difference and has a great role in prevalence of T2DM and its complications.

- Screening of vitamin D could be considered for diabetic care.

LIMITATIONS

This study was an observational study from a single center; confounders like diet and physical activity were not included.

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