

## Association of serum Vitamin D level with Glycemic Status in Patients of Type 2 Diabetes Mellitus

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### Abstract

**Introduction:** For development of Type 2 Diabetes mellitus, Vitamin D is thought to be a risk factor. Various studies have established the fact that Vitamin D replenishment improves glycemic status and insulin secretion in patients with Type 2 Diabetes mellitus with established hypovitaminosis D. This study was done to find out the degree of association between glycemic status and vitamin D levels in type 2 Diabetes Mellitus patients in a tertiary care center.

**Patient and methods:** The study was done in the Department of Biochemistry, SCB Medical College, and Cuttack 48 patients of type 2 Diabetes Mellitus were taken as cases 42 healthy subjects were taken as controls. Biochemical parameters like FBS, PPBS, Urea, Creatinine, HbA1c, Lipid profile parameters were measured in both cases and controls.

**Results:** The serum urea and creatinine levels were significantly elevated in complicated type 2 Diabetes mellitus patients as compared to healthy controls. Serum cholesterol, triglycerides, LDL Cholesterol levels also showed significant increase Vitamin D and FBS levels showed a significant negative correlation in cases and vitamin D levels were decreased in cases as compared to controls.

**Conclusion:** As Vitamin D and FBS levels showed a significant negative correlation, and vitamin D levels were decreased in cases as compared to controls, so it can be proved that vitamin D can lead to good glycemic control and hypovitaminosis D can thereby lead to Type 2 Diabetes Mellitus.

**Keywords:** Diabetes mellitus; Vitamin D; Glycosylated hemoglobin (HbA1C); Glycemic status

### Introduction

In 2010, an estimated 25.8 million people (8.3%) in the United States had diabetes mellitus, of which approximately 1 million have type 1 diabetes and most of the rest have type 2 diabetes. A third group that was designated as "other specific types" by the American Diabetes Association (ADA) number only in the thousands. Among these are the rare monogenic defects of either B cell function or of insulin action, primary diseases of the exocrine and medication-induced diabetes.

Out of these three types, the number of type 2 diabetes mellitus cases is increasing day to day by leaps and bounds. The main cause of this increased incidence is increased incidence of obesity. Though by changing environmental factors, we can counter obesity, but still we need to look for other factors for preventing diabetes.

One of these factors is vitamin D. This vitamin is also known as sunshine vitamin as sun is the main primary source. The main marker of vitamin D status is 25-hydroxy cholecalciferol, synthesized in liver. The epidemiology of vitamin D status is inverse to diabetes, since level of 25-hydroxy cholecalciferol declines with age and in obese persons [1-3].

### Aim and Objectives

To find out the association between the vitamin D level and glycemic status in patients of type 2 Diabetes Mellitus.

### Patient and Methods

This study was conducted in the Department of Biochemistry in collaboration with the Department of Medicine, S.C.B. Medical College and Hospital Cuttack.

Fasting plasma glucose, glycosylated hemoglobin (HbA1C) and serum vitamin D levels were estimated in 48 patients of type 2 diabetes mellitus and compared with 42 age and sex matched healthy controls.

### Exclusion Criteria

- Diabetics with acute complications.
- Patients on vitamin supplementation.
- Patients of Gestational Diabetes Mellitus and diabetics with pregnancy.
- Patients with any other endocrinopathies.

Three ml of blood was collected after overnight fasting of 8 hours from all enrolled patients and healthy controls for the assessment of lipid profile, urea and creatinine levels. Demographic characteristics (name, age, sex), history of risk factors (smoking, family history,

medications, alcohol intake etc.), systolic and diastolic blood pressures, were recorded in detail.

- Statistical analysis was done using SPSS and Microsoft Excel 10 software.

**Following methods were used for estimation of the different parameters**

- Fasting plasma glucose and post prandial plasma glucose (GOD-POD method).
- Serum urea (GLDH/Kinetic method), Serum creatinine (Modified Jaffe method).
- Serum cholesterol (CHOD-PAP method), serum triglycerides (enzymatic method), serum HDL (turbidometric immunoassay method), serum LDL (Friedwald’s formula), serum VLDL (calculated).
- Estimation of 25-hydroxy vitamin D was done by ELISA method, HbA1C level estimation (%) was done by HPLC method and other parameters were estimated using standard biochemical methods.
- All the case records were collected in a specified preformat. Written informed consent was obtained from all subjects.

**Results**

Diabetes mellitus is a clinically and genetically heterogeneous group of disorders characterized by abnormally high levels of glucose in the blood (hyperglycemia). It is the most common endocrine disease, characterized by metabolic abnormalities and long term complications involving the eyes, kidneys, nerves and blood vessels.

In our study 48 type 2 diabetes mellitus patients were selected. 27 of them were uncomplicated cases and 21 complicated. Mean age in years was 56.3 ± 7.3. Majority of uncomplicated cases were within 51-58 years. Majority of complicated cases were within 59-66 years.

Occurrence of complications was lower in younger age group (35-50 years) with male predominance. Complications were higher in older age group (59-74 years) and were slightly higher in females (Tables 1-4) (Figure 1).

Parameter	Control Group (n=42) Mean ± SD	Study Group (n=48) Mean ± SD	
		Uncomplicated Cases (n=27)	Complicated Cases (n=21)
Fasting Plasma Glucose(FPG)	83.09 ± 7.57	149.5 ± 14.85*	207.26 ± 27.96*
Post Prandial Plasma Glucose(PPPG)	104.72 ± 10.87	189.5 ± 19.77*	263.5 ± 38.53*
Serum Urea	27.3 ± 4.18	32.05 ± 2.86	56.3 ± 12.01*
Serum Creatinine	0.82 ± 0.15	1.01 ± 0.16	1.94 ± 0.45*

(\*p value<0.05, which is statistically significant in comparison with controls)

**Table 1:** Biochemical parameters in study group and control group.

Parameter	Control Group (n=42) Mean ± SD	Study Group (n=48)	
		Mean ± SD	Mean ± SD
Total Cholesterol	151.5 ± 16.37	176.3 ± 18.67	218.7 ± 28.78*
Triglycerides	118.5 ± 20.76	129.8 ± 21.35	170.9 ± 34.56*
HDLc	44.28 ± 2.16	40.78 ± 4.18	37.61 ± 2.70
LDLc	91.58 ± 15.4	119.8 ± 19.33	150.3 ± 33.75*
VLDLc	27.44 ± 3.56	27.91 ± 3.98	34.49 ± 6.64

**Table 2:** Comparison in lipid profile parameters in study group and control group.

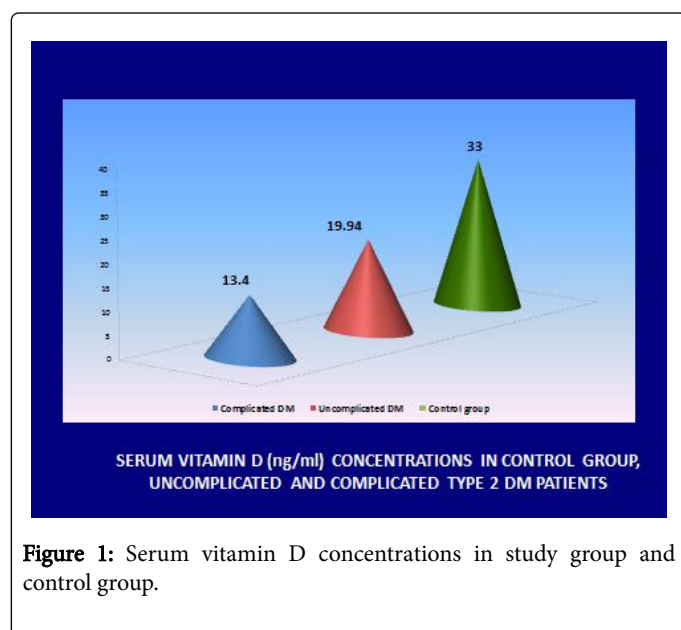
Parameter	Controls(n=42)	Cases (n=48)	P value
	Mean ± SD	Mean ± SD	
Serum Vitamin D	33 ± 3.33	16.94 ± 3.87	<0.001
HbA1C (%) level	4.67 ± 0.39	7.95 ± 0.75	<0.001

(p value<0.001, which is statistically significant in cases in comparison with controls)

**Table 3:** Serum Vitamin D and HbA1c levels in study group and control group.

Serum Vitamin D v/s	r value	p value
Fasting Plasma Glucose	-0.3336	0.046

**Table 4:** Correlation between vitamin D and FBS levels in study group.



**Figure 1:** Serum vitamin D concentrations in study group and control group.

## Discussion

Type 2 Diabetes Mellitus (DM) is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. Worldwide prevalence of DM has risen dramatically over past two decades. IDF projects that 438 million individuals will have the disease by the year 2030. Prevalence is rising rapidly due to, increasing obesity, reduced activity levels as countries become more industrialized. This is true in most countries, as six of the top ten countries with the highest rates are in Asia. Several environmental and dietary factors are associated with Vitamin D deficiency.

Animal studies published nearly 30 years ago identified a pancreatic receptor to the active metabolite [4] and showed that vitamin D deficiency decreased insulin secretion [5]. Since then various human studies have been published, but results have been mixed.

In the present study, lower 25(OH)D3 levels were observed in a type 2 diabetes mellitus patient group than in a control group and an inverse relationship was observed between glycosylated hemoglobin levels and 25(OH)D3 levels in the patient group, implying that 25(OH)D3 levels may affect glucose control in type 2 diabetes mellitus. Interestingly, an inverse relationship was found between vitamin D levels and glycosylated hemoglobin in the whole population studied, type 2 diabetes mellitus patients and controls when analyzed together.

It appears that vitamin D may be related to glucose control in type 2 diabetes mellitus.

Vitamin D receptors have been found in pancreatic beta cells, which additionally have been found to express the enzyme 1- $\alpha$ -hydroxylase, an enzyme that is usually present in kidney activating vitamin D leading to the production of its biologically active form. Vitamin D facilitates the secretion of insulin from pancreatic beta cells, thus appearing to regulate insulin secretion.

### Vitamin D increases insulin secretion from $\beta$ cells of pancreas

- Below are the probable explanations that have been tried for this.
- Insulin secretion is a calcium-dependent process.
- Vitamin D contributes to normalization of extracellular calcium, ensuring normal calcium flux through cell membranes and adequate  $Ca^{2+}$  ion pool.

Therefore vitamin D deficiency may be related to impaired insulin secretion in type 2 diabetes mellitus. In addition, as vitamin D stimulates the expression of the insulin receptor, vitamin D deficiency may be related with insulin resistance.

Based on these studies, vitamin D supplementation can be given to patients with type 2 diabetes mellitus to achieve good glycemic control. But this also has shown conflicting results. In some studies vitamin D supplementation was found to improve glucose control in type 2 diabetes mellitus [6,7], while in others no such effect was observed [8,9].

Vitamin D deficiency appears to be widespread and associated with ethnicity and economic status. Geography is the key to virtually all national statistics. It provides a structure for collecting, processing, storing and aggregating data. Linking geographic data to laboratory data allows analysis of the association of laboratory data with economic indicators. Accumulating research suggests that circulating concentrations of Vitamin D may be inversely related to prevalence of diabetes, plasma concentration of glucose, insulin resistance. It has also been shown that Vitamin D replenishment improves glycemic status and insulin secretion in patients with Type 2 DM with established Hypovitaminoses D.

The evidence of association between vitamin D and Diabetes comes from different intervention studies [10-12]. But still the actual reason behind this association is yet to be established.

The findings in this study have therapeutic applications. In patients with type 2 DM, vitamin D supplementation can improve glycemic control in type 2 DM patients. On the other hand in patients with low vitamin D, vitamin D supplementation can reduce the risk of developing type 2 DM in future.

The facts can be further established by incorporating more number of cases. As ours is a cross sectional study, we cannot determine causation. But if well-designed trials are carried out and confirm a protective effect from vitamin D, it could be used by the general

population as a simple and cheap solution to help prevent the diabetes epidemic.

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