

# Vitamin D Status in Type 2 Diabetes Mellitus

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## ABSTRACT

**Background:** Type 2 Diabetes Mellitus (T2DM) is a progressive disease characterized by both insulin resistance and  $\beta$ -cell dysfunction. Several studies have revealed the inverse relationship between vitamin D deficiency and T2DM. Vitamin D deficiency is thought to influence insulin resistance and the pathogenesis of T2DM by affecting either insulin sensitivity or  $\beta$ -cell function or both. It has been shown that vitamin D replenishment improves insulin sensitivity in patients with T2DM and also decreases the progression of diabetic neuropathy. The presence of vitamin D receptors (VDR) and vitamin D binding proteins (DBP) in pancreatic tissue and the relationship between certain allelic variation in the VDR and DBP genes with glucose tolerance and insulin secretion have further supported this hypothesis.

**Aim:** To examine the association between vitamin D deficiency and T2DM.

**Materials and Methods:** The Study design is a case-control study. 60 non-diabetic individuals were taken as controls and 60 individuals with known DM were taken as cases. Each group consisted of both sexes and the participants were between age of 30-60 years. Various parameters like plasma FBS, 2 hour PPBS, Serum levels of 25(OH)-vitamin D level were measured in both groups. The data were collected and analyzed.

**Result:** Vitamin D level was found to be significantly low in diabetic group compared with controls ( $p$  value < 0.05)

**Conclusion:** There is inverse association between vitamin D status and Type 2 Diabetes Mellitus.

**Key words:** Vitamin D, TYPE 2 Diabetes Mellitus, Vitamin D receptor, Vitamin D binding protein

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## INTRODUCTION

T2DM is a progressive disease characterized by insulin resistance,  $\beta$ -cell dysfunction ultimately leads to altered insulin secretion<sup>(1)</sup>. The pathogenesis of T2DM is multi-factorial. Environmental factors play important role either as triggers or even have protective role<sup>(1)</sup>. The incidence of coronary heart disease and other atherosclerotic disease manifestations are common in individuals with T2DM compared to controls. T2DM is also associated with 2-4 fold higher risk for mortality from CHD than in age matched non-diabetic subjects<sup>(2)</sup>. Therefore increasing burden of T2DM incidence and its associated complications highlights the need for innovative approaches for its prevention and management.

One among the environmental factors which may play a role in T2DM pathogenesis is vitamin D deficiency<sup>(3)</sup>. Vitamin D plays wide range of functions in our body such as regulation of mineral homeostasis, bone remodeling and also plays role in immune system<sup>(15)</sup>. Apart from these well known functions, many studies have shown that vitamin D also plays important role in  $\beta$ -cell function, insulin sensitivity and secretion by both direct and indirect actions.

Presence of vitamin D receptor (VDR) and vitamin D binding protein (DBP) on pancreatic  $\beta$ -cells suggests the role of vitamin D in insulin secretion<sup>(1)</sup>. Vitamin D directly acts on VDR, enhances the transcriptional activation of insulin

gene, thus increases insulin secretion. Also vitamin D directly stimulates expression of insulin receptor and thus improves insulin sensitivity<sup>(1)</sup>. Indirectly vitamin D increases insulin secretion by regulating calbindin, a cytosolic calcium binding protein present in  $\beta$ -cells. By regulating intracellular calcium, vitamin D acts as modulator of depolarization-stimulated release of insulin<sup>(15)</sup>.

Vitamin D is thought to modulate the expression and activity of cytokines and hence protect  $\beta$ -cells against cytokine-induced apoptosis<sup>(1,8)</sup>. Vitamin D also regulates nuclear PPAR (peroxisome proliferative activated receptor) that has an important role in the insulin sensitivity. Indirectly vitamin D can affect insulin resistance by regulating RAAS. In the tissue of vascular and skeletal muscle, action of insulin is inhibited by Angiotensin II thus causes impaired glucose uptake. Vitamin D suppresses rennin and pancreatic RAAS formation, hence it could be a negative endocrine regulator of RAAS<sup>(15)</sup>.

All the above factors suggest a role of vitamin D in the pathogenesis of T2DM. Therefore the present study is conducted to examine the association between vitamin D deficiency and T2DM.

## MATERIALS AND METHODS

The study design is a case-control study. A total of 120 participants were included in the study. 60 T2DM individuals between the age group of 30-60 years were taken as cases. 60 healthy normoglycemic

individuals with no T2DM or any other illness between the age groups 30- 60 years were taken as controls.

Patients with known history of renal disease, bone disease or any other systemic illness were excluded from the study. Study protocol was accepted by the institutional ethics committee and informed consent was obtained from all the participants.

Plasma fasting and post prandial blood sugar levels were measured using Glucose-oxidase peroxidase method. Serum 25- OH Vitamin D was measured using chemiluminescent immunoassay (CLIA).

Statistical analysis was done using SPSS software version 15. Intergroup comparisons of variables were made using independent sample T-test. P value of <0.05 is considered statistically significant.

## RESULTS

After statistical analysis it was found that both the groups were similar in age (p-value of 0.05). The fasting and the post prandial blood sugar levels were found to be significantly higher in cases compared with the controls, with the p-value of 0.000. The vitamin D level was found to be significantly lower in the cases than the controls with the p value of 0.000.

**Table 1: Patient Characteristics**

	Case	Control	P Value
<b>AGE (in years)</b>	48.92±7.320	47.82±8.850	0.500
<b>FBS (in mg/dL)</b>	182.46±76.73	93.56±10.64	0.000*
<b>PPBS (in mg/dL)</b>	235.21±85.07	104.46±14.46	0.000*
<b>25(OH)vit D (in ng/mL)</b>	16.34±5.26	46.89±26.04	0.000*

p-value of FBS, PPBS, 25(OH)Vitamin D were 0.000\* (which is <0.05): statistically significant.

Vitamin D level < 20 ng/mL: Deficiency  
 Vitamin D level 20 – 30 ng/mL: Insufficiency  
 Vitamin D level > 30 ng/mL: Normal

In this study, few individuals from the healthy control group had vitamin D insufficiency and rest of the others had normal vitamin D level. Similarly in the case group, few individuals had vitamin D insufficiency and rest of them had vitamin D deficiency. The detail of the above mentioned criteria is given below in the Table 2.

**Table 2**

	Normal vitamin D level	Vitamin D insufficiency	Vitamin D deficiency
<b>Healthy controls (60)</b>	48	12	-
<b>Serum Vitamin D mean ± SD</b>	51.47 ± 26.21	23.98 ± 2.84	-
<b>Cases (60)</b>	-	8	52
<b>Serum Vitamin D mean ± SD</b>	-	23.34 ± 2.98	14.59 ± 3.85

## DISCUSSION AND CONCLUSION

Diabetes mellitus is a metabolic disorder with high prevalence across the world. T2DM has become a significant global health care problem<sup>(16)</sup>. Many prospective and cross sectional studies suggests that there is an inverse relationship between T2DM and vitamin D status, pointing to a direct link between the risk of T2DM and vitamin D deficiency<sup>(15,17)</sup>. The present study showed that the vitamin D level was found to be significantly low in diabetic group compared with non diabetic healthy controls (p < 0.000).

In the current study population, out of 60 cases, 52 individuals were found to have vitamin D deficiency with the vitamin D level < 20 ng/mL and 8 individuals were found to have vitamin D insufficiency with the vitamin D level between 20 to 30ng/mL. Among the control group 48 individuals had the normal vitamin D level of >30 ng/mL and 12 individuals were found to have vitamin D insufficiency with the vitamin D level between 20 to 30 ng/mL.

The vitamin D insufficiency which was seen among the control group may be due to the insufficient exposure to sunlight or may be due to the sedentary life style of those individuals.

Increasing interest in finding the role of vitamin D in T2DM pathogenesis has led to large number of studies. Many studies suggests that vitamin D plays a strong role in  $\beta$ - cell well being, insulin production and sensitivity<sup>(12,13,15)</sup>. In-vitro experiments of pancreatic islet cells have shown that 1,25(OH)<sub>2</sub>D is required for normal insulin release partly by effect on PTH and by increasing intracellular calcium movement<sup>(7,8)</sup>.

A cross-sectional study conducted in elderly population suggested that, high level of vitamin D not only protects younger individuals but also protects subjects older than 70 years against Type 2 DM. They also suggest an inverse association between HbA1C and vitamin D level in elderly population.<sup>(17)</sup>

Many studies have also done several tests to estimate the insulin resistance like, HOMA-IR, HOMA  $\beta$ - index, Fasting plasma Insulin level

etc<sup>(12,14,17)</sup>. In the current study these parameters are not measured.

Furthermore, it has been demonstrated in both vitamin D deficient humans and animal models, vitamin D supplementation has improved insulin sensitivity and secretion<sup>(3,7)</sup>.

Vitamin D exerts its action through vitamin D receptor (VDR), a member of steroid hormone receptor family. VDR is a transcriptional activator of many genes<sup>(11)</sup>. It was shown that VDR and vitamin D dependent calcium binding protein are present in  $\beta$ -cells and this suggests that vitamin D plays a physiological role in insulin secretion.<sup>(4)</sup> Furthermore some studies have suggested that VDR polymorphism is related to diabetes, obesity, insulin secretion and sensitivity<sup>(11)</sup>. Insulin secretion is modulated by vitamin D, hence genetic variants of VDR gene leads to the development of T2DM<sup>(10)</sup>. Several studies have also shown that low levels of vitamin D binding proteins are also associated with insulin deficiency<sup>(2)</sup>.

Since altered vitamin D status or action affects insulin sensitivity and  $\beta$ -cell function, it has been shown by many studies that vitamin D deficiency plays a significant role in T2DM.<sup>(1)</sup> However currently there is only insufficient data to support that vitamin D supplementation can improve T2DM. Hence to confirm the beneficial role of vitamin D on T2DM and to test the hypothesis that vitamin D status is a direct contributor to the pathogenesis of T2DM, large clinical trials in well-defined population should be conducted and if it is proven to be effective, could have substantial public health implications<sup>(15)</sup>.

To conclude, this study showed that there is a significant inverse association between vitamin D status and T2DM. It is thus suggested that low level of vitamin D might play a significant role in T2DM pathogenesis and supplementation with vitamin D might improve the insulin sensitivity in T2DM.

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