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## Incidence and severity of vitamin d insufficiency among type diabetes patients and the impact of hyperglycemia on serum vitamin d levels: A case control study

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### Abstract

**Aim:** The aim of the present study was to assess the prevalence and severity of vitamin D deficiency in type 2 DM as well as to record the effect of hyperglycaemia on serum vitamin D level.

**Methods:** The present study was conducted in the Department of General Medicine. Total 200 participants were enrolled in the study out of which 100 healthy people were enrolled as case (Group A) and 100 type 2 diabetic patients as controls (Group B). Controls include age and sex matched healthy individuals. Patients younger than 18 years, patients with chronic kidney disease, patients taking calcium supplements or vitamin D supplements within last 3 months, patients suffering from any known chronic illness were excluded from this study.

**Results:** Frequency Distribution of Participants according to Severity of Vitamin D level noted. Prevalence of low vitamin D level in healthy population was only 20% in the study, while prevalence was 80% in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (64%) were having insufficiency, only 20% were having overt vitamin D deficiency in Diabetic patients. In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 24%, 60% and 15% respectively, where in patients with uncontrolled diabetes it was 10%, 68% and 22% respectively. More number of diabetic patients with uncontrolled status (22%) was having overt vitamin D deficiency in comparison to controlled status (16%). There was a significant association between the maintenance of euglycemia and severity of Vitamin D level in diabetic patients, as the p value was less than 0.05.

**Conclusion:** Vitamin D deficiency is highly prevalent in diabetic patients as compared to normal healthy population. All patients with type 2 diabetes mellitus must be screened for vitamin D levels and those found to be having insufficiency or deficiency of vitamin D should be started on vitamin D supplements.

**Keywords:** Serum vitamin D level, Type 2 diabetes mellitus, vitamin D deficiency

### Introduction

The worldwide epidemic of Diabetes Mellitus (DM) is a serious current health problem because of the high toll of vascular complications associated with the condition. It has been estimated that 380 million individuals would be affected with diabetes worldwide by the year 2025. The incidence & prevalence of Type-2 Diabetes Mellitus (T2DM) is increasing rapidly. There were greater than 285 million patients worldwide with diabetes in 2010, increasing to approximately 438 million by 2030 [1]. Asian Indians are at a high risk for developing insulin resistance, the metabolic syndrome, T2DM and coronary heart disease [2]. Diabetes mellitus (DM) is a group of diseases with common feature of hyperglycaemia and associated with disturbance of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action or both [3]. Vitamin D deficiency is increasingly recognized as a global problem and it has been estimated that nearly one billion people have either vitamin D deficiency or insufficiency [4]. Possible explanations include lack of adequate sun exposure in urban areas, lack of intake of fortified foods and obesity [5, 6]. Vitamin D is a pleiotropic hormone known to play an immunomodulatory role [7, 8], in addition to Ca and bone metabolism. Receptors for its activated form have been identified on pancreatic  $\beta$  cells and immune cells [9, 10].

Evidence is available linking vitamin D deficiency with bacterial and viral infections [11, 12]. Foot infection accounts for 20% of hospitalization of diabetic patients annually [13]. Immunological defects [14] in addition to neuropathy and vascular abnormality are the prime contributors in the pathogenesis of diabetic foot and subsequent infections. Different studies have shown that deficiency of vitamin D leads to immune cell dysfunction,  $\beta$  cell damage and impaired insulin production [15, 16]. Few research reported association of that Vitamin D deficiency has been associated with a myriad of metabolic abnormalities, including hypertension, diabetes, dyslipidaemia and obesity [17]. As vitamin D has been showed to have effect on pathophysiology of diabetes and diabetics having very high prevalence of vitamin D deficiency.

The aim of the present study was to assess the prevalence and severity of vitamin D deficiency in type 2 DM as well as to record the effect of hyperglycaemia on serum vitamin D level.

### Methods

The present study was conducted in the Department of General Medicine. Total 200 participants were enrolled in the study out of which 100 healthy people were enrolled as case (Group A) and 100 type 2 diabetic patients as controls (Group B). Controls include age and sex matched healthy individuals. Patients younger than 18 years, patients with chronic kidney disease, patients taking calcium supplements or vitamin D supplements within last 3 months, patients suffering from any known chronic illness were excluded

from this study. The patients fulfilling the above mentioned criteria were selected after informed consent. All participants included in this study were subjected to complete history and clinical examination. Routine laboratory Investigations like CBC, FBS, RBS, PP2BS, HbA1C, blood urea, serum creatinine, lipid profile, urine albumin and Vitamin D3 levels were done by standard methods in central laboratory of Hospital. The value of serum vitamin D level was further divided in following category: sufficient = 30-100 ng/ml, insufficient=20-29 ng/ml, deficiency = less than 20ng/ml. Data were analyzed by using SPSS-20 and MS-Excel-2016 version.

### Results

**Table 1:** Severity grading of vitamin D deficiency in cases and controls

Severity grading of vitamin D	Case	Controls
Deficiency	10 (20)	0
Insufficient	32 (64)	10 (20)
Sufficient	8 (16)	40 (80)

Frequency Distribution of Participants according to Severity of Vitamin D level noted. Prevalence of low vitamin D level in healthy population was only 20% in the study, while prevalence was 80% in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (64%) were having insufficiency, only 20% were having overt vitamin D deficiency in Diabetic patients.

**Table 2:** The association of severity of vitamin D level with the category of diabetes control

Diabetes control	Vitamin D Level			p value
	Sufficient	Insufficient	Deficiency	
Controlled Diabetic (N = 50)	12 (24%)	30 (60%)	8 (16%)	0.002
Uncontrolled Diabetic (N= 50)	5 (10%)	34 (68%)	11 (22%)	

Test applied: chi-square test

In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 24%, 60% and 15% respectively, where in patients with uncontrolled diabetes it was 10%, 68% and 22% respectively. More number of diabetic patients with

uncontrolled status (22%) was having overt vitamin D deficiency in comparison to controlled status (16%). There was a significant association between the maintenance of euglycemia and severity of Vitamin D level in diabetic patients, as the p value was less than 0.05.

**Table 2:** Subgroup analysis- mean vitamin D level in diabetes patients in relation with age, gender and associated co-morbidities

Parameters (Number of patients)	Mean value of vitamin D	p value
Age group	35-60 (64)	23.97±6.06
	>60 (36)	24.48±3.14
Gender	Male (70)	26.64±6.16
	Female (30)	25.35±4.88
HTN	Yes (20)	23.17±3.16
	No (80)	25.45±7.63
IHD	Yes (10)	28.12±4.06
	No (90)	26.64±6.44

Test applied: chi-square test

These findings suggest that duration of having diabetes has no effect on vitamin D levels. We also compared the mean value of vitamin D deficiency with the duration of Diabetes, but there was no significant relation between duration of diabetes and serum vitamin D deficiency (p value >0.5). Diabetic nephropathy was the most common micro vascular

complication seen in type 2 diabetic patients. It was found that all three important microvascular complications. Diabetic retinopathy, diabetic nephropathy and peripheral neuropathy did not have any significant correlation with serum vitamin D level as p value is greater than 0.05 for all three parameters.

**Table 3:** Comparison of mean vitamin D level with duration and micro vascular complication of diabetes mellitus

	Parameters		Mean value of vitamin D (ng/dl)	p value
Duration of diabetes	1-5 years		25.55±5.89	0.274
	6-10 years		26±6.08	
	>10 years		25.8±3.14	
Micro-vascular complication	Diabetic Retinopathy	Present	24.26±4.86	0.084
		Absent	25.95±5.78	
	Diabetic Neuropathy	Present	28.62±4.86	0.064
		Absent	25.65±5.95	
	Peripheral neuropathy	Present	24.56±5.10	0.116
		Absent	26.14±6.14	

These findings suggest that duration of having diabetes has no effect on vitamin D levels. We also compare the mean value of vitamin D deficiency with the duration of Diabetes, but there was no significant relation between duration of diabetes and serum vitamin D deficiency (P value >0.5). Diabetic nephropathy was the most common micro vascular complication seen in type 2 diabetic patients. it was found that all three important microvascular complications: - diabetic retinopathy, diabetic nephropathy and peripheral neuropathy did not have any significant correlation with serum Vitamin D level as p value is greater than 0.05 for all three parameters.

### Discussion

The global prevalence of vitamin D insufficiency is a significant health concern. According to a study conducted by Pfortnhauer KM *et al.*, the global prevalence of Vitamin D insufficiency is around 15% [18]. Given the shown impact of vitamin D on the pathophysiology of diabetes and the high incidence of vitamin D insufficiency, this study aims to investigate the reciprocal relationship between these two prevalent conditions. Numerous studies conducted across many geographical regions and cultural contexts have revealed a wide spectrum of prevalence rates for vitamin D insufficiency among individuals with diabetes, ranging from 67% to 98.8% [19]. India has been officially designated as the "Capital of Diabetes." Diabetes mellitus is recognized as a significant developing pandemic in India, given the present prevalence of 41 million individuals diagnosed with diabetes, a number projected to increase to 70 million by the year 2025. Given the shown impact of vitamin D on the pathogenesis of diabetes and the significant incidence of vitamin D insufficiency, this study aims to investigate the reciprocal influence of these two very prevalent conditions. The present study examines the frequency distribution of participants based on the severity of their observed vitamin D levels. The study revealed that the prevalence of low vitamin D levels in the healthy population was found to be 20%, however in the diabetic group, the prevalence was significantly higher at 80%. The study found that a significant proportion of diabetes individuals with inadequate Vitamin D levels exhibited insufficiency (64%), whereas a smaller percentage demonstrated overt vitamin D deficiency (20%). The study observed the prevalence of adequate, inadequate, and deficient levels of Vitamin D in patients with managed and uncontrolled diabetes, as determined by HbA1C criteria. Among patients with controlled diabetes, the prevalence of sufficient Vitamin D was 24%, while insufficient and deficient levels were seen in 60% and 15% of patients, respectively. In contrast, among patients with uncontrolled diabetes, the prevalence of sufficient Vitamin D was 10%, while insufficient and

deficient levels were observed in 68% and 22% of patients, respectively. A higher proportion of diabetes patients with uncontrolled state (22%) had overt vitamin D insufficiency, as opposed to those with managed status (16%). A noteworthy correlation was seen between the preservation of euglycemia and the severity of Vitamin D levels in individuals with diabetes, as shown by a p value below 0.05. Our study, along with the investigations conducted by Bashir *et al* and Ifigenia-Kostoglou A *et al*, has demonstrated a greater occurrence of vitamin D insufficiency in persons with diabetes mellitus in comparison to those who are healthy. However, two other studies have indicated that there is no significant disparity in the prevalence of vitamin D deficiency between diabetic and healthy populations. We have conducted a comparative analysis of the average blood vitamin D levels between individuals diagnosed with diabetes and those belonging to a healthy population across many studies. Various research, including our own investigation, have observed a significantly lower average level of vitamin D in individuals with diabetes when compared to the general population of healthy individuals [20, 21].

The study involved a comparison of the average level of vitamin D insufficiency in connection to the length of Diabetes. However, the analysis did not reveal a statistically significant association between the duration of diabetes and the presence of blood vitamin D deficiency (p value >0.5). Diabetic nephropathy emerged as the prevailing microvascular consequence observed among individuals diagnosed with type 2 diabetes. It has been discovered that all three significant microvascular problems were present. There was no significant link seen between blood vitamin D level and diabetic retinopathy, diabetic nephropathy, and peripheral neuropathy, as shown by p values larger than 0.05 for all three measures. The findings of our study indicate that there is a statistically significant difference in the mean vitamin D levels between patients with uncontrolled diabetes and patients with managed diabetes (p value=0.004, Chi Square test). Specifically, the mean vitamin D level was found to be lower in patients with uncontrolled diabetes. Mukherjee B *et al.* demonstrated comparable findings. The average concentration of vitamin D is significantly lower in uncontrolled diabetes patients (19.47±4.76) compared to managed diabetic patients (23.63±3.71) [21]. The study conducted by Modi KD *et al* revealed that those with managed diabetes had an average vitamin D level of 22.4±18.6, whereas those with uncontrolled diabetes had a lower average level of 19.9±18.3. This difference in vitamin D levels between the two groups was shown to be statistically significant [22]. The duration of diabetes and the existence of microvascular complications do not appear to have a significant impact on

blood vitamin D levels. There was no observable impact of advancing age on the vitamin D levels of diabetes patients, and we were unable to identify a similar correlation in other research. Female diabetes patients had lower levels of vitamin D in comparison to their male counterparts. This disparity may be attributed to reduced sun exposure resulting from increased engagement in household activities. In our study, we observed that hypertension was the prevailing comorbidity among diabetes patients, with a prevalence rate of 17.14%. The research conducted by Shalini P and colleagues revealed a higher prevalence of Vitamin D insufficiency (80.4%) among those diagnosed with hypertension compared to those who are considered healthy (67.7%) [23].

Additionally, we conducted a comparison of the average vitamin D deficiency levels with the length of Diabetes. However, our analysis revealed no statistically significant association between the duration of diabetes and serum vitamin D deficiency (P value >0.5). Diabetic nephropathy emerged as the prevailing microvascular consequence observed among individuals diagnosed with type 2 diabetes. The study revealed that there was no significant association between blood Vitamin D level and the three key microvascular sequelae, namely diabetic retinopathy, diabetic nephropathy, and peripheral neuropathy. This conclusion is supported by the p-values, which were all larger than 0.05 for these three variables. There is no significant association between the duration of diabetes and the occurrence of microvascular complications with serum vitamin D levels. There was no observable impact of increasing age on vitamin D level in diabetes patients, and a similar connection was not seen in other investigations. Female diabetes patients had lower levels of vitamin D in comparison to their male counterparts. This disparity may be attributed to less sun exposure resulting from household activities. In our investigation, hypertension emerged as the prevailing comorbidity among individuals with diabetes. The research conducted by Shalini P *et al* revealed a higher prevalence of Vitamin D insufficiency (80.4%) among those diagnosed with hypertension compared to those who are considered healthy (67.7%) [23]. In the present investigation, it was observed that hypertension diabetes patients exhibited a comparatively lower level of vitamin D in comparison to non-hypertensive diabetic patients. This disparity was found to be statistically significant, as shown by a p-value of 0.047. Ischemic heart disease was identified as a comorbidity in conjunction with diabetes; however, no statistically significant disparity in the average Vitamin D levels was seen between diabetic individuals with and without ischemic heart disease.

### Conclusion

The prevalence of vitamin D insufficiency is significantly higher among individuals with diabetes compared to those who are considered to be in a state of normal health. It is important to do vitamin D level screenings for all individuals diagnosed with type 2 diabetes mellitus. If a patient is discovered to have insufficient or deficient levels of vitamin D, it is recommended to initiate vitamin D supplementation. Moreover, it is important to maintain rigorous control over diabetic state as a means of mitigating the risk of developing vitamin D insufficiency.

### Conflict of Interest

Not available

### Financial Support

Not available

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