

A Case Control Study to Examine Vitamin D Insufficiency in type 2 Diabetes and the Impact of Hyperglycemia on Blood Vitamin D Levels

Shachindra Kumar Astik¹, Bindu Arya²

¹Associate Professor, Department of General Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India

²Assistant Professor, Department of Obstetrics and Gynecology, Nalanda Medical College and Hospital, Patna, Bihar, India

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Corresponding author: Dr. Bindu Arya

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Abstract

Aims: The aim of the study 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. **Material and methods:** A case-control study was conducted in the Department of General Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India from August 2019 March 2020. Total 240 participants were including in the study out of which 120 healthy people were include as case (Group A) and 120 type 2 diabetic patients as controls (Group B). 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 Institute. **Results:** Prevalence of low vitamin D level in healthy population was only 23.33 % in my study, while prevalence was 85.83 % in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (65%) were having insufficiency, only 20.83% were having over 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 18.51%, 61.11% and 16.67% respectively, where in patients with uncontrolled diabetes it was 10.60%, 68.18% and 24.24% respectively. More number of diabetic patients with uncontrolled status (24.24%) was having overt vitamin D deficiency in comparison to controlled status (16.67%). There is a significant association between the maintenance of euglycemia and severity of Vitamin D level in diabetic patients, as the p value is less than 0.05. **Conclusion:** control of diabetic status is mandatory in order to prevent vitamin D deficiency. **Keywords:** Serum vitamin D level, Type 2 diabetes mellitus, Vitamin D deficiency.

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Introduction

T2DM is a chronic metabolic condition whose incidence is progressively growing globally.

The worldwide diabetes population is predicted to reach 562 million by 2030[1].

Although T2DM is spreading globally, it is mostly affecting the poor world, where it is quickly becoming an epidemic.

The pathophysiology of T2DM is being studied again because to the rising

worldwide burden of T2DM. It is caused by genetic and environmental factors interacting. T2DM prevalence varies geographically owing to lifestyle and risk factors.

Other than obesity, inactivity, high calorie diets and stress, the relevance of specific dietary variables in T2DM aetiology is a newer notion. Several cross-sectional studies demonstrate that vitamin D is vital in blood glucose regulation and that its shortage may induce T2DM.

Vitamin D is a misnomer since its active form is a hormone that is involved in bone metabolism as well as many non-skeletal physiological functions. The direct influence of vitamin D on pancreatic-cells and insulin sensitive organs has been hypothesised, as has an indirect effect on calcium homeostasis[2,3].

In the largest epidemiological study from the NHANES population, a dose-dependent inverse relationship has been observed between vitamin D and type 2 DM with the highest number of metabolic syndrome patients having the lowest quartiles of vitamin D[4]. The main source of vitamin D in humans is exposure to sunlight, natural diet and dietary supplements. Vitamin D from the skin and diet are metabolised in the liver to 25-hydroxy vitamin D [25 (OH)D] which is used to determine the patient's vitamin D status. Although there is no definite consensus about the normal level of vitamin D, most experts define vitamin D deficiency as less than 20 ng/ml. A level of 20 - 29 ng/ml is considered to indicate a relative insufficiency of vitamin D and a level of 30 ng/ml or greater can be considered as sufficient[5,6]. According to this definition, 1 billion people worldwide are suffering from vitamin D deficiency or insufficiency. Even in the sunniest countries including India, vitamin D deficiency is very common as most of the body surface is shielded from the sun. India is a country where both T2DM and hypovitaminosis D are prevalent. But relatively scarce data is available observing the

correlation between the two. The aim of the study 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.

Material and Methods

A case-control study was conducted in the Department of General Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India from August 2019 March 2020, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient or the relatives.

Methodology

The technique, risks, benefits, results and associated complications of the procedure were discussed with all patients. Total 240 participants were included in the study out of which 120 healthy people were included as case (Group A) and 120 type 2 diabetic patients as controls (Group B). Controls include age and sex matched healthy individuals. 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. 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 Institute. The value of serum vitamin D level was further divided in following category: sufficient = 30-100ng/ml, insufficient = 20-29ng/ml, deficiency = less than 20ng/ml.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages and means. Test applied for the analysis was chi-square test.

Results

In the study population, the mean age of group A (case) was 52.42±10.25 years while that of group B (control) was 50.12±11.88 years. Total 140 males and 100 females were enrolled in study. 65% of group A were male and 35 females. Group B (control) had 60% males and 40 females. On evaluation of investigation profile of both group A and group B, mean values of haematological parameters in form of haemoglobin, total count and platelet were within normal limit and comparable in both groups. Surprisingly mean value of renal function test parameters, blood urea and serum creatinine were within normal range for diabetic group also, though 10.5% of

patients had abnormal serum creatinine value and it range from 2.22 to 4.2 mg/dl. Mean value of all lipid profile component were in normal limit in both the group, but 35% of diabetic patients had dyslipidaemia and commonest dyslipidaemia was hypertriglyceridemia in 30% patients. Frequency Distribution of Participants according to Severity of Vitamin D level noted. Prevalence of low vitamin D level in healthy population was only 23.33 % in my study, while prevalence was 85.83 % in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (65%) were having insufficiency, only 20.83% were having overt vitamin D deficiency in Diabetic patients (table 1.)

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

	Case =120	%	Control=120	%
Deficiency	25	20.83	nil	-
Insufficient	78	65	28	23.33
Sufficient	17	14.17	92	76.67

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

Diabetes control	Vitamin D Level			Chi Sq (p value)
	Sufficient	Insufficient	Deficiency	
Controlled			9	3.12 (0.003)
Diabetic (N = 54)	10(18.51%)	33 (61.11%)	(16.67%)	
Uncontrolled Diabetic (N= 66)	7(10.60%)	45 (68.18%)	16 (24.24%)	

In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 18.51%, 61.11% and 16.67% respectively, where in patients with uncontrolled diabetes it was 10.60%, 68.18% and 24.24% respectively. More number of diabetic patients with uncontrolled status (24.24%) was having overt vitamin D deficiency in comparison to controlled status (16.67%). There is a significant association between the maintenance of euglycemia and severity of

Vitamin D level in diabetic patients, as the p value is less than 0.05 (Table 2).

Pearson correlation test showed negative correlation between HbA1C level and mean vitamin D level in Diabetic group as r = - 0.266, p value = <0.001. It suggests as HbA1c level increase, the level of vitamin D decreases, so more severe the hyperglycaemia and poorer the control of diabetes status, there was more severe the vitamin D deficiency.

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 (Table 3).

Table 2: 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	0-5 years		25.77±6.85	0.265
	5-10 years		27±5.85	
	>10 years		26.12±3.82	
Micro-vascular complication	Diabetic	Present	24.11±5.02	0.077
	Retinopathy	Absent	26.31±5.22	
	Diabetic	Present	27.11±5.45	0.057
	Nephropathy	Absent	25.41±6.35	
	Peripheral	Present	24.24±4.69	0.102
	Neuropathy	Absent	27.25±5.88	

Hypertension was most common co-morbidity found in diabetic group (18.33%) followed by ischemic heart disease (5.83%). Serum vitamin D level was measured in all participants. 85.83% of diabetic population was having less than normal vitamin D level, while only 23.33% had less than normal vitamin D level in group B(control). Mean value of vitamin D in type 2 Diabetic patients was 26.33±6.94 ng/dl and mean value of vitamin D in healthy individuals was 35.67±4.88 ng/dl.

Table 3: 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	Below40 (91)	25.32±5.75
	>40 (29)	25.02±3.19
Gender	Male (78)	28.65±5.86
	Female (42)	25.09±4.68
HTN	Yes (22)	21.66±4.22
	No (98)	25.68±6.81
IHD	Yes (7)	28.23±4.72
	No (113)	26.17±5.82

Discussion

Vitamin D deficiency is a major health problem worldwide. The overall worldwide Vitamin D deficiency prevalence is around 15% according to study done by Pfothnerhauer KM et al.[7] However the prevalence of vitamin D deficiency in India is around 50-90% in normal healthy population[8]. In my study, prevalence of

vitamin D deficiency is 23.33% in normal population which is similar to worldwide prevalence but very less in comparison to prevalence shown in Indian studies. This low prevalence in healthy population was contradictory to other Indian studies. Another on-going study on vitamin D level done in similar region had also showed 16% prevalence of vitamin D deficiency in healthy population. Vitamin D exerts its

effect on calcium metabolism and hence affects skeletal system; however, it also has extra skeletal effects like that on cardiovascular system, endocrine disorders and autoimmune disorder. Several reports have ascribed an active role to vitamin D in the functional regulation of the endocrine pancreas, particularly the beta-cells.

India is already declared as 'Capital of Diabetes'. Diabetes mellitus is accepted as major emerging epidemic in India, as India is having 41 million of diabetic patients currently and it will go up to 70 million by year 2025. As vitamin D has been showed to have effect on pathophysiology of diabetes and have very high prevalence of vitamin D deficiency, so we have taken up this study to see effect of both high prevalence diseases on each other.

Various studies done in different geographical region and cultural background have shown varied range of prevalence of vitamin D deficiency in diabetic group ranging from 67%-98.8% [8-11]. Our study along with Bashir et al and Ifigenia-Kostoglou A et al studies had shown higher prevalence of vitamin D deficiency in diabetes mellitus patients compared to healthy individuals, but two other studies had shown no difference of prevalence between diabetic and healthy population [8-11]. So, we have compared the mean value of serum vitamin D level in diabetic patients and in healthy population of various study. Various studies including our study had low mean level of vitamin D for diabetic patients in comparison to healthy population [8,11,12].

In our study, mean vitamin D level is lower in patients with uncontrolled diabetes than patient with controlled diabetes (p value=0.003 Chi Sq test). Similar results was shown by Mukherjee B et al. Mean level of vitamin D is low in uncontrolled diabetic patients (19.47 ± 4.76) as compared to controlled diabetic patients (23.63 ± 3.71) [12]. Modi KD et al found that vitamin D levels in patients with controlled diabetes was 22.4 ± 18.6 while in

uncontrolled diabetic patients it was lower, 19.9 ± 18.3 which is statistically significant [13]. Overall insufficiency is more common than deficiency state in diabetic patients regardless of diabetic control status, but severe vitamin D deficiency is more prevalent when patients were having uncontrolled diabetes than controlled diabetes (24.24% and 16.67% respectively). On Pearson correlation, the study has demonstrated negative correlation between HbA1C level and serum vitamin D level. It is suggesting that as HbA1C level increase, there is decrease in serum vitamin D level. Ifigenia-Kostoglou A et al had also found that 25(OH) D3 levels were inversely associated with HbA1c when the patient and control groups were analysed together (p = 0.008, $r^2 = 0.058$, linear regression analysis).¹¹ Study by Mukherjee B et al also indicates there is a definite negative correlation between Vitamin D levels and diabetes (r = -0.94 and -0.97) and poorly controlled diabetics have further lower values of Vitamin D [12]. A study by Akshay kumar SV et al showed a negative negligible correlation between vitamin D levels and HbA1C, which was not statistically significant (r = 0.017, p value 0.741) [10]. The inverse relationship between vitamin D level and glycaemic control in this study support an active role of vitamin D in pathogenesis of type 2 diabetes mellitus.

Duration of diabetes and presence of microvascular complication do not have effect on serum vitamin D level. No effect of increasing age was observed on vitamin D status in diabetic patients and we could not able to find such association in other studies. Female diabetic patients were having lower vitamin D level compared to male counterparts; the reason might be less exposure to sun due to household activity. Hypertension was the most common comorbidity found in diabetic patients (18.33%) in our study. Study by Shalini P et al found that Vitamin D deficiency is more prevalent (80.4%) in hypertensive patients than healthy (67.7%)

individuals[14]. Hypertensive diabetic patients had lower vitamin D level than non-hypertensive diabetic patients in my study, which is statistically significant as p value was 0.033. Ischemic heart disease was another comorbidity found with diabetes, but there was no significant difference in mean Vitamin D level was recorded in diabetic patients with or without ischemic heart disease.

Conclusion

Vitamin D levels should be checked in all patients with type 2 diabetes, and those found to be inadequate or deficient should be given vitamin D supplements. Also, diabetics must be closely monitored to avoid vitamin D insufficiency. We hope this research will help us better understand the relationship between vitamin D and type 2 diabetes and assist diabetic individuals avoid vitamin D insufficiency.

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