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Original Research Article

Prevalence and severity of vitamin D deficiency in type 2 diabetic patients

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ABSTRACT

Background: The current worldwide epidemic of diabetes mellitus is a serious health problem because of the high toll of vascular complications. Vitamin D deficiency as emerging epidemic have effect on pathophysiology of diabetes mellitus by various mechanisms, so we have taken up this study with aim to see effect of both high prevalent diseases on each other and to observe prevalence and pattern of vitamin D deficiency in diabetics.
Methods: In this case-control study 70 type 2 diabetic patients were taken as cases and 70 healthy individuals as controls. All participants included in this study were subjected to complete history taking and clinical examination and routine laboratory Investigations were done for all participants. The data was analyse using appropriate statistical tests.
Results: The prevalence of low vitamin D level (inclusive of insufficiency and deficiency) was 18.57% in healthy controls, while 84.29% in diabetic group. Mean level of vitamin D in cases was 25.73±7.27 while 34.55±5.17 in healthy population (p value <0.05). Vitamin D deficiency is more seen in uncontrolled diabetes patients. Inverse correlation was recorded between HbA1C and serum vitamin D level (r = - 0.281, p value = <0.001).
Conclusions: Vitamin D deficiency is highly prevalent in diabetic patients as compare to normal healthy population. All patients of type 2 Diabetes patients must have screened for serum vitamin D level and if found deficient than it should be treated promptly with vitamin D supplements for better control of hyperglycaemia.

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

INTRODUCTION

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.[1] The worldwide epidemic of diabetes mellitus 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. In India alone 41 million individuals are affected, and this is likely to go up to 70 million by the year 2025.[2] Along with Insulin resistance and relative insulin Deficiency, Inflammatory factors, reactive oxygen species and autoimmune reactions have all strongly emerged as the major pathogenic effectors for diabetes.

Vitamin D deficiency is also a major health problem worldwide. The prevalence of vitamin D deficiency in India is around 50-90% in normal healthy population.[3] As the major regulator for calcium homeostasis, vitamin D

directly and indirectly improves insulin exocytosis via activating calcium-dependent endopeptidases, Hence Vitamin D also improves glucose tolerance.[4] Few Research reported association of that Vitamin D deficiency has been associated with a myriad of metabolic abnormalities, including hypertension, diabetes, dyslipidaemia and obesity.[5] As vitamin D has been showed to have effect on pathophysiology of diabetes and diabetics having very high prevalence of vitamin D deficiency. this study was carried out with aim to see effect of both high prevalent diseases on each other. The objectives were 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

Sumandeep Vidyapeeth, a tertiary care Centre at Vadodara, Gujarat after obtaining Ethics committee clearance. Total 140 participants were enrolled in the study out of which 70 healthy people were enrolled as case (Group A) and 70 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 Dhiraj Hospital. 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. Appropriate statistical methods were used to analyse the results.

RESULTS

In the study population, the mean age of group A (case) was 53.86±9.26 years while that of group B (control) was 49.74±12.4 years. Total 82 males and 58 females were enrolled in study. 60% of group A were male with sex ratio of 1:0.6 while group B (control) had 57.1% males with sex ratio of 1:0.75.

Hypertension was most common co-morbidity found in diabetic group (17.14%) followed by Ischemic Heart Disease (5.71%). Serum vitamin D level was measured in all participants. Almost 3/4th (74.3%) of diabetic population was having less than normal vitamin D level, while only 18.6% had less than normal vitamin D level in group B(control). Mean value of vitamin D in type 2 Diabetic patients was 25.73±7.27 ng/dl and mean value of vitamin D in healthy individuals was 34.55±5.16 ng/dl.

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 8.5% of patients had abnormal serum creatinine value and it range from 2.10 to 3.9 mg/dl. Mean value of all lipid profile component were in normal limit in both the group, but 32% of diabetic patients had dyslipidaemia and commonest dyslipidaemia was hyper-triglyseridemia in 28.57% patients.

Frequency Distribution of Participants according to Severity of Vitamin D level noted. Prevalence of low vitamin D level in healthy population was only 18.57 % in my study, while prevalence was 84.29 % in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (65.72%) were having insufficiency, only 18.57% were having overt vitamin D deficiency in Diabetic patients (Figure 1).

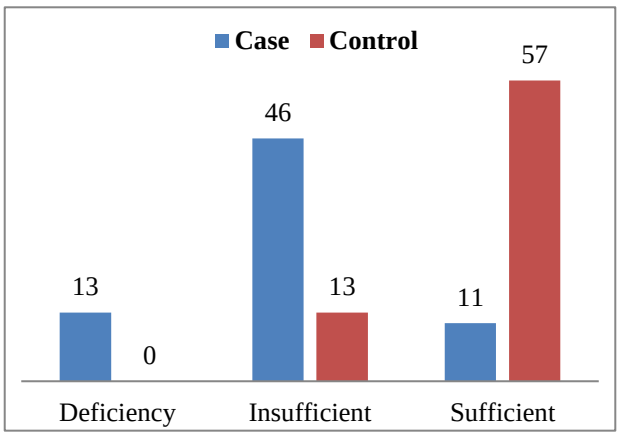

Figure 1: Severity grading of vitamin d deficiency in cases and controls.

Table 1: 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 Diabetic (N = 29)	6 (24.13%)	19 (62.06%)	4 (13.79%)	2.614 (0.004)
Uncontrolled Diabetic (N= 41)	5(12.19%)	27 (65.85%)	9 (21.95%)	

In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 24.13%, 62.06% and 13.79% respectively, where in patients with uncontrolled diabetes it was 12.19%, 65.85% and 21.95% respectively. More number of diabetic patients with uncontrolled status (21.95%) was having overt vitamin D deficiency in comparison to controlled status (13.79%). 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 1).

Pearson correlation test showed negative correlation between HbA1C level and mean vitamin D level in Diabetic group as r = -0.281, 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 (Figure 2).

Out of 26 patients having diabetes duration of less than 5 years, 25.7% were have insufficiency of vitamin D level and 8.6% had deficiency, while out of 10 patients having long duration of diabetes (> 10 years), 8.6% patients have insufficiency and 1.4% patients have deficiency of vitamin D level. 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 (Table 2).

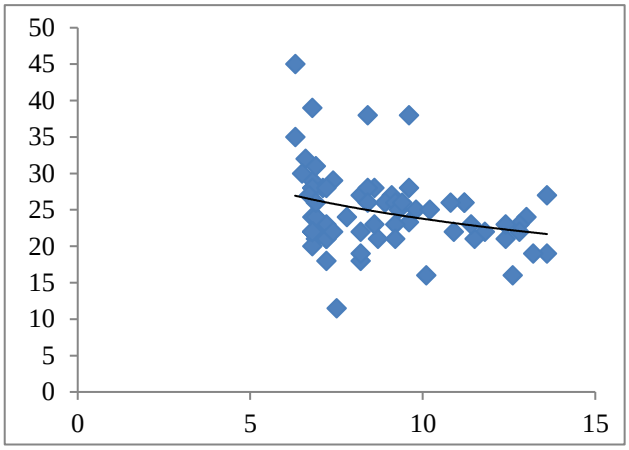

Figure 2: Correlation between vitamin D deficiency and HbA1C.

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	1-5 years		24.52±5.83	0.285
	6-10 years		26±6.01	
	>10 years		25.8±3.65	
Micro-vascular complication	Diabetic retinopathy	Present	23.21±4.81	0.084
		Absent	25.91±5.78	
	Diabetic nephropathy	Present	27.63±4.89	0.064
		Absent	24.65±5.90	
	Peripheral neuropathy	Present	24.60±5.10	0.124
		Absent	26.18±6.11	

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	35-60 (53)	24.91±6.07	0.337
	>60 (17)	24.43±3.09	
Gender	Male (42)	27.77±6.19	0.021
	Female (28)	24.38±4.83	
HTN	Yes (12)	22.15±3.89	0.047
	No (58)	26.48±7.60	
IHD	Yes (4)	27.10±4.07	0.185
	No (66)	25.66±6.42	

Out of 26 patients having diabetes duration of less than 5 years, 25.7% were have insufficiency of vitamin D level and 8.6% had deficiency, while out of 10 patients having long duration of diabetes (> 10 years) ,8.6% patients have insufficiency and 1.4% patients have deficiency of vitamin D level. 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 (Table 3).

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 Pfotrnhauer KM et al.[6] However the prevalence of vitamin D deficiency in India is around 50-90% in normal healthy population.[3] In my study, prevalence of vitamin D deficiency is 18.6% 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%.[3,7-9] 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.[3,7-9] 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.[3,9,10]

In our study, mean vitamin D level is lower in patients with uncontrolled diabetes than patient with controlled diabetes (p value=0.004 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).[10] 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.[11] 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 (25% and 13.4% respectively). On Pearson correlation, the study has demonstrated negative correlation between HbA1C level and serum vitamin D level. It 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).[9] 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.[10] A study by Akshaykumar SV et al showed a negative negligible co-relation between vitamin D levels and HbA1C, which was not statistically significant (r = 0.017, p value 0.741).[8] 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 micro-vascular 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 (17.14%) 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.[12] Hypertensive diabetic patients had lower vitamin D level than non-hypertensive diabetic patients in my study, which is statistically significant as p value was 0.047. 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.

Limitation of my study was inability to nullify the effect of confounding factors for vitamin D level like duration of sun exposure and complexion of the skin. We had not analysed association of BMI with vitamin D level in our study while analysing study data.

CONCLUSION

Vitamin D deficiency is highly prevalent in diabetic patients as compared to normal healthy population. All patients of type 2 diabetes patients 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. Also strict control of diabetic status is mandatory in order to prevent vitamin D deficiency. We sincerely wish this study will be an important step in understanding association of Vitamin D level with type 2 diabetes mellitus and help in preventing vitamin D deficiency in diabetic patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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