

To Study The Pattern Of Vitamin D Levels In Newly Diagnosed Type 2 Diabetes Mellitus Patients.

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ABSTRACT

Background: Diabetes mellitus is a metabolic disease, linked to deficiency of insulin occurring really or relatively can have an effect on almost body's every organ system. Untreated diabetes can lead to majority of the complications. Vitamin D, fat-soluble secosteroids, are related to absorption of calcium, iron, magnesium, phosphate and zinc at intestine level to be increased. Vitamin D deficiency, appears to be related to the process of initiating type 2 DM. Mild to moderate vitamin D deficiency has been postulated to be a risk factor for type 2 diabetes. AIM: The present study was conducted to study serum vitamin D levels in patients with recently diagnosed type 2 diabetes mellitus in comparison with controls of similar age and gender. **Methods:** A total of 100 patients were included in the study among which 50 patients were diabetic and 50 were age and gender matched healthy non-diabetic controls. Patients in the age group of 30-65 yrs., who were diagnosed with type 2 diabetes within last 6 months were included in the study. Patients with Diagnosed cases of Type 2 diabetes mellitus on treatment for more than 6 months, known case of Cancer/ liver /renal dysfunction, medication that affect vitamin D metabolism/its absorption (Phenytoin, Rifampicin, Isoniazid, Ketoconazole, Carbamazepine, Phenobarbitone, valproic acid, Primidone, Prednisolone, Dexamethasone, Efavirenz, Atorvastatin, Orlistat, Cholestyramine, Estrogen, Thiazides, Antacids, Verapamil), Type 1 diabetes mellitus, Patients on vitamin D Supplementation were excluded from the study. **Result:** Optimal Vitamin D2 level was found among none (0) and 36.0% (18) subjects with diabetes and without diabetes respectively, Insufficient Vitamin D2 level was found among 14% (7) subjects each with diabetes and without diabetes and Deficient Vitamin D2 level was found among 86.0% (43) and 50.0% (25) subjects with diabetes and without diabetes respectively. **Conclusion:** Vitamin-D deficiency/insufficiency is common among individuals with diabetes.

Keywords: Vitamin D, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus(DM) is a metabolic disease that either caused by absolute deficiency of insulin known as Type 1 DM or by relative deficiency of insulin along with insulin resistance known as Type 2 DM.^[1,2] Literature has shown that 380 million individuals will be affected by diabetes across the world by 2025. In India, diabetics are likely to be 109 million by year 2035.^[3,4] More than half the number of diabetics, according to International Diabetes Federation (2013), are in 3 countries with China having the maximum at 98.4 million,^[5] after which, India has the next highest at 65.1 million and USA follows it with 24.4 million diabetics. It affects nearly every organ system causing severe complications.

- a. Acute complications are diabetic ketoacidosis and non-ketotic hyperosmolar coma.

- b. Severe complications that last longer are cardiac disease, stroke, kidney diseases, foot ulcers and damaging eyes respectively.

Prevalence of diabetic neuropathy and diabetic nephropathy are 5-100% and 5-40%.^[6-11] For pathogenesis of diabetes, Vitamin D has led to extreme enthusiasm, having a protective outcome on β cell mass. The β cell apoptosis increase might be due to increase in any one of the following: excessive production of ROS, glucotoxicity or lipotoxicity are often present.^[12] Vitamin D prevents apoptosis of β cells and prevents apoptosis of β cell mass. Riachy et al has shown that 1,25(OH)₂ D₃ leading to human islets insulin preservation, expression of MHC-I, production of IL-6 and release of NO by increasing gradient of antiapoptotic protein in rat cells and also human islets for cytokines.^[13]

Mechanism of action of Vitamin D are^[14]

1. Directly, leading to induction of beta cell insulin secretion, through non-selective voltage dependent calcium channels by concentration raise of intracellular calcium.

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2. Endopeptidases are activated which depend on beta cell calcium leading to insulin converting from pro-insulin.

The current study was conducted to assess the serum vitamin D levels in newly detected type 2 diabetes mellitus comparing with the age and gender similar controls.

Aim of The Study

To study serum vitamin D levels in patients with recently diagnosed type 2 diabetes mellitus in comparison with controls of similar age and gender.

Objective

- To study the levels of serum Vitamin D levels in type 2 Diabetic in comparison to non-diabetic, healthy controls.
- To correlate Vitamin D levels with blood glucose status.

MATERIALS AND METHODS

Study Setting

The study was conducted on 100 patients either attending OPD or being admitted indoors in the department of Internal Medicine, TMMC & RC, TMU, MORADABAD, U.P.,INDIA meeting the inclusion criteria during the study Period of one year.

Sample Size

- 50 newly diagnosed diabetic patients.
- 50 age and gender matched controls.

Study Design: The present study was a cross-sectional observational study.

Inclusion Criteria

- Newly detected Type 2 diabetes mellitus (<6months)
- 30-65 years of age.

Diagnostic Criteria For Diabetes Mellitus

- Fasting blood glucose ≥ 126 mg/dl
- Glycated hemoglobin $\geq 6.5\%$
- Symptoms of diabetes mellitus-polyuria, polydipsia, fatigue, weight loss with (RBS > 200 mg/dl).

Exclusion Criteria

- Diagnosed cases of Type 2 diabetes mellitus on treatment for more than 6 months
- Known case of Cancer/ liver /renal dysfunction
- Medication that affect vitamin D metabolism/its absorption (Phenytoin, Rifampicin, Isoniazid, Ketoconazole, Carbamazepine, Phenobarbitone, valproic acid, Primidone, Prednisolone, Dexamethasone, Efavirenz, Atorvastatin, Orlistat, Cholestyramine, Estrogen, Thiazides, Antacids, Verapamil)
- Type 1 diabetes mellitus.
- Patients on vitamin D Supplementation.

Study Plan

- The data used for the study will be recorded from the history, examination and investigations of the patients.

- Range of expected values.

Status	25-(OH) vitamin D
Deficient	< 20 ng/ml
Insufficient	20-29 ng/ml
Sufficient	30-100 ng/ml
Potential toxicity	>100 ng/ml

Investigations

- Fasting blood sugar
- Post prandial blood sugar
- Glycated Hb levels
- Serum 25 (OH) cholecalciferol levels
- Blood Urea
- Serum Creatinine
- Urine Routine and Microscopy
- Fundoscopy
- ECG
- LFT
- X-ray Chest
- Lipid Profile
- CBC

Stastical Methods

- Pearson's Chi-Square test
- Measures of Dispersion
- Measures of Central Tendency
- Graphical representation of the data
- Shapiro-Wilk Test
- One-way ANOVA test
- Post-hoc Bonferroni test

RESULTS

A total of 100 patients were included in the study among which 50 patients were diabetic and 50 were age and gender matched healthy non-diabetic controls. There were 58.0% (58) males and 42.0% (42) females in the over-all study population. Among Diabetics, there were 54.0% (27) males and 46.0% (23) females and among Non-Diabetics, there were 62.0% (31) males and 38.0% (19) females.

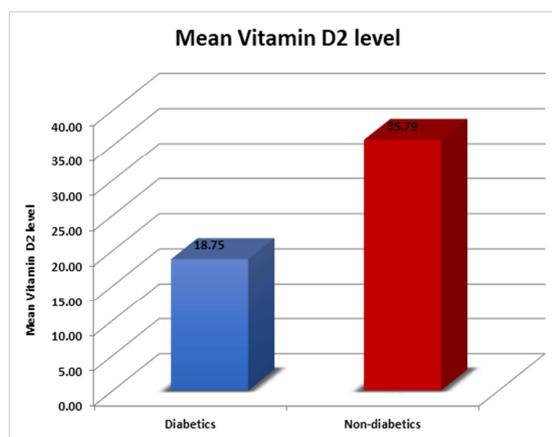


Figure 1: Comparison of mean Vitamin D2 level among Diabetics and Non-diabetics

Table 1: Distribution of the study population according to Gender, Marital status, Education and Occupation.

		Groups		p-value
		Diabetics	Non-diabetics	
Gender	Male	27 (54.0%)	31 (62.0%)	0.159
	Female	23 (46.0%)	19 (38.0%)	
	Age (in years)	49.08±9.08	45.24±8.92	0.035*
Marital status	Married	50 (100.0%)	50 (100.0%)	1.000
Education	Educated	30 (60.0%)	28 (56.0%)	0.685
	Uneducated	20 (40.0%)	22 (44.0%)	
Occupation	Businessman	5 (10.0%)	4 (8.0%)	0.001*
	Clerk	0 (0%)	1 (2.0%)	
	Driver	4 (8.0%)	3 (6.0%)	
	Farmer	5 (10.0%)	4 (8.0%)	
	Housewife	22 (44.0%)	17 (34.0%)	
	Labourer	1 (2.0%)	5 (10.0%)	
	Plumber	1 (2.0%)	5 (10.0%)	
	Retired	1 (2.0%)	2 (4.0%)	
	Shopkeeper	9 (18.0%)	6 (12.0%)	
	Teacher	2 (4.0%)	2 (4.0%)	
	Unemployed	0 (0%)	1 (2.0%)	

Table 2: Comparison of mean Vitamin D2 level among Diabetics and Non-diabetics

	Diabetics	Non-diabetics			
	Mean±S.D.	Mean±S.D.	Mean Difference	t-test value	p-value
Vitamin D2 level	18.75±9.93	35.79±15.46	-17.04	-6.559	< 0.001*

Table 3: Comparison of mean vitamin D 2 level between patients with different levels of fasting sugar

Fasting blood sugar level	Vitamin D2 level				F-value	p-value	Post-hoc comparisons
	Number	Mean	Std. Deviation				
1 < 100	43	36.97	16.38	14.713	0.001*	1>2,3>4>5	
2 101-125	7	28.57	1.51				
3 126-140	17	25.70	10.79				
4 141-199	19	17.87	6.78				
5 ≥ 200	14	13.19	7.46				

Table 4: Comparison of mean vitamin D 2 level between patients with different levels of HbA1c (%)

HbA1c (%)	Vitamin D2 level				F-value	p-value	Post-hoc comparisons
	Number	Mean	Std. Deviation				
1 < 6.5	51	35.45	15.50	13.579	0.001*	1>2>3>4	
2 6.5-7.0	5	25.05	5.40				
3 7.1-7.5	9	20.18	11.09				
4 ≥ 7.5	35	15.13	10.29				
Total	100	27.27	15.50				

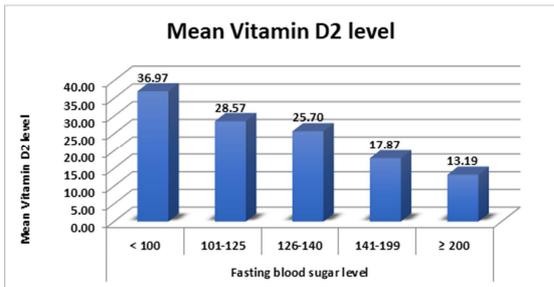


Figure 2: Comparison of mean vitamin D 2 level between patients with different levels of fasting sugar

Table 5: Distribution of Vitamin D deficiency among Diabetics and Non-diabetics

Vitamin D level	Groups	
	Diabetics	Non-diabetics
Optimal	0	18
	.0%	36.0%
Insufficient	7	7
	14.0%	14.0%
Deficient	43	25
	86.0%	50.0%
	100.0%	100.0%

Chi-square value = 16.931, p-value = 0.001*

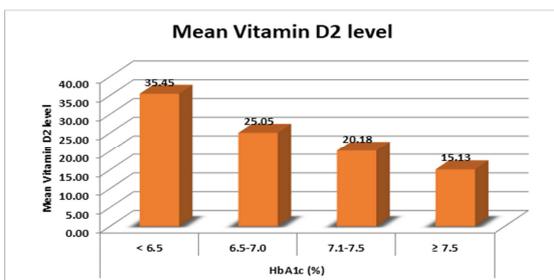


Figure 3: Comparison of mean vitamin D 2 level between patients with different levels of HbA1c(%)

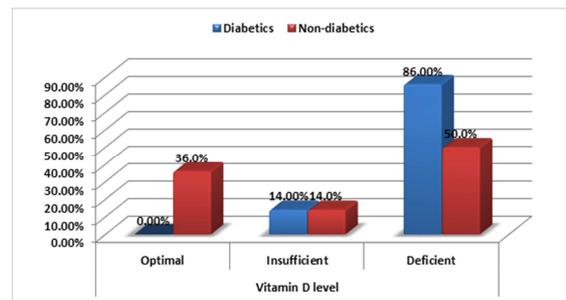


Figure 4: Distribution of Vitamin D deficiency among Diabetics and Non-diabetics

DISCUSSION

Vitamin D is a vitamin, which, is related to metabolism of the bone, being a secosteroid, which, is synthesized in skin by the sun's ultraviolet irradiation. Its extraskelatal effects are currently the focus of research efforts.^[15] Vitamin D has been related to immune system enhancing the tolerance of immune system,^[16] autoimmune diseases such as multiple sclerosis, rheumatoid arthritis and diabetes mellitus type 1 have been linked to vitamin D.^[17] Of late, the relation between vitamin D and type 2 diabetes mellitus and metabolic syndrome has been debated.^[18-21] It has been shown that Vitamin D was related to glucose metabolism and the development of diabetes mellitus type 2 and the metabolic syndrome.^[20,21]

The mean Age (in years) of the diabetics was 49.08±9.08 and Non- diabetics was 45.24±8.92. This was similar to the studies by Modi et al,²² the mean age of the study participants was 43.2 ± 13.6 years, Knekt et al,^[23] “the study population consisted of men and women aged 40-74 years and free of diabetes at baseline and Gagnon et al,^[24] the mean age of the subjects was 51 years”.

There were 58.0% males and 42.0% females in the over-all study population.

In the current study, the mean Vitamin D2 level was significantly higher among Non- Diabetics (35.79±15.46) than Diabetics (18.75±9.93). This was similar to the studies by Chaudhary et al,^[25] the mean serum vitamin D level among Type 2 DM cases was 19.09±5.34 ng/ml. There might be many pathways for the action of vitamin D on secretion of insulin.^[26] Vitamin D affects secretion of insulin and also its synthesis, which relates to b-cell calcium dependent endopeptidases, facilitating the process of converting of proinsulin to insulin.^[27] Calcium is not only required for exocytosis of insulin, but also has role in b-cell glycolysis, for controlling glucose level in blood.^[27] Resistance to insulin and inadequate insulin secretion are the characteristics of type 2 diabetes mellitus, although its aetiopathogenesis is not known. Hypovitaminosis D, because of depletion or relative vitamin D resistance, has been suspected to be a risk factor for glucose intolerance. The prolonged treatment with vitamin D for osteomalacia can lead to an increase in the secretion of insulin and improvement of the glucose tolerance.^[10,27]

Furthermore, increased bone mineral density in subjects with diabetes and without diabetes has been suggested to be associated with hyperinsulinemia. On the other hand, administration of a single high dose of vitamin D leads to increase in blood glucose levels in patients with diabetes.^[28] Among subjects without vitamin D deficiency, no benefits in glucose tolerance have been found with vitamin D supplementation.^[29] Lower levels of vitamin D, as per analysis of the literature, are mainly responsible for occurrence of type 2 DM.

Our study showed that the mean vitamin D2 levels were relatively more among subjects with fasting sugar level < 100 mg/dl (36.97±16.38) in comparison to subjects with 101-125 (28.57±1.51) and 126-140 mg/dl (25.70±10.79) which was significantly more than subjects with 141-199 mg/dl (17.87±6.78) which was significantly more than subjects with ≥ 200 mg/dl (13.19±7.46). The similar results were reported in the study by Kumar et al,^[27] lower vitamin D level was associated with higher fasting blood sugar levels (among patients with serum vitamin D level < 15 and 15-29.9, 88.9% and 90% had FBS level at >126 mg/dl, respectively, serum vitamin D level > 30, 41.7% had FBS level 100-126 and 58.3% had FBS level > 125 mg/dl). The mean vitamin D2 level was significantly more among subjects with post-prandial sugar level < 140 mg/dl sugar level in comparison to 141-199 which was significantly more in comparison to ≥ 200 mg/dl sugar level. Similar findings were reported by Scragg et al,^[30] 25 (OH) D was found to be significantly lower in individuals with newly diagnosed IGT or diabetes as compared to normal individuals and Kumar et al.^[27]

In current study, the mean vitamin D2 level was relatively higher among subjects with < 6.5% level (35.45±15.50) in comparison to 6.5-7.0% level (25.05±5.40) which was significantly more than 7.1-7.5% level (20.18±11.09) which was significantly more than ≥ 7.5% level (15.13±10.29).

A higher prevalence of deficiency of vitamin D, in our study, among diabetics (86.0%) in comparison to the people without diabetics (50.0%) was in accordance with Isaia et al,^[31] As compared with the normal population, Vitamin D deficiency was found to be more prevalent and severe in type 2 diabetic patients. “Kant et al.^[32] found high prevalence of Vitamin D deficiency in patients of Vitamin D deficiency in type 2 diabetic patients (91%) and Vitamin D deficiency was inversely related to glycemic control (HbA1c)”.

The findings in our study has therapeutic implications. The normal levels of vitamin D might help in controlling the glucose among type 2 diabetes patients. Also, among people with chances of developing type 2 diabetes mellitus, the optimum vitamin D levels in blood might lead to the retardation of the clinical development of diabetes type 2.

Macdonald et al.^[33] suggested that status of vitamin D may not be the marker, which can only be considered, for poor health, but it can also be an indicator of an individual's lifestyle of such as working indoor, which has restricted exposure to sunlight, lesser mobility, food habits, which, can have an affect on the long-term health. The usual office hours in our country are from 11 -7 pm in evening, the maximum exposure to sun and absorption occurs from 11 am-2 pm with UV index of 7-9, adequate for converting 7-dehydrocholesterol

to pre-vitamin D3. It is difficult to believe as summers in India are very hot, enforcing maximum people to stay indoor. As a result, low exposure to the sunlight attributes to very low vitamin D status in community

The reciprocating relation was approved by Liu et al.^[34] predicted 25 hydroxy Vitamin D score and incident type 2 DMs in the Framingham offspring study there was a reduced in the risk of type 2 DM with rise in the Vitamin D levels. Major weakness in the study design that it does not establish whether improved Vitamin D status is cause or consequence of type 2 diabetes mellitus.

Two randomized studies have reported better glycemic control in patients with T2D who either received vitamin D alone or yogurt drink fortified with Vitamin D while another study detailed decrease gradient levels of inflaming markers following supplementation of vitamin D in Type 2 diabetic patients.^[35]

Epidemiological studies disclosed that vitamin D deficiency alongwith type 2 diabetes carries higher risk cardiovascular mortality.^[36,37] Vitamin D receptors being found in tissue types all throughout the body, inclusive of vascular smooth muscle, the endothelium, and cardiomyocytes. In many observational studies, cardiometabolic risk factors such as endothelial dysfunction and diabetes were strongly associated with Vitamin D deficiency.^[38,39]

In the current study, there were lower vitamin D2 levels among type 2 diabetes compared to non-diabetics and glycosylated haemoglobin levels and 25(OH)D3 levels had an inverse relationship among diabetics, which, implied that level of 25(OH)D3 affects the control of glucose among type 2 DM subjects. However, there was a reciprocative relationship reported between vitamin D levels and glycosylated haemoglobin among total population and type 2 DM patients. This depicts that vitamin D is related with type 2 DM. Also, significantly more type diabetes 2 patients than the control population were having inadequacy of vitamin D

There are many limitations in the current study. It is an observational study and therefore no decision can be made for cause and effect relationship between deficiency of vitamin D and type 2 DM. In addition, serum vitamin D2 was chosen as a vitamin D deficiency marker, which, is recently used. But, vitamin D is in circulation in many forms in our blood and the most active form being 1,25 (OH)2D3. However, many studies are required utilizing better tools for determining deficiency of vitamin D deficiency among diabetics.

CONCLUSION

Vitamin-D deficiency/insufficiency is common among individuals with diabetes. Prospective studies are needed to evaluate whether supplementation of vitamin-D and correction of deficiency/insufficiency delays the development of diabetes.

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