

# A study of co-relation of vitamin D level and risk factors in a patient of diabetes mellitus

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## Abstract

**Background:** Vitamin D insufficiency has long been suspected as a risk factor for type 1 Diabetes based on animal and human observational studies. The study under discussion was undertaken to determine the correlation of Vitamin D level to the other risk factor of Diabetes, glycemic control, and duration of Diabetes and treatment of Diabetes. **Materials and Methods:** A study of co-relation of Vitamin D level and other risk factors of Diabetes in patients attending the outpatient department and indoor department of civil hospital, Ahmedabad was done using Vitamin D level in year 2017-2019. All the patients and the control subjects underwent a through clinical examination. The following investigations were done HbA1c, S cholesterol, S triglyceride estimation, Fasting blood sugar after an overnight fast, Post prandial blood sugar 2 hours after lunch and Vitamin D level estimation in all subjects. **Results:** Patient with well controlled Diabetes (HbA1c < 7) had a mean Vitamin D level 28.48(ng/ml) which was on higher side as compared to patient with poorly controlled Diabetes. In control group one subject had deficient Vitamin D, 11 having insufficient and 18 had adequate level of Vitamin D. Hypovitaminosis D is 4.12 times more common in diabetic patient as compared to age and gender matched control. In our study 73% diabetic patient had insufficient Vitamin D level as compared to 40% in control group. In our study mean Vitamin D level in diabetic patients was 24.25(ng/ml) and in control group 32.21(ng/ml). **Conclusion:** Vitamin D deficiency appears to be detrimental to beta-cell function, and leads to glucose intolerance in animal models and humans, consequently type 2 Diabetes. In our study we found that Vitamin D co-related with other risk factors of Diabetes. Vitamin D deficiency was common in patients with Diabetes Mellitus and deficiency was much more in patients having more than one risk factor for Diabetes. Vitamin D deficiency is associated with poor Glycemic control.

**Key Words:** Diabetes mellitus, Vitamin D deficiency, HbA1C, BMI, Cholesterol

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## INTRODUCTION

Diabetes is now emerging as a world wide epidemic. Type 2 Diabetes mellitus is the predominant form of Diabetes worldwide, accounting for 90% of cases globally. Although our current methods of treating Type 2

Diabetes Mellitus and its complications have improved, prevention of the disease is preferable. Indeed, epidemiologic data suggest that 9 out of 10 cases of type 2 Diabetes could be attributed to habits and forms of modifiable behavior. Recent evidence suggests that Vitamin D and calcium have also been suspected as modifiers of Diabetes risk. Vitamin D insufficiency has long been suspected as a risk factor for type 1 Diabetes based on animal and human observational studies. More recently, there is accumulating evidence to suggest that altered Vitamin D and calcium homeostasis may also play a role in the development of Type 2 Diabetes Mellitus. The study under discussion was undertaken to determine the correlation of Vitamin D level to the other risk factor of Diabetes, glycemic control, duration of Diabetes and treatment of Diabetes.

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## MATERIAL AND METHODS

A study of co-relation of Vitamin D level and other risk factors of Diabetes in patients attending the outpatient department and indoor department of civil hospital, Ahmedabad was done using Vitamin D level in year 2017-2019. This is a descriptive case control study with total number of 60 patients and 30 controls.

### INCLUSION CRITERIA:

- Age : 40-75 years
- Diabetes Mellitus Type II diagnosed as per WHO criteria
- Diabetic patients either on oral treatment or insulin therapy

### EXCLUSION CRITERIA

- Age > 75 years
- S Creatinine > 1.4 mg/dl
- Bl. Urea > 50 mg/dl
- Parathyroid disorder
- Malignancy
- Chronic liver or kidney disease

### CONTROL

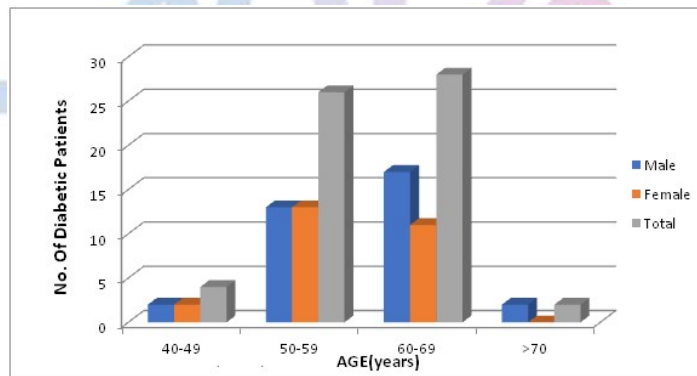
A random sample of 30 patients 19 male and 11 female was selected.

### The criteria for inclusion were:

- Age and Sex were comparable to the study group.
- FBS < 126 mg/dl, PPBS < 200 mg/dl, Glycosylated Haemoglobin (HbA1c) < 6.5%
- S .cholesterol < 240 mg/dl, S. Triglyceride < 150 mg/dl

All the patients and the control subjects underwent a thorough clinical examination with special emphasis on Symptoms: Body ache, Depression, Bone pain, weakness, Tingling and numbness in feet and hands, Burning sensation in hands and feet, Blurring of vision, Polyuria/Polydypsia. Duration of Diabetes. Treatment received : OHA and/or insulin. General Examination was done specially looking for Height, Weight, Body Mass Index, features of hyperlipidemia, Blood Pressure. Cardiovascular, respiratory and Central Nervous system examination was done to exclude any clinical abnormality. The following investigations were done HbA1c, S cholesterol and S triglyceride estimation, Fasting blood sugar after an overnight fast, Post prandial blood sugar 2 hours after lunch. Vitamin D level estimation in all subjects.

## OBSERVATION AND RESULTS



Age and sex wise distribution of Diabetic cases

**Table 1:** Mean Age in various study groups of diabetic patients

Study Group	Mean Age in Years
Vinereanu <i>et al</i> <sup>1</sup> (n=70)	57
Aldo Study <sup>2</sup> (n=49)	59
Kyong <i>et al</i> <sup>3</sup> (n=103)	60
Donbouchi <i>et al</i> <sup>4</sup> (n=100)	51.3
Our Study(n=60)	57.17

**Table 2:** Relationship between duration of Diabetes and Vitamin D level

Duration of Diabetes (years)	No. Of Patients	Mean Vitamin D Level (ng/ml)
<5	22	25.99
6-10	27	22.27
>10	11	25.61

**Table 3:** Gender Distribution and Vitamin D level:

Gender	Number of Diabetic Patients	Mean Vitamin D Level (ng/ml)
Male	34	24.93
Female	26	23.35

**Table 4:** BMI distribution in Diabetic patient and control:

BMI (kg/m <sup>2</sup> )	Diabetic		Control	
	Male	Female	Male	Female
Healthy (20-24.9)	12	10	12	9
Pre-Obese (25-29.9)	12	9	7	2
Obese (>30)	10	7	0	0

**Table 5:** Co-relation of BMI and Vitamin D Level in Diabetic Patients

BMI (kg/m <sup>2</sup> )	No. Of Diabetic Patients	Mean Vitamin D Level (ng/ml)
Healthy(20-24.9)	22	28.71
Pre-Obese(25-29.9)	21	22.66
Obese(>30)	17	20.41

**Table 6:** ANOVA test (analysis of variance) for correlation between BMI and mean Vitamin D level

BMI(kg/m <sup>2</sup> )	Healthy (BMI 20-24.9)	Pre-obese (BMI 25- 29.9)	Obese (BMI > 30)
Mean	M1=28.71	M2=22.66	M3=20.41
Standard deviation	SD1=7.11	SD2=9.68	SD3=9.63
Sample size	N1=22	N2=21	N3=17

F value of ANOVA test is 4.78 and corresponding p value is 0.012 (<0.05) suggest significant difference of Vitamin D level in obese, pre-obese and healthy diabetic patient and shows inverse correlation between BMI and Vitamin D level. This is probably explained by as Vitamin D is fat soluble vitamin and stored in adipose tissue. Blum *et al* showed that the concentration of Vitamin D in fat is approximately ten times higher than in the blood stream. In patient of obesity it becomes difficult for body to retrieve stored vitamin because it is less bio-available when it imbedded in deeper adipose tissue. Also Vitamin D metabolizing enzyme has been demonstrated in human adipose tissue, the expression level of 25-hydroxy cyp2j2 and 1 $\alpha$  hydroxylase cyp27b1 is decreased in adipose tissue of obese subject.

**Table 7:** Comparison of BMI in various Study Groups

Study Groups	Mean BMI(kg/m <sup>2</sup> )	
	Diabetes	Control
Cigolini <i>et al</i> <sup>6</sup> (n=459)	29	26
JA Sugden <i>et al</i> (n=17)	31.7	28
Kyong <i>et al</i> <sup>3</sup> (n=103)	25.6	23.4
Donbouchi <i>et al</i> <sup>4</sup> (n=100)	26.1	25
M Usitupa <i>et al</i> <sup>7</sup> (n=70)	28.7	26.4
Present Study (n=90)	27.14	22.77

P=0.0049

**Table 8:** Comparison of HbA1c and Vitamin D in Diabetic Patients.

HbA1c(%)	No. of Diabetic Patients	Mean Vitamin D level (ng/ml)
6 - 6.9	20	28.48
7 - 8.9	31	21.95
>9	9	22.71

Study done by pittas *et al* and Schwalfenberg *et al* shows inverse co-relation between HbA1c and Vitamin D level. In our study, mean value of HbA1C in diabetic was 7.64 as compared to 5.56 of control group. Mean value of HbA1C in study carried out by Kyong *et al* was 7.62 as compared to 5.3 of control group. This value is almost similar to our finding. Mean value of HbA1c in study carried out by JA Sugden *et al* was 7.5 as compared to 5.4 of control group. Mean value of HbA1C in study by Vinereanu *et al*, and Mohammmd *et al* was 8 which were higher than control group.

**Table 9:** Mean HbA1C level according to Vitamin D levels

Vitamin D status	No of patients	Mean HBA1c(%)
Hypovitaminosis D	44	7.71
Normal	16	7.4

**Table 10:** Comparison between Vitamin D level and HBA1C in various study groups

Study Group	Mean HBA1C in Diabetes patients	
	Normal Vitamin D	Hypovitaminosis D
Cigolini <i>et al</i> <sup>6</sup> (n=454)	7.0	7.4
Krugs' <i>et al</i> <sup>8</sup> (n=123)	7.1	8.1
Our study (n=60)	7.4	7.7

In our study mean HbA1c in patients with hypovitaminosis D was 7.7 which was higher than HbA1c of 7.4 in patient having Vitamin D in normal range. In study done by Krugs' *et al* mean HbA1c was 7.1 in patients with normal Vitamin D level and mean HbA1c of 8.1 in patients with hypovitaminosis D.

**Table 11:** Comparison between Mode of Treatment and Vitamin D level

Treatment	No. of Diabetic Patient	Mean Vitamin D level(ng/ml)
OHA	34	25.32
Insulin (30\70)	17	22.3
Basal Bolus	9	23.88

**Table 12:** Age distribution and Vitamin D level

Age (years)	No. of Diabetic Patient	Mean Vitamin D level (ng/ml)
40-49	4	26.4
50-59	26	26.42
>60	30	22.00

Inverse relationship between age of patient and Vitamin D level is demonstrated in the study. Patient with age < 60 having mean Vitamin D level of 26.4 much higher than mean Vitamin D level of 22 in patient with age more than 60. This could be explained by decreased capacity in old people to produce Vitamin D, decreased capacity of intestine to absorb dietary Vitamin D.<sup>9,10</sup>

**Table 13:** Co-relation of Hypertension and Vitamin D level in Diabetic Patients

Hypertension	No. of Diabetic Patient	Mean Vitamin D level (ng/ml)
Present	25	22.756
Absent	35	25.18

In our study 25 patients were hypertensive having mean Vitamin D level of 22.75 as compared to mean Vitamin D level of 25.18 in non-hypertensive diabetic patient. Thus Vitamin D level having inverse correlation with blood pressure. Many studies have been conducted in order to establish a relationship between hypertension and Vitamin D levels. A recent review article demonstrates that eight out of ten observational studies and three randomized controlled trials strongly support an inverse relation between Vitamin D level and blood pressure.<sup>11</sup> 1.25-OH-D decreases the production of renin in the kidneys, as well as decreasing the inflammatory factors involved in chronic heart disease, including C-reactive protein and IL-10.<sup>12</sup> This modulation occurs by way of suppressing renin gene expression via VDR, and low calcitriol concentrations may result in an up-regulation of the renin-angiotensin system.<sup>13-15</sup>

**Table 14:** Co-relation of cholesterol and Vitamin D level in diabetic patients

Cholesterol (mg/l)	No. of diabetic patient	Mean Vitamin D level (ng/ml)
<200	30	24.81
200-240	24	25.18
>240	6	17.33

In our study mean Vitamin D is significantly lower 17.33 in patients with cholesterol > 240, as compared to mean Vitamin D levels of 25.18 in patients having cholesterol level between 200-240 and mean Vitamin D level of 24.81 in patients having cholesterol level <200. Mean cholesterol level of our 60 diabetic patient was 202.

**Table 15:** Co-relation of triglyceride and Vitamin D level in diabetic patients

Triglyceride (mg/l)	No. of diabetic patient	Mean Vitamin D level (ng/ml)
<150	27	24.11
151-199	15	28.30
>200	18	21.01

Mean triglyceride level in 60 diabetic patient was 174. Out of 60, 27 patient had triglyceride level < 150 with mean Vitamin D level of 24.11. While 15 patients had triglyceride level between 151-199 with mean Vitamin D level of 28.33, and 18 patients had triglyceride level of >200 with mean Vitamin D level of 21.01. No linear co-relation was established in our study between Triglyceride and Vitamin D level.

**Table 16:** Prevalence of Vitamin D deficiency in diabetic patient

Vitamin D level(ng/ml)	Case (n =60)	Control(n=30)
Deficiency (<10)	5 (8.3%)	1 (3.3%)
Insufficiency(10-30)	39 (65%)	11 (36.7%)
Adequate(30-100)	16 (26.7%)	18 (60%)
High(>100)	0	0

In our study 5 patients were Vitamin D deficient (<10), 39 patient had insufficient Vitamin D level (10-30), and 16 patient had Vitamin D level of normal range. Thus total 44 out of 60 [73.3%] diabetic patients had hypovitaminosis D. In control group 1 subject had deficient Vitamin D, 11 having insufficient and 18 had adequate level of Vitamin D. Thus 12 control out of 30 [40%] had hypovitaminosis D.

**Table 17:** Calculation of odds ratio of hypovitaminosis D in diabetic patients

Vitamin D status	case	Control
Hypovitaminosis D	44	12
Normal Vitamin D	16	18
<b>Total</b>	<b>60</b>	<b>30</b>

Odd ratio=4.12, suggest that hypovitaminosis D is 4.12 times more common in diabetic patient as compared to age and gender matched control.

**Table 18:** Prevalence of hypovitaminosis D in various study groups

Study groups	Case	Control
Barissova Am <i>et al</i> (n 90) <sup>16</sup>	70%	46%
Subramanian <i>et al</i> (n 92) <sup>17</sup>	84%	48%
Cigolini <i>et al</i> (n 459) <sup>6</sup>	60%	42%
Krug's <i>et al</i> (n 123) <sup>8</sup>	91%	56%
Daga <i>et al</i> (n 72) <sup>18</sup>	91%	58.5%
Our Study (n 90)	73.3%	40%

In our study 73% diabetic patient had insufficient Vitamin D level as compared to 40% in control group, which is comparable to study done by Barissova Am *et al* 70% in case and 46% in control group. In study done by krugs *et al* and Daga *et al* 91% diabetic patient were having hypovitaminosis D which was more than control group.

**Table 19:** Mean Vitamin D level in various study groups

Various study groups	Case	Control
Ja sudgen <i>et al</i> (n17)	16.4	31.4
Kostoglou <i>et al</i> (n120) <sup>19</sup>	19.2	25.4
Scragg <i>et al</i> <sup>20</sup>	18	26
Cigolini <i>et al</i> (n459) <sup>6</sup>	19.7	24
Subramanian <i>et al</i> (n92) <sup>17</sup>	11	15.5
Daga <i>et al</i> (n72) <sup>18</sup>	7.88	16.64
Our study (n90)	24.25	32.21

In our study mean Vitamin D level in diabetic patients was 24.25 and in control group 32.21. In study done by Ja Sudgen *et al* mean Vitamin D level in diabetic patients was 16.6 which was lower than our study, but in control group level was comparable to our study.



**Table 20:** Z test for correlation between Vitamin D level and Diabetes

	Case	Control
Mean Vitamin D	M1= 24.25	M2=32.9
Standard deviation	SD2=9.35	SD2=15.74
Sample size	N1=60	N2=30

Z test value 2.77, and corresponding p value <0.005. This shows relation between Diabetes and hypovitaminosis D although not causal but a definite and important association.

The correlation further warrants larger prospective studies addressing hypovitaminosis D and Diabetes association.

## DISCUSSION

The mean age of diabetic patients was 58.6 years and controls was 57.4 years. The male to female ratio was 1.33:1 in diabetic group and 1.31: 1 in controls. 22 patients out of 60 had Diabetes duration of 5 years. 27 patients had duration of Diabetes between 6 to 10 years, while 11 patients had Diabetes duration more than 10 years. Mean Vitamin D of patients with Diabetes duration between 6 to 10 years was 22.27(ng/ml), of < 5 year was 25.88(ng/ml) and patient with Diabetes duration > 10 was 25.61(ng/ml). Male had mean Vitamin D level of 24.93 and female patients had 23.95(ng/ml). 38 patients were in over weight group and only 9 controls were in over weight group. Mean BMI of diabetic patients was 27.14(kg/m<sup>2</sup>) as compared to 22.77(kg/m<sup>2</sup>) of control group. Diabetic patient with BMI<25 had mean Vitamin D level of 28.71(ng/ml) whereas mean Vitamin D level was 22.66(ng/ml) in pre-obese and 20.41(ng/ml) in obese diabetic patients. Patient with well controlled Diabetes (HbA1c < 7) had a mean Vitamin D level 28.48(ng/ml) which was on higher side as compared to patient with poorly controlled Diabetes. In our study, mean value of HbA1C in diabetic was 7.64 as compared to 5.56 of control group. In our study mean HbA1c in patients with hypovitaminosis D was 7.7 which was higher than HbA1c of 7.4 in patient having Vitamin D in normal range. Patient on OHA having Vitamin D level on higher side as compared to patient on insulin. Hypertensive patients had mean Vitamin D level of 22.75(ng/ml) as compared to mean Vitamin D level of 25.18(ng/ml) in non-hypertensive diabetic patient. Mean Vitamin D is significantly lower 17.33(ng/ml) in patients with cholesterol > 240(mg/l), as compared to mean Vitamin D levels of 25.18(ng/ml) in patients having cholesterol level between 200-240(mg/l) and mean Vitamin D level of 24.81(ng/ml) in patients having cholesterol level <200(mg/l). Mean cholesterol level of our 60 diabetic patient was 202.63(mg/l). Mean triglyceride level in 60 diabetic patient was 174(mg/l). 5 patients were Vitamin D deficient (<10), 39 patient had insufficient Vitamin D level (10-30), and 16 patient had Vitamin D level of normal range. In control group 1 subject had deficient Vitamin D, 11 having insufficient and 18 had adequate level of Vitamin D. Hypovitaminosis D is 4.12 times

more common in diabetic patient as compared to age and gender matched control. In our study 73% diabetic patient had insufficient Vitamin D level as compared to 40% in control group. In our study mean Vitamin D level in diabetic patients was 24.25(ng/ml) and in control group 32.21(ng/ml).

## CONCLUSION

Vitamin D is a hormone of multiple importance to the body and its role in various disease processes is being appreciated. The present study evaluated the co-relation between Vitamin D level and other risk factors of Diabetes Mellitus. Vitamin D deficiency appears to be detrimental to beta-cell function, and leads to glucose intolerance in animal models and humans, consequently type 2 Diabetes. Vitamin D and its related metabolic and immune pathways may be involved in the pathogenesis of Diabetes at environmental and genetic levels. Studies on Vitamin D supplementation on prevention of Diabetes are inconclusive. In our study we found that Vitamin D co-related with other risk factors of Diabetes. Vitamin D deficiency was common in patients with Diabetes Mellitus and deficiency was much more in patients having more than one risk factor for Diabetes. Vitamin D deficiency is associated with poor Glycemic control. Further prospective study are required to ascertain the role of Vitamin D deficiency in pathogenesis of Diabetes Mellitus.

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