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**COMPARISON OF VIT D LEVELS AND HBA1C IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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**ABSTRACT**

**Introduction:** Diabetes mellitus is a prevalent endocrine disorder associated with numerous complications. Vit D maintains the levels of calcium in the body and its deficiency leads to inhibition of insulin synthesis seen in diabetes mellitus.

**Aim:** The aim of the current study was to compare and correlate the levels of Vit D with FBS, PPBS and HbA1c.

**Material & Methods:** A total of 100 participants divided into Group-I normal patients and Group II patients with diabetes mellitus. Patients >18yrs with type II diabetes mellitus without complications were included and patients with other types of diabetes, on Vit D supplement, bisphosphonate, pregnant women were excluded from the study. 5ml of venous sample was obtained and serum was used to analyze FBS, PPBS, HbA1c, vitamin D were measured and the values were compared and statistically analyzed using unpaired t test and Pearson coefficient correlation. A p value of 0.05 was considered to be statistically significant.

**Results:** The participants of the study were predominantly females (63) and in the age group of 18-60 years. The values of FBS, PPBS, HbA1c and Vit D were compared among Group I and Group II and were statistically significant. 36 patients of Group II had Vit D deficiency, 9 patients had insufficient Vit D and only 5 patients had sufficient Vit D. Vit D showed an inverse relationship with HbA1c more strongly than other parameters.

**Conclusion:** An inverse relationship between serum Vit D level and HbA1c, FBS and PPBS. Vit D supplementation in patients with T2DM is associated with improved glycemic control.

**Key words:** Diabetes mellitus, FBS, HbA1c, PPBS, Vit D

## **Introduction**

Diabetes mellitus DM is an exceedingly prevalent major public health issue of current times. It is an endocrine disorder which is causing a global impact both economically and socially.[1] Diabetes results from defective or deficient Insulin in the body resulting in hyperglycemia which leads to numerous complications like neuropathy, nephropathy and retinopathy. There are around 40.9 million diabetics in India which is expected to rise to 66.9 million by 2025 as estimated by The International Diabetes Federation (IDF).[2] Addressing management of diabetes is a herculean task due to lack of awareness, limited facilities, expensive treatment, lack of control of hyperglycemia, prevalence in both urban and rural areas and diabetic complications. [3] Vitamin D is a fat soluble vitamin which plays a role in maintaining calcium levels in the body and bone. The physiologically active forms are Vit D<sub>2</sub> (ergocalciferol) and Vit D<sub>3</sub> (cholecalciferol) which are produced through exposure to sunlight and the main circulating form is 25-hydroxyvitamin D 25OH D<sub>3</sub> which is converted to 1,25 dihydroxyvitamin D in the kidneys. Vitamin D deficiency has been linked to infections, fracture, obesity, cardiovascular disease as well as diabetes mellitus. [4] Low levels of Vitamin D causes  $\beta$  cell dysfunction in the pancreas which leads to inhibition of insulin synthesis and secretion with insulin resistance associated with Diabetes mellitus.[5] It is also shown that Vit D deficiency raises the inflammatory markers thereby increasing inflammation which is known to cause impaired glycemic control demonstrating anti- diabetic properties of Vit D. [6]

Thus the aim of the present study was to compare and correlate the levels of Vit D with FBS, PPBS and HbA1c.

## **Material and Method**

The present study was a cross sectional prospective study conducted in a private clinical set up for over a period of 1 year from 2022-2023. This study was in accordance with local and global ethical norms. The total number of participants in the present study was 100 and was divided into two groups; Group I Normal patients and Group II Patients with Type 2 Diabetes mellitus (T2DM). Patients visiting the OPD with diagnosis of T2DM were randomly selected for the study based on inclusion and exclusion criteria.

### Inclusion and exclusion criteria

All patients >18yrs old with an established diagnosis of T2DM without diabetic complications were included in the present study. Patients with other types of diabetes, patients on oral supplements of Vit D, bisphosphonates or others, pregnant females, patients with hyperthyroidism, hyperparathyroidism or kidney diseases were excluded from the study.

### Sample collection and testing

The procedure was explained to all patients and written consent was obtained from selected patients. 5ml of venous blood sample was collected from patients under strict aseptic conditions. Sodium fluoride serum samples were used to measure FBS and PPBS; EDTA serum sample was used to measure HbA1c and Vitamin D. The blood samples were centrifuged at low speed and serum samples were collected, stored and used for assessment. FBS and PPBS were assessed using Transasia (fully automatic analyser); HbA1c was assessed using BIORAD D10 HbA1c analyser; and Vitamin D was measured using ECLIA assay.

In the study serum sample level of Vit D <20ng/ml was considered as deficiency, 20-30ng/ml was considered insufficiency and >30ng/ml was considered as sufficiency.

The values obtained were entered and stored in excel sheet and submitted for statistical analysis. Unpaired t test was applied to compare the values of FBS, PPBS, HBA1c and Vitamin D in Group I and Group II. Pearson coefficient correlation was used to compare levels of Vit D with FBS, PPBS and HBA1c. A p value of 0.05 was considered to be statistically significant.

### Results

In the present study there were 100 participants of which 50 were in Group I (Normal subjects) and 50 were in Group II (Patients with T2DM). There were 37 males and 63 females in the present study. The mean age for the study participants was 54.55 and the standard deviation was 5.91. (Table 1)

Characteristic of the study			
	Group I (n=50)	Group II (n=50)	P value
Age	34.5±13.4	54.55±5.91	0.01
Gender	Males 19	Males 18	0.01
	Females 32	Females 31	

Table 1 showing distribution of age and gender in Group I and Group II

In Group I the mean and standard deviation of FBS was 95.38±8.7; PPBS was 121.48±47.91; HbA1c was 5.52±0.58 and Vit D 36.45±13.23. In Group II the mean and standard deviation of FBS was 139.48 ±65.7; PPBS was 253.72±48.56; HbA1c was 9.52±1.03 and Vit D was 13.65±5.20.

Unpaired t test showed that the difference in FBS, PPBS and HbA1c in Group I and Group II were statistically significant with a p value of 0.01. Whereas unpaired t test comparing levels of Vit D in Group I and Group II was very significant with a p value of 0.001. (Table 2)

	<b>FBS (mg/dl)</b> ± S.D	<b>PPBS (mg/dl)</b> ± S.D	<b>HbA1c (%)</b> ± S.D	<b>Vit D ng/ml</b> ± S.D
Normal patients Group I (N=50)	95.38 ±8.71	121.48 ±47.91	5.52 ±0.58	36.45 ±13.23
Patients with Diabetes mellitus Group II (N=50)	139.48 ±65.73	253.72 ±48.56	9.52 ±1.03	13.65 ±5.20
P value	<b>0.01*</b>	<b>0.01*</b>	<b>0.01*</b>	<b>0.001**</b>

\* Significant \*\* very significant

Table 2: showing unpaired t test comparing values of FBS, PPBS, HbA1c and VitD in Group I and Group II.

In the study it was noted that Vit D was deficient in 36 participants, insufficient in 9 participants and sufficient only in 5 participants. In patients with < 7% HbA1c 5 showed deficiency of Vit D, 3 had insufficient Vit D and only 2 had sufficient Vit D. In patients with > 7% HbA1c 31 showed deficiency of Vit D, 6 showed insufficient Vit D and only 3 showed sufficient Vit D. (Table 3) It was noted that Vit D levels were generally lower in patients where HbA1c was >7%. (Chart 1)

<b>Vitamin D</b>	<b>HbA1c &lt;7%</b>	<b>HbA1c &gt;7%</b>	<b>Total</b>
<20ng/ml Deficient	5	31	36
20-30ng/ml Insufficient	3	6	9
>30ng/ml Sufficient	2	3	5

Table-3: showing levels of Vit D in HbA1c <7% and HbA1c >7%

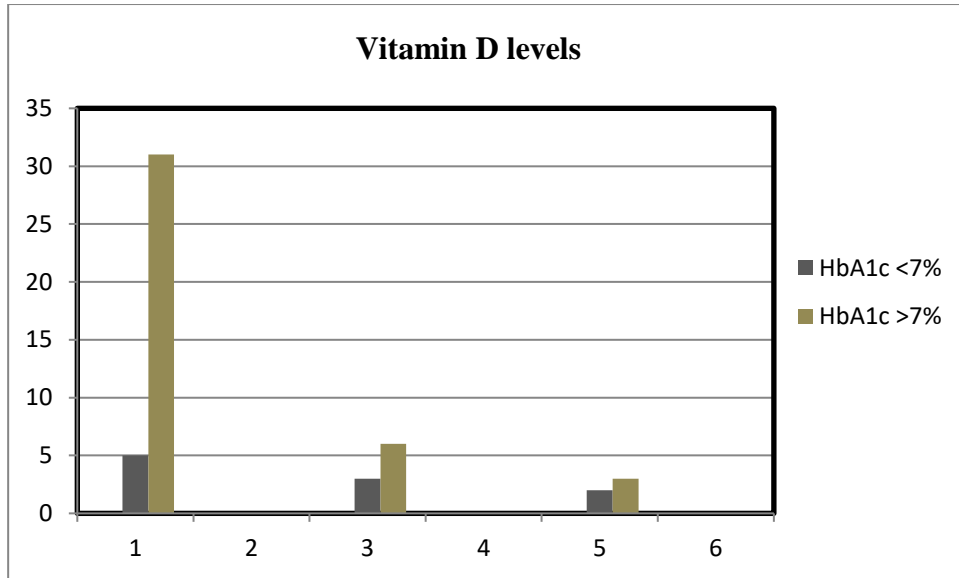


Chart 1 Bar Graph showing relationship of Vit D with HbA1c levels

Pearson correlation coefficient was used to compare Vit D with FBS, PPBS and HbA1c and we noted r value was negative for all three parameters which signify an inverse correlation of Vit D with other parameters. The correlation of Vit D with FBS showed r value of -0.0106; with PPBS r value was -0.1183 and HbA1c r value was -0.1289. The inverse relationship of Vit D and HbA1c showed high correlation than compared to other parameters. (Chart 2)

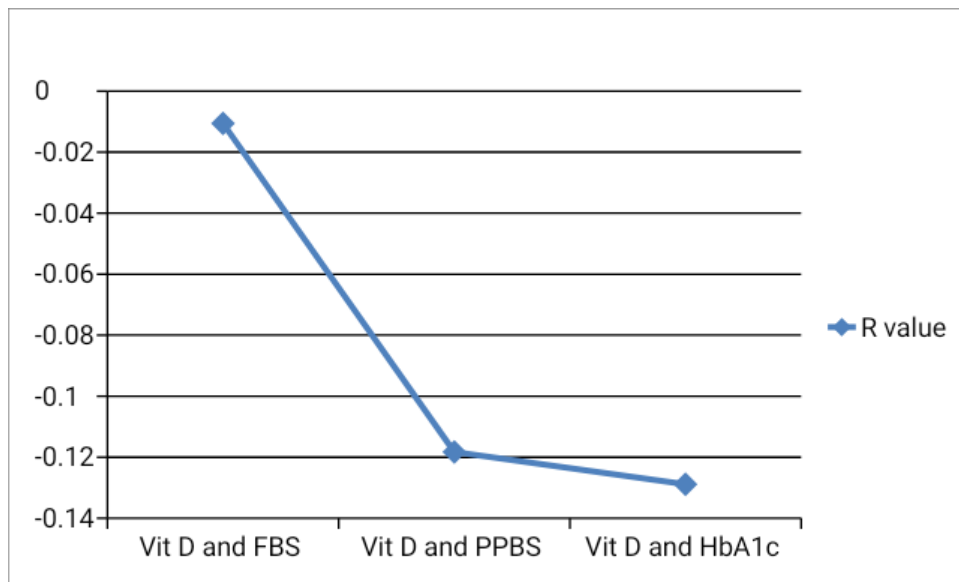


Chart 2 Line graph showing negative Correlation of Vit D with FBS, PPBS and HbA1c

## Discussion

Vitamin D deficiency is a highly prevalent condition but is by far still underdiagnosed and undertreated nutritional deficiency unrelated to age, gender and geography. There has recently been a vested interest in Vitamin D as it plays a crucial role in many diseases from cardiovascular to cancer to diabetes. Vit D deficiency is associated with increased risk of T2DM and supplementation of Vit D reduces risk of development and progression of T2DM as well as complications like diabetic retinopathy, nephropathy and peripheral neuropathy. Vitamin D levels can be assessed from serum levels of D3.[7] Diabetes mellitus has shown increase in its incidence worldwide and the complications and management has been very challenging. There is significant risk of blindness, heart attack, stroke, amputation, kidney failure and premature mortality. [8]

Hence there is constant look out for treatment modalities which may decrease the incidence of occurrence and complication.

The participants of the study were in the age range of 32-73 years and showed more number of females than males in both Group I and Group II and was found to be statistically significant. Higher prevalence of females noted in the study was similar to findings of Mihardja 2014 and Azlin 2019 who suggested that diabetes affects women more commonly than men due to their higher fat deposits in the body.[9,10] It is suggested that prevalence of diabetes increases with increase in age and the peak is noted at 55-64 years.[11] FBS and PPBS are used commonly to detect short term blood glucose whereas HbA1c is used to detect long term blood glucose levels. The HbA1c test is easy and is widely used to monitor T2DM and is accepted as diagnostic criteria for T2DM by WHO in 2011. [12]

In the present study we found that Vit D deficiency was seen in patients with increased HbA1c levels. As the level of HbA1c increased there was a corresponding decrease in Vit D level. This finding of the study was consistent with previous studies of Niyati Mehta 2016. [13] The correlation of Vit D in the present study represented an inverse relationship with PPBS. This correlation of the present study was similar to the findings of Pitta 2010, Neeta 2020 who also found similar inverse correlation of Vit D and PPBS. [14,15]

Wang et al in their case-control study, found an inverse relationship between serum levels of Vit D and impaired fasting glucose; they explained this negative relationship to be due to altering lipid metabolism.[16] In the largest cross-sectional study to date from the National Health and Nutrition Examination Survey (NHANES) data, serum Vit D3 concentration was inversely associated with diabetes prevalence in a dose-dependent pattern in non-Hispanic whites whereas there was no such correlation among non-Hispanic blacks. This lack of correlation is explained due to difference in Vit D, calcium and PTH homeostasis among whites and blacks. Priyaranjan 2023 in their comparative

study noted that deficiency of Vit D was significantly associated with retinopathy and neuropathy but not nephropathy. [17]

There have been numerous advances in the therapies to treat diabetes recently along with new insights for prevention and management of T2DM. Of late Vit D has gained substantial importance in the outcome of many diseases including diabetes due to its anti-diabetic property.

However there is conflicting evidence on the role of Vit D in diabetes and thereby raising concerns on the necessity to supplement Vit D in diabetic patients.

The findings of our study indicate that low levels of Vit D is associated with T2DM and is like minded with observations from cross sectional cohort studies of Matilla 2007, Forouhi 2008, Wang 2020, Ahmed 2020. [18-20] But findings of Zhao 2013 found no association between Vit D intake and T2DM and thus contrasted with our findings. [21]

Overall we observed that serum Vit D levels were lesser in group where HbA1c was  $> 7\%$  than when compared to group where HbA1c was  $< 7\%$ . This finding of ours is similar to the findings of Mehmet 2023.[12] Meta-analysis conducted by Mohammad Ashraf 2023 has pointed out that there were significantly reduced levels of FBS noted in patients with long term supplementation of Vit D. It was also found that high dose of Vit D supplementation is necessary for ideal results. The decrease in blood glucose is obtained when Vit D is used as a supplement along with other diabetic drugs than when used only. [22] Meta analysis by Mohammad Ashraf and Chunhua Wu suggest that Vit D supplementation was associated with decrease in FBS and HbA1c. [23]

The greatest reduction in blood glucose levels in T2DM following Vit D supplementation was observed among Asians and Europeans whereas other continent did not show such a difference. This heterogeneous response is due to Vit D binding protein polymorphism which shows increased susceptibility of T2DM in Asians than Caucasians. [24]

Mitri et al examining the effect of vitamin D supplementation in adults at high risk of diabetes concluded that short-term supplementation with cholecalciferol did not have a significant effect on HbA1c. [25] Supplementation of Vit D<sub>3</sub> has been done in various doses from 400-800 IU daily to 60,000IU weekly and the calculation of the dose is dependent on the gender, age, ethnic background, BMI, Life style etc. However the recommended supplementation of 40ng/ml or 60ng/ml is preferred to achieve a normal serum Vit D level and should never be more than 60ng/ml. [26] Mohammad Ashraf 2023 suggested that Vit D supplementation reduces FBS and HbA1c in patients with vitamin deficiency more than that in Vit D insufficiency and sufficiency patients. [23]

Limitations of the present study is that it was a single center study, and is just a cross sectional study and not a randomized clinical trial. Higher sample size will strengthen the statistical analysis.

## Conclusion

In the present study it was noted that there was an inverse relationship between Serum Vit D and HbA1c, FBS and PPBS. Vit D deficiency might be considered as a risk factor for patients with T2DM with high HbA1c levels. Vit D supplementation is administered to patients with T2DM and is seen to be associated with improved glycemic control.

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