

Vitamin D Status in Relation to Glycaemic Management in Type 2 Diabetes Mellitus**Tushar Singh¹, Kashish², Shivani Bansal³, Ashok Kumar⁴, Lalit Kumar Tyagi⁵**^{1,2}Junior Resident, Department of General Medicine, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad³Professor, Department of General Medicine, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad⁴Professor and Head of Department, Department of General Medicine, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad⁵Senior Resident, Department of General Medicine, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad

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Conflict of interest: Nil

Abstract**Objectives:** The study aims to evaluate vitamin D levels in individuals with type 2 diabetes mellitus (T2DM) and healthy non-diabetic controls, and to determine its impact on glycemic management in those with T2DM, a prevalent global issue linked to bone disorders, cancers, infectious illnesses, and autoimmune diseases.**Methods:** A Total of 252 participants were taken, out of which 126 were known case of diabetes and 126 were taken as controls which were non diabetic.**Results:** The mean age in case group was 53.48 years (SD= 9.14) and in control group was 51.79 years (SD=11.22). The case group 83 females (65.9%) and 43 males (34.1%), while the control group had 85 females (67.5%) and 41 males (32.5%). The case group had a mean vitamin D level of 12.79 ng/mL (SD=8.11), while the control group had a mean of 18.05 ng/mL (SD=12.50). In the case group, 88.9% (112) were vitamin D deficient, 8.7% (11) had insufficient levels, and only 2.4% (3) had normal vitamin D levels which was significantly different between both groups ($p = 0.0001$). A negative correlation was observed between vitamin D and glycemic parameters [HbA1c, FBS, PPBS] which was not significant. However, a moderate negative correlation was observed (Pearson correlation = -0.277), between vitamin D and duration of diabetes which was statistically significant ($p = 0.002$).**Conclusion:** The study found a higher prevalence of vitamin D deficiency in type 2 diabetics, with a significant inverse relationship between vitamin D levels and diabetes duration, suggesting longer diabetes durations lead to lower levels.**Keywords:** Diabetes Mellitus, Vitamin D, HbA1c, Glycemic Control, Dyslipidemia.

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Introduction

Diabetes comprises a group of metabolic disorders characterized by elevated blood glucose levels due to impairments in insulin production, function, or a combination of both. Type 2 diabetes mellitus (T2DM) presents a significant global public health challenge, particularly in developing nations.

The most recent figures reported by the International Diabetes Federation (IDF) reveal a concerning trend, with the worldwide occurrence of type 2 diabetes mellitus (T2DM) among adults reaching 536.6 million individuals (10.5%) in 2021. Estimates indicate this figure will escalate to 783.2 million (12.2%) by 2045. [1] Prolonged elevated blood sugar levels in diabetic individuals

can give rise to macrovascular issues such as coronary artery disease and strokes, along with microvascular complications like nerve damage, vision impairment, and kidney disease.[2] These complications advances and results in severe outcomes such as, heart attacks, kidney failure, vision loss and limb amputations.[3]

Vitamin D, a fat-soluble hormone, is derived through dietary sources and synthesized through the skin upon exposure to sunlight. It has two primary forms: vitamin D2 (ergocalciferol) produced in plants via photochemical reactions, and vitamin D3 (cholecalciferol) which is generated in the skin of animals and humans upon

exposure to ultraviolet B rays within the 270– 300 nm wavelength range [4-5]

Vitamin D insufficiency is a growing health issue worldwide, affecting around one billion individuals globally, with its prevalence continuing to rise.[6] Vitamin D is essential in maintaining calcium levels and bone health while also contributing to various functions within the endocrine system.[7] The prevalence of vitamin D deficiency is widespread globally, as humans primarily acquire it through sunlight exposure or dietary intake. Low levels of vitamin D have been linked to decreased insulin sensitivity, as it stimulates insulin production. [8] Moreover, individuals with low vitamin D concentrations are at a higher risk of developing diabetic complications, including cardiovascular disease, renal impairment, and peripheral arterial disease.[9-11]

The cut-off values for classifying vitamin D status based on 25(OH) concentrations are as follows: Normal Vitamin D: ≥ 30 ng/mL, Insufficiency Vitamin D: 21-29 ng/mL, Deficient: ≤ 20 ng/mL.[12]

Growing research indicates a connection between low vitamin D levels and diabetes, yet the relationship between vitamin D levels and glycemic control, as well as the impact of blood sugar on vitamin D levels, has not been well explored. This study investigates the link between vitamin D status and glycemic parameters in Type 2 Diabetes Mellitus patients. It aims to identify vitamin D as a therapeutic adjunct in diabetes management, potentially improving glycemic control, reducing complications, and improving patient outcomes. Early detection and correction could contribute to a more comprehensive and cost-effective diabetes care strategy. Hence, the current study aims to assess vitamin D levels in individuals with type 2 diabetes mellitus (T2DM) and healthy non-diabetic controls as well as to determine its effect on glycemic management in those with T2DM.

Methods

This was a cross sectional observational study conducted at Santosh Medical College and Hospital, Ghaziabad, after obtaining approval from the Institutional Ethics Committee over a period of one year. Total 252 participants were taken, out of which 126 were known case of diabetes and 126 were taken as controls which were non diabetic.

Study population included in the study were based on the following criteria: Age more than 35 years of either gender, Patient with T2DM. The study excludes pregnant women, Type 1 diabetics, vitamin D supplementation-using patients, hospitalized patients, chronic diseases, steroid use, metabolic bone and parathyroid disorders, malabsorption syndromes, active malignancy, and

active infections. It also excludes those with metabolic or malabsorption syndromes.

Demographic details of the patients were recorded. Smoking, Body mass index (BMI) and dyslipidemia were examined. Routine laboratory investigations were performed and these included: Liver function tests, renal function tests, electrolytes, complete blood picture and lipid profile. HbA1c was chromatographically separated on a cation exchange cartridge. Glycemic control was assessed by Fasting blood sugar and HbA1c. Levels of 25(OH)D3 were measured by radioimmunoassay (RIA) in a two-step procedure.

Statistical Analysis: The study collected data using a predesigned template and compiled it into an Excel spreadsheet. The data was analyzed using SPSS 24th version, and quantitative and categorical variables were compared using Student t-test, ANOVA, Chi square, and Fisher's exact tests. Pearson correlation was used to study the relationship between vitamin D levels, HbA1c, and diabetes duration.

Results

The demographic details of the patients, along with the findings related to vitamin D levels, diabetes, and BMI, are presented below:

In the case group, 93 participants (73.8%) were aged ≤ 60 years and 33 participants (26.2%) were aged > 60 years. In the control group, 97 participants (77.0%) were aged ≤ 60 years and 29 participants (23.0%) were aged > 60 years. In terms of gender, the case group included 83 females (65.9%) and 43 males (34.1%), while the control group had 85 females (67.5%) and 41 males (32.5%). For smoking status, 65 participants (51.6%) in the case group were smokers, while 61 participants (48.4%) in the control group reported smoking as shown in Table 1.

The mean age in the case group was 53.48 years (SD = 9.14) and in the control group was 51.79 years (SD = 11.22). The mean BMI in the case group was 23.43 (SD = 2.75), while in the control group, the mean BMI was 22.89 (SD = 2.85). There was no significant differences between the case and control groups in terms of age, gender distribution, smoking status, and BMI which suggests that the two groups were well-matched for these potential confounders.

The mean HbA1c level was 8.04% (SD = 1.36) in the case group and 5.93% (SD = 0.43) in the control group, showing a significant difference ($p = 0.0001$). The mean fasting blood sugar (FBS) level was 125.65 mg/dL (SD = 38.57) in the case group and 86.75 mg/dL (SD = 13.15) in the control group ($p = 0.0001$) and the Postprandial blood sugar levels also differed significantly, with a mean of

202.11 mg/dL (SD = 69.83) in the case group and 144.07 mg/dL (SD = 20.13) in the control group ($p = 0.0001$). The case group had a mean vitamin D level of 12.79 ng/mL (SD = 8.11), while the control group had a mean of 18.05 ng/mL (SD = 12.50) showing a statistically significant difference ($p = 0.0001$) as shown in Table 2.

In the case group, 88.9% (112 participants) were vitamin D deficient, 8.7% (11 participants) had insufficient levels, and only 2.4% (3 participants) had normal vitamin D levels. In the control group, 54.0% (68 participants) were deficient, 31.0% (39 participants) had insufficient levels, and 15.0% (19

participants) had normal levels. This distribution was significantly different between both groups ($p = 0.0001$) as shown in Table 3 and Graph 1. A weak negative correlation was observed between vitamin D levels and HbA1c, vitamin D levels and FBS and vitamin D and PPBS, which was not significant.

However, a moderate and statistically significant negative correlation was found between vitamin D levels and the duration of diabetes. The correlation between serum Vitamin D levels and glycemic parameters as well as the duration of diabetes in diabetic patients is shown in Table 4.

Table 1: Characteristics of Participants

| Categories | Case | | Controls | | P-value |
|----------------|-------|-------|----------|-------|---------|
| | count | % | count | % | |
| Age ≤60 years | 93 | 73.8% | 97 | 77.0% | 0.559 |
| >60 years | 33 | 26.2% | 29 | 23.0% | |
| Gender: Female | 83 | 65.9% | 85 | 67.5% | 0.789 |
| Male | 43 | 34.1% | 41 | 32.5% | |
| Smoking: No | 61 | 48.4% | 65 | 51.6% | 0.614 |
| Yes | 65 | 51.6% | 61 | 48.4% | |

Table 2: Comparison of baseline variables in T2DM in cases and controls

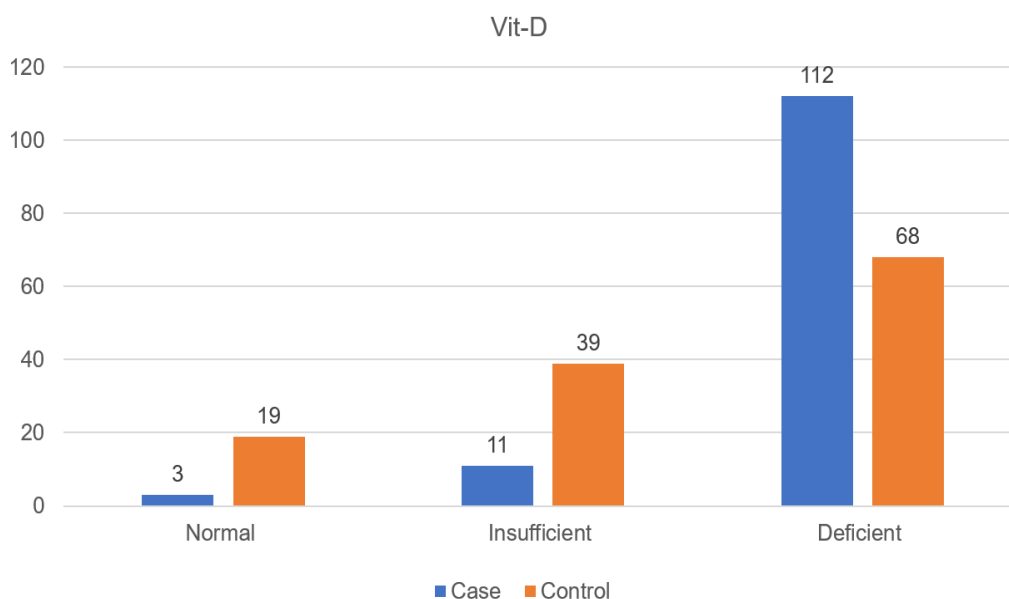
| Parameter | Case | | Control | | p-value |
|--------------------------|---------|---------|---------|----------|---------|
| | Mean | SD | Mean | SD | |
| Age | 53.48 | 9.141 | 51.79 | 11.223 | 0.191 |
| BMI | 23.4304 | 2.75234 | 22.8905 | 2.85651 | 0.128 |
| Hemoglobin | 11.767 | 2.3333 | 12.059 | 2.3383 | 0.320 |
| SGOT | 42.944 | 27.4524 | 28.794 | 12.7989 | 0.0001* |
| SGPT | 39.825 | 26.8200 | 27.492 | 13.2700 | 0.0001* |
| Urea | 25.119 | 9.3626 | 30.373 | 15.5583 | 0.001* |
| Creatinine | .813 | .3014 | .882 | .2376 | 0.043* |
| Sodium | 135.263 | 4.0607 | 136.375 | 3.4510 | 0.020* |
| Potassium | 4.1663 | .48167 | 4.0740 | .47114 | 0.125 |
| Calcium | 8.5910 | .65358 | 8.6690 | .60114 | 0.325 |
| HbA1c | 8.0421 | 1.36072 | 5.9382 | .43342 | 0.0001* |
| FBS | 125.659 | 38.5769 | 86.754 | 13.1561 | 0.0001* |
| Postprandial Blood Sugar | 202.119 | 69.8391 | 144.079 | 20.1358 | 0.0001* |
| TC | 159.984 | 29.1994 | 147.722 | 27.0018 | 0.001* |
| LDL | 88.833 | 22.1048 | 84.769 | 17.0215 | 0.103 |
| TG | 161.810 | 65.3946 | 135.706 | 67.1150 | 0.002* |
| Vit -D | 12.7971 | 8.11085 | 18.0597 | 12.50673 | 0.0001* |

Table 3: Comparison of Vit-D between both groups:

| Vit-D | Case | | Control | | p-value |
|--------------|-------|-------|---------|-------|---------|
| | Count | % | Count | % | |
| Normal | 3 | 2.4% | 19 | 15.0% | 0.0001 |
| Insufficient | 11 | 8.7% | 39 | 31.0% | |
| Deficient | 112 | 88.9% | 68 | 54.0% | |

Table 4: Correlation of Vit-D with HbA1c and FBS, PPBS and duration of diabetes in diabetes patients:

| | | VIT D |
|----------------------------------|---------------------|---------|
| HBa1c | Pearson Correlation | -.115 |
| | p-value | .200 |
| | N | 126 |
| FBS | Pearson Correlation | -.028 |
| | p-value | .753 |
| | N | 126 |
| Postprandial Blood Sugar (mg/dL) | Pearson Correlation | -.121 |
| | p-value | .176 |
| | N | 126 |
| Duration of Diabetes (years) | Pearson Correlation | -.277** |
| | p-value | .002 |
| | N | 126 |

**Graph 1: Comparative distribution graph of cases and controls based on Vitamin D levels**

Discussion

Vitamin D, a fat-soluble vitamin, plays a crucial role in maintaining bone health and regulating calcium-phosphorus metabolism. Recent research has highlighted its potential involvement in glucose metabolism and insulin sensitivity, linking Vitamin D deficiency to type 2 diabetes mellitus (T2DM).

T2DM is a chronic metabolic disorder characterized by hyperglycemia, insulin resistance, and progressive β -cell dysfunction. Glycemic control, assessed through parameters such as fasting blood sugar (FBS), post prandial blood sugar (PPBS) and glycated hemoglobin (HbA1c), is critical for preventing complications in diabetic patients.

Vitamin D is hypothesized to influence glycemic control through mechanisms such as enhancing β -cell function, modulating inflammation, and improving insulin action. However, the relationship between Vitamin D levels and glycemic parameters

remains inconsistent across studies. Understanding the correlation between Vitamin D deficiency and glycemic markers in T2DM patients can provide insights into its role in diabetes management and potential therapeutic implications, necessitating further exploration in this domain. In this study we had taken 252 participants out of which 126 participants were controls and 126 participants were cases having type 2 diabetes. Our study demonstrated a mean age of 53.48 ± 9.14 years in the case group and 51.79 ± 11.22 years in the control group, with no significant difference between groups ($p = 0.191$). This age distribution closely aligns with several comparative studies in the literature. The age categorization in our study revealed that 73.8% of cases were aged ≤ 60 years, while 26.2% were >60 years. This distribution pattern provides valuable insights into the age-related presentation of T2DM and its relationship with vitamin D metabolism. This finding becomes particularly relevant when considering that aging

affects both glucose homeostasis and vitamin D synthesis.

Our study population exhibited a notable female predominance, with 65.9% of cases being female. This finding aligns with but shows a slightly higher female representation than Salih et al.'s study [13], which reported 56.1% female participants. Our analysis of Body Mass Index (BMI) revealed no significant difference between cases (23.43 ± 2.75) and controls (22.89 ± 2.85). This finding presents an interesting contrast to several comparative studies in the literature. Salih et al. (2021)[13] reported a notably higher prevalence of obesity in their T2DM population, while Mousa et al. (2017)[14] specifically focused their research on overweight and obese individuals, with a mean BMI of $30.9 \pm 4.4 \text{ kg/m}^2$.

The study found no significant differences between the case and control groups in terms of age, gender distribution, smoking status, and BMI. This suggests that the two groups were well-matched for these potential confounders.

The case group had significantly lower mean vitamin D levels compared to the control group (12.79 vs. 18.05 ng/mL). Furthermore, a staggering 88.9% of diabetic participants were vitamin D deficient, 8.7% insufficient while only 2.4% had normal levels. In contrast, the control group had a more even distribution, with 54% being deficient, 31% having insufficient levels, and 15% having normal levels. These findings suggest a high prevalence of vitamin D deficiency among type 2 diabetics.

The significantly lower vitamin D levels in diabetic participants are consistent with the literature. Kostoglou-Athanassiou et al. (2013)[15] found that 25(OH)D3 levels were significantly lower in patients with T2DM compared to controls. Similarly, Salih et al. (2021) [13] observed vitamin D insufficiency and deficiency in 71% of cases and 40.6% of controls. Our study demonstrated significantly higher HbA1c levels in the case group ($8.04\% \pm 1.36$) compared to controls ($5.93\% \pm 0.43$, $p = 0.0001$). This finding aligns closely with Kostoglou-Athanassiou et al.'s [15] research, which also reported significant differences in glycemic control between diabetic and non-diabetic populations. The mean fasting blood sugar levels showed significant differences between cases ($125.65 \pm 38.57 \text{ mg/dL}$) and controls ($86.75 \pm 13.15 \text{ mg/dL}$, $p = 0.0001$). This finding was further supported by significant differences in postprandial blood sugar levels ($202.11 \pm 69.83 \text{ mg/dL}$ vs $144.07 \pm 20.13 \text{ mg/dL}$, $p = 0.0001$).

The study found a weak negative correlation between vitamin D levels and HbA1c, but it was not statistically significant. Similarly, a weak

negative correlation was observed between vitamin D levels and FBS, vitamin D and PPBS, which was also not significant. However, a moderate and statistically significant negative correlation was found between vitamin D levels and the duration of diabetes. This suggests that longer durations of diabetes are associated with lower vitamin D levels.

The lack of a significant correlation between vitamin D levels and HbA1c or FBS is somewhat inconsistent with previous research. Kostoglou-Athanassiou et al. (2013)[15] found an inverse relationship between 25(OH)D3 levels and HbA1c in T2DM patients, which persisted when both patient and control groups were analyzed together. Similarly, Hu et al. (2019)[16] reported that short-term vitamin D supplementation led to decreased HbA1c, insulin resistance, and insulin levels in T2DM patients. The significant negative correlation between vitamin D levels and diabetes duration aligns with the findings of Salih et al. (2021)[13], who observed a significant difference in serum 25(OH)D levels between patients with a diabetes duration of more than 5 years and those with a duration of less than 5 years. Kostoglou-Athanassiou et al. (2013)[15] and Hu et al. (2019)[16] both found significantly lower vitamin D levels in T2DM patients compared to controls, which aligns with the current study. However, they also reported significant inverse relationships between vitamin D levels and glycemic control parameters, which were not observed in the current study.

Salih et al. (2021)[13] found a high prevalence of vitamin D deficiency among T2DM patients, particularly those with poor glycemic control and longer diabetes durations. This is consistent with the current study's findings. However, they also observed a significant negative correlation between FBS and Vit D, which was not found in the current study.

Krul-Poel et al. (2015)[17] and Gulseth et al. (2017)[18] conducted randomized controlled trials investigating the effect of vitamin D supplementation on glycemic control in T2DM patients. Both studies found no significant improvements in HbA1c or other glycemic control parameters after vitamin D supplementation. These findings suggest that the relationship between vitamin D status and glycemic control may be more complex than a simple cause-and-effect relationship. Overall, the current study's findings are generally consistent with the literature regarding the high prevalence of vitamin D deficiency in T2DM patients and its potential association with glycemic control parameters. However, the lack of significant correlations between vitamin D levels and HbA1c or FBS differs from some previous studies. This discrepancy highlights the need for further research

to clarify the complex relationship between vitamin D status and glycemic control in type 2 diabetes.

This study highlights the importance of vitamin D in glycemic control among Type 2 Diabetes Mellitus patients, potentially improving metabolic outcomes and reducing long-term complications. It emphasizes the use of objective biochemical markers like HbA1c and serum vitamin D, and has the potential to influence clinical practice and public health strategies. However, limitations include cross-sectional design, single-center study, and the potential influence of confounding factors like sun exposure, diet, and physical activity.

Conclusion

This study investigated the vitamin D status of type 2 diabetic patients and explored its relationship with glycemic control parameters. The findings reveal a high prevalence of vitamin D deficiency among type 2 diabetics, with 88.9% of participants in the case group being vitamin D deficient. The study also found a significant negative correlation between vitamin D levels and the duration of diabetes, suggesting that longer durations of diabetes are associated with lower vitamin D levels. However, no significant correlations were observed between vitamin D levels and HbA1c or fasting blood sugar.

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