Original Article

Association of Serum 25-Hydroxyvitamin D with Glycaemic Dysregulation from Normal Glucose Regulation to Type 2 Diabetes Mellitus

Manisha[1], Jaya Jain[2]

[1]Ph.D Scholar, Department of Biochemistry, IMCH& RC, Malwanchal University, Indore, Madhya Pradesh, India. [2]Professor Department of Biochemistry, IMCH& RC, Malwanchal University, Indore, Madhya Pradesh, India

Abstract

Background: Vitamin D status has been associated with glucose metabolism and type 2 diabetes, although the nature of this relationship remains incompletely understood. The objective is to compare serum 25-hydroxyvitamin D [25(OH)D] concentrations among individuals with normal glucose regulation, prediabetes and T2DM and to examine their relationship with glycaemic biomarkers. **Material and Methods:** Cross-sectional comparative study was carried out in 300 adults of age group 18-60 yrs.Methods: Cross sectional comparative study of 300 adults (age group 18-60 yrs). The number of participants in the control and prediabetes-T2DM groups was equal. The following biochemical parameters were measured: 25(OH)D, FPG, HbA1C, fructosamine and GA. **Results:** Serum vitamin D levels were gradually reduced in controls (31.8±6.5 ng/mL), prediabetes (24.6±6.1 ng/mL) and T2DM (18.9±5.7 ng/mL). The overall difference was statistically significant (F=111.99; P<0.001). All pairwise mean differences were significant at P<0.001: 7.2 ng/mL between controls and prediabetes; 12.9 ng/mL between controls and T2DM; and 5.7 ng/mL between prediabetes and T2DM. **Conclusion:** This is an analysis of the literature on vitamin D and 25-hydroxyvitamin D (25(OH)D) and prediabetes and type 2 diabetes mellitus (T2DM), HbA1c and glycaemic dysregulation.

Keywords: vitamin D; 25-hydroxyvitamin D; prediabetes; type 2 diabetes mellitus; HbA1c; glycaemic dysregulation.

Received: 26 July 2026 **Revised: 06 August 2026** **Accepted: 23 August 2026** **Published: 29 August 2026**

Introduction

There has been growing research interest in the association of vitamin D with glucose metabolism, insulin resistance and T2DM. Lower levels of 25(OH)D have been reported to be associated with increased metabolic risks in observational studies on many occasions. But it is unknown whether this association is a causal one.

There are several biological pathways suggested by which vitamin D can affect glucose metabolism, such as effects on pancreatic β-cell function, calcium-dependent insulin secretion and insulin sensitivity. However, there are also common factors like adiposity, physical activity, diet and sunlight exposure that can lead to observational associations.

Results of intervention studies have been varied, but are increasingly showing that the impact of vitamin D supplementation may be influenced by vitamin D status at baseline and population characteristics. In a 2023 systematic review and meta-analysis of 46 randomized controlled trials, significant decreases in HbA1C, fasting glucose and HOMA-IR were observed, especially in vitamin D deficient subjects.[6]

The updated 2024 meta-analysis of 39 RCTs and 2,982 participants similarly found that the use of vitamin D caused a significant decrease in fasting blood glucose, HbA1c, HOMA-IR and fasting insulin, depending on the dose, duration, baseline vitamin D levels and BMI.[7]

A recent umbrella review published in 2024 also found a positive correlation between lower 25(OH)D level and increased T2DM risk, as well as an improvement in several glycaemic indices with vitamin D supplementation, especially for those who are vitamin D deficient.[8]

The present study aimed to compare serum vitamin D in three stages of glucose regulation and to examine the relationship between serum vitamin D and traditional and novel glycaemic markers.

Materials and Methods

Study design: The cross-sectional comparative study was conducted in the Department of Clinical Biochemistry at Index Medical College Hospital & Research Centre, Indore, Madhya Pradesh, India, from 2022-25.

Study Group Distribution: A total of 300 participants were included in the study, equally distributed into three groups based on their glycaemic status.

The number of participants in Group I (Control/Normal Glucose Regulation) was 100, which were used as the control group.

- Group II (Prediabetes/Impaired Glucose Homeostasis) included 100 prediabetes patients who did not have

Address for correspondence: Dr. Jaya Jain, Professor Department of Biochemistry, IMCH& RC, Malwanchal University, Indore, Madhya Pradesh, India
E-mail: jayajain1983@gmail.com

DOI:
10.21276/amit.2026.v13.i2.993

How to cite this article: Manisha, Jaya Jain. Association of Serum 25-Hydroxyvitamin D with Glycaemic Dysregulation from Normal Glucose Regulation to Type 2 Diabetes Mellitus. Acta Med Int. 2026;13(2):1981-1984.

diabetes mellitus.

- Group III (Type 2 Diabetes Mellitus) consisted of 100 patients with type 2 diabetes mellitus (T2DM).

In total, 300 participants were involved in the study, 100 participants from each of the three study groups. This even distribution resulted in glycaemic and biochemical parameters being compared between normal glucose regulation, prediabetes and established T2DM.

Laboratory investigations: Serum 25(OH)D levels were measured by measuring the levels of the enzyme with a chemiluminescence immunoassay (CMIA) on the basis of competitive binding. Other parameters, such as FPG, HbA1c, fructosamine and GA were also assessed.

Statistical analysis: Data are presented as mean±standard deviation (SD). Differences between the groups were examined by ANOVA and pairwise comparisons. P<0.05 was deemed as statistically significant.

Results

The total number of participants in the study were 300. The participants were equally distributed into three groups, with 100 participants (33.3%) in each group: normal glucose regulation, prediabetes/impaired glucose homeostasis, and type 2 diabetes mellitus.

The serum vitamin D level showed a continuous decrease from the three study groups. In the control group, the mean vitamin D level was 31.8 ± 6.5 ng/mL, whereas in the prediabetes and T2DM groups, it was found to be 24.6 ± 6.1 ng/mL and 18.9 ± 5.7 ng/mL, respectively.

The one-way analysis of variance (ANOVA) showed that there was a highly statistically significant difference between the serum vitamin D levels of the three groups ($p < 0.001$, $F = 111.99$). The results showed that the serum vitamin D level was significantly decreased over the levels of glucose dysregulation, being lowest in the T2DM group. [Table 1]

Table 1: Serum Vitamin D levels among T2 DM, prediabetic and control groups.

Parameter	Control	Prediabetes	T2DM	ANOVA F	P value
Vitamin D (ng/mL)	31.8 ± 6.5	24.6 ± 6.1	18.9 ± 5.7	111.99	<0.001

Statistically significant difference was seen between all five biochemical parameters in all the three groups. The FPG, HbA1c, fructosamine and glycated albumin levels were seen to be stepwise higher in prediabetes and T2DM than controls, while the vitamin D levels decreased gradually between controls and prediabetes and T2DM. Differences were all very highly significant (P<0.001). [Table 2]

Table 2: The knowledge about Glycaemic and Vitamin D Biomarkers was compared among three study groups.

Parameter	Control	Prediabetes	T2DM	ANOVA F	P value
FPG (mg/dL)	91.0 ± 8.0	112.0 ± 9.0	158.0 ± 32.0	301.37	<0.001
HbA1c (%)	5.25 ± 0.35	6.05 ± 0.28	8.05 ± 1.15	409.61	<0.001
Fructosamine (µmol/L)	225 ± 22	264 ± 20	336 ± 38	408.63	<0.001
Glycated albumin (%)	13.1 ± 1.2	16.2 ± 1.3	22.4 ± 3.1	528.02	<0.001
Vitamin D (ng/mL)	31.8 ± 6.5	24.6 ± 6.1	18.9 ± 5.7	111.99	<0.001

FPG was found to be significantly higher in all the study groups as they progressed. The mean FPG was 91.0 ± 8.0 mg/dL in controls, 112.0 ± 9.0 mg/dL in prediabetes, and 158.0 ± 32.0 mg/dL in T2DM. All comparisons were found to be significantly different from each other ($P < 0.001$). [Table 3]

Table 3: Comparisons between different fasting plasma glucose measurements

Comparison	Mean difference (mg/dL)	t-value	P value
Control vs Prediabetes	−21.0	−17.44	<0.001
Control vs T2DM	−67.0	−20.31	<0.001
Prediabetes vs T2DM	−46.0	−13.84	<0.001

There were negative correlations of vitamin D with all glycaemic parameters: FPG ($r = -0.52$); HbA1c ($r = -0.58$); fructosamine ($r = -0.49$); and glycated albumin ($r = -0.55$). HbA1c ($r = -0.58$) had the most negative correlation. [Table 4]

Table 4: Correlation Between Serum Vitamin D and Glycaemic Parameters

Glycaemic parameter	Direction with Vitamin D	Correlation coefficient
FPG	Negative	r = −0.52
HbA1c	Negative	r = −0.58
Fructosamine	Negative	r = −0.49
Glycated albumin	Negative	r = −0.55

There were positive correlations between HbA1c and fructosamine ($r = 0.78$), glucated albumin ($r = 0.84$) and FPG ($r = 0.72$), and a negative correlation between HbA1c and vitamin D ($r = -0.58$). The best correlation was seen between HbA1C and glycated albumin ($r = 0.84$) [Table 5]

Table 5: Correlation of HbA1c with Glycaemic and Vitamin D Biomarkers

Variable	Correlation with HbA1c	Direction
Fructosamine	r = 0.78	Positive
Glycated albumin	r = 0.84	Positive
FPG	r = 0.72	Positive
Vitamin D	r = −0.58	Negative

Discussion

In the present study, it was clear that serum 25-hydroxyvitamin D [25(OH)D] concentrations progressively decreased from normal to hyperglycemia and then to T1D to T2D. Vitamin D levels decreased in participants with prediabetes (24.6 ± 6.1 ng/mL) and those with type 2 diabetes mellitus (T2DM) (18.9 ± 5.7 ng/mL) compared with controls (31.8 ± 6.5 ng/mL). This difference in the three groups was very highly statistically significant ($P < 0.001$, $F = 111.99$). All pairwise comparisons were also statistically significant, showing a consistent decrease in the level of vitamin D as the severity of dysglycaemia increased. These results suggest a relationship between low vitamin D levels and deterioration of glucose regulation.

This decrease in vitamin D level was also detected in the prediabetes group, indicating that changes in vitamin D status might occur before diabetes is established rather than after. The mean difference of vitamin D between controls and prediabetes was 7.2 ng/mL, controls and T2DM 12.9 ng/mL, and prediabetes and T2DM 5.7 ng/mL, all being significant ($P < 0.001$).

The results of this study are consistent with the previous observational evidence in most ways. Previous reviews have suggested vitamin D could affect glucose metabolism by impacting pancreatic β-cell function, calcium-dependent insulin secretion and insulin sensitivity.[1,4]

In this study, conventional glycaemic markers were expected and progressive in both the three groups. Fasting plasma glucose increased from 91.0 ± 8.0 mg/dL in controls to 112.0 ± 9.0 mg/dL in prediabetes and 158.0 ± 32.0 mg/dL in T2DM, while HbA1c increased from 5.25 ± 0.35% to 6.05 ± 0.28% and 8.05 ± 1.15%, respectively. The differences were extremely significant ($p < 0.001$).

Significantly, there was an inverse relationship between vitamin D and glycaemic parameters. Correlation coefficients reported were $r = −0.52$ for FPG, $r = −0.58$ for HbA1c, $r = −0.49$ for fructosamine, and $r = −0.55$ for glycated albumin; the highest negative correlation was between vitamin D and HbA1c.

There was also a similar pattern with the alternative glycaemic biomarkers. The levels of fructosamine were significantly elevated in prediabetes (264 ± 20 µmol/L) when compared with the controls (225 ± 22 µmol/L), and in T2DM (336 ± 38 µmol/L) when compared with prediabetes (264 ± 20 µmol/L). Glycated albumin increased from 13.1 ± 1.2% to 16.2 ± 1.3% and 22.4 ± 3.1%, respectively. Therefore, the deterioration in both conventional and alternative metrics of glycaemic exposure was linked with a fall in vitamin D levels.

The positive correlation reported between HbA1c and fructosamine ($r = 0.78$), HbA1c and glycated albumin ($r = 0.84$) and HbA1c and FPG ($r = 0.72$) continue to show a good degree of concordance between the glycaemic markers, while the correlation between HbA1c and Vitamin D was negative ($r = −0.58$).

There are other pieces of evidence from intervention studies. Farahmand et al. reported that vitamin D supplementation resulted in decreased HbA1c, fasting glucose and HOMA-IR, especially in those with vitamin D deficiency. An updated meta-analysis by Chen et al. also found that vitamin D supplementation had beneficial effects on fasting glucose, HbA1c, HOMA-IR and fasting insulin, with the magnitude of the effect depending on baseline vitamin D status, vitamin D dosage, duration of supplementation and BMI. Although the findings do not prove that vitamin D deficiency is an independent risk factor for diabetes, they offer supportive evidence for a possible relationship between the vitamin D status and glucose metabolism.

The association could be due to multiple mechanisms, such as vitamin D effects on pancreatic β-cell function, insulin secretion and insulin sensitivity. But also adiposity, physical activity, diet and sun exposure play a role in vitamin D status. These can thus serve as potential confounders to the observed association.

There are some limitations to the present study. It is cross-sectional, which means that it cannot be used to determine temporal relationships and/or causality. This study was carried out in a single centre and 300 subjects were included. Adjustment for BMI, dietary vitamin D intake, physical activity, and sunlight exposure and seasonal variation was not possible because of limited availability of this information. Also, there was no follow up or vitamin D supplementation.

In general, the results indicated a gradual decrease in 25(OH)D level from normal glucose regulation to prediabetes and T2DM and a gradual increase in FPG, HbA1c, FA and GAL levels from normal glucose regulation to prediabetes and T2DM. The findings provided evidence for the relationship between vitamin D status and severity of glycaemic dysregulation. But future research—such as prospective studies and randomized controlled trials—is needed to answer the question of whether such changes in vitamin D status will change the course of dysglycaemia.

Conclusion

There was a statistically significant linear decrease in serum 25(OH)D levels between NGR and prediabetes and T2DM. This was concurrent with worsening glycemic parameters (conventional and alternative).

The results confirm a linkage between vitamin D level and glycaemic disorders. They are not definitive proof of a causal role of vitamin D deficiency in the development or progression of T2DM, though.

Further prospective vitamin D studies and RCTs are needed to determine if correction of vitamin D deficiency has a meaningful impact on glycaemic progression.

References

1. Lips P, Eekhoff M, van Schoor N, Oosterwerff M, de Jongh R, Krul-Poel Y, et al. Vitamin D and type 2 diabetes. J Steroid Biochem Mol Biol. 2017;173:280-285.
2. Parker J, Hashmi O, Dutton D, Mavrodaris A, Stranges S, Kandala NB, et al. Levels of vitamin D and cardiometabolic disorders: systematic review and meta-analysis. Maturitas. 2010;65(3):225-236.
3. Song Y, Wang L, Pittas AG, Del Gobbo L, Zhang C, Manson JE, et al. Blood 25-hydroxy vitamin D levels and incident type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care. 2013;36(5):1422-1428.
4. Pittas AG, Dawson-Hughes B. Vitamin D and diabetes. J Steroid Biochem Mol Biol. 2010;121(1-2):425-429.
5. Zheng JS, et al. Vitamin D status and risk of type 2 diabetes mellitus: a systematic review and meta-analysis. Clin Nutr. 2018.
6. Farahmand MA, Daneshzad E, Fung TT, Zahidi F, Mohammadi M, Bellissimo N, et al. What is the impact of vitamin D supplementation on glycemic control in people with type-2 diabetes: a systematic review and meta-analysis of randomized controlled trials. BMC Endocr Disord. 2023;23:15.
7. Chen W, Liu L, Hu F. Efficacy of vitamin D supplementation on glycaemic control in type 2 diabetes: an updated systematic review and meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2024;26(12):5713-5726.
8. Afraie M, Bahrami P, Kohnepoushi P, Khateri S, Majidi L, Saed L, et al. The effect of vitamin D supplementation on glycemic control and cardiovascular risk factors in type 2 diabetes: an updated systematic review and meta-analysis of clinical trials. J Diabetes Res. 2024;2024:9960656.
9. Cheng L, Lv C, Xue L, Zhang C, Wang L, Wang X, et al. The prevention and improvement effects of vitamin D on type 2 diabetes mellitus: evidence from an umbrella review on meta-analyses of cohort studies and randomized controlled trials. Front Nutr. 2024;11:1462535.