RESEARCH PAPER

Effect of Vitamin D Level on Glycemic Control in Type 2 Diabetes Mellitus: A Prospective Observational Study

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ABSTRACT

Background: Type 2 diabetes mellitus is a health issue of global concern whose prevalence is increasing especially in India. There exists some evidence that vitamin D deficiency may also be responsible in poor glycemic control although the association between the two is not always stable across populations. The paper examined the relationship between the serum levels of vitamin D and the glycemic control indicators, and the effect of vitamin D supplementation on the HbA1c value of patients with type 2 diabetes mellitus.

Methods: A prospective observational case study was carried out in one of the tertiary care hospitals that included 100 patients with type 2 diabetes mellitus. The baseline measurements consisted of demographic data, anthropometric measurement, HbA1c levels, and serum 25-hydroxyvitamin D3 levels. Vitamin D deficient or insufficient patients were given standard vitamin supplementation (60,000 IU a week, 8 weeks, then monthly maintenance). Three-month follow-ups were conducted to determine the improvement of vitamin D condition and glycemic control.

Results: The cohort of the study included 53 and 47 percent female and male participants respectively with mean age of 56.9 ± 2.13 years. Baseline testing showed that 40% of the participants had too little vitamin D (<20 ng/mL) and 49% had too little (20-29 ng/mL) and only 11% had enough (30 ng/mL or higher). Baseline HbA1c was 8.5 ± 1.48 with 61% exhibiting fair glycemic control and 29% exhibiting poor glycemic control. There was a strong negative relationship between the baseline vitamin D3 and HbA1c ($r = -0.356$, $p = 0.0001$). After the vitamin D supplementation, the mean level of vitamin D3 went up, but the level itself rose to 45.06 ± 20.70 ng/mL (mean 0.0001), and the HbA1c dropped to 7.50% (mean 0.96, $p < 0.0001$). The correlation between vitamin D3 and HbA1c was also significant after the intervention ($r = -0.262$, $p = 0.008$).

Conclusion: The present research shows that vitamin D deficiency is rather widespread in patients with type 2 diabetes mellitus and that there is a strong negative correlation between the state of vitamin D and the state of glycemic control. The supplementation with vitamin D led to significant increases in the levels of vitamin D and HbA1c which indicates that this nutrient can be used as a possible adjunctive treatment in the management of diabetes. The results suggest regular testing of vitamin D deficit and intensive supplementation of diabetic groups to maximize metabolic results.

Keywords: Type 2 diabetes mellitus, Vitamin D deficiency, HbA1c, Glycemic control, Vitamin D supplementation, Insulin resistance

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Introduction

Diabetes mellitus is one of the greatest metabolic diseases of the twenty-first century, which is defined by persistent hyperglycemia that is caused by the inhibited secretion of insulin, the disrupted insulin participation, or both[1]. Diabetes type 2 (T2DM) is

thought to be the cause of about 90-95% of all diabetes and has become an epidemic in the world[2]. The International Diabetes Federation reports that the prevalence rate in the world has now grown exponentially, as there were 382 million people with this condition in 2013 and the number is expected to rise to 592 million by 2035[3]. India has a very huge burden with the number of diabetic patients being the highest in the world as it is currently. The ICMR-INDIAB national study reported 62.4 million individuals with type 2 diabetes and 77 million with pre-diabetes in India and projections showed that this number would rise to 101 million by 2030[4]. Pathophysiology Type 2 diabetes mellitus is a complex interaction of the genetic predisposition and the environment. Although conventional risk factors such as obesity, sedentary lifestyle, and dietary habits have been fully described, recent studies have shed some light on the possible contribution of vitamin D deficiency in the occurrence and propagation of this metabolic disorder[5][6]. This relationship has attracted a lot of scientific attention because the lack of vitamin D has become widespread in all parts of the world, and it may be a contributing factor to the increasing cases of type 2 diabetes. With long-standing reputation as a very important vitamin in maintaining calcium balance and bone processes, vitamin D has proven to have numerous far-reaching impacts other than on bone health. In the last twenty years, there has been an accumulation of evidence to establish the role of vitamin D in many physiological functions such as immune system, cardiovascular health, and metabolism[7]. Direct mechanistic connections between the status of vitamin D and glucose metabolism are implied by the identification of vitamin D receptors (VDR) in insulin-sensitive tissues such as pancreatic beta cells, skeletal muscle, adipose tissue, and hepatocytes[8]. Activation of these receptors by the active form of vitamin D, which is 1, 25-dihydroxyvitamin D, can regulate gene expression that is associated with insulin secretion, insulin sensitivity, and glucose homeostasis. Various mechanistic pathways support the role of vitamin D in the pathogenesis of diabetes as it is biologically plausible. Vitamin D has been associated with insulin resistance that is the characteristic of type 2 diabetes mellitus in several ways. Vitamin D could increase the expression of insulin receptors, boost insulin-signaling pathways and translocation of glucose transporters in the peripheral tissues[9]. Moreover, the anti-inflammatory effects of vitamin D may also be used to manage chronic inflammation of low grade that is a major cause of insulin resistance[10]. The pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-a) and nuclear factor-kappa B (NF-kB) activation, have also been reported to be suppressed by vitamin D and may, therefore, help relieve insulin resistance caused by inflammation[11]. Another very crucial area through which vitamin D has its effect is in the pancreatic beta-cell functioning. It has been shown through experimental research that vitamin D could directly influence the survival of the beta-cells, as well as, its proliferation and insulin secretion capability[12]. Pancreatic islets contain vitamin D receptors and 1-alpha-hydroxylase enzyme, which allows a direct conversion of 25-hydroxyvitamin D to its active form, which indicates the presence of autocrine and paracrine regulation. Deficiency of vitamin D has been linked with the reduced glucose-stimulated insulin secretion as well as augmented beta-cell apoptosis in animal models and explain the protective effect on maintaining the mass and function of beta-cells[13]. Adipose tissue malfunction is an important cause of insulin resistance among type 2 diabetes mellitus. Vitamin D affects the adipogenesis, adipocyte differentiation, and adipokine secretion which can control insulin sensitivity via these mechanisms[14]. Research indicates that vitamin D may have an influence on the levels of adiponectin, an insulin-sensitising adipokine with positive metabolic properties, as well as decreasing the release of pro-inflammatory adipokines like leptin and resistin[15]. Also, the vitamin D implication in the renin-angiotensin-aldosterone system (RAAS) could be linked to the enhanced insulin sensitivity since increased RAAS levels have been linked to the development of insulin resistance[16].

Hemoglobin A1c (HbA1c) has emerged as the gold standard biomarker for assessing long-term glycemic control in diabetes management. HbA1c reflects average blood glucose concentrations over the preceding 2-3 months and correlates strongly with the risk of diabetic complications[17]. The American Diabetes Association has endorsed HbA1c ≥6.5% as

a diagnostic criterion for diabetes and recommends target levels below 7% for most adults with diabetes to minimize complication risks[18]. The relationship between vitamin D status and HbA1c has been explored in numerous studies, though results have been inconsistent across different populations and study designs.

Despite growing interest in the vitamin D-diabetes relationship, several important questions remain inadequately addressed. The precise nature and strength of the association between serum vitamin D levels and glycemic control markers, particularly HbA1c, vary considerably across published literature[19]. This variability may stem from differences in study populations, baseline vitamin D status, genetic factors, environmental influences, and methodological approaches. Furthermore, intervention studies examining the efficacy of vitamin D supplementation on glycemic outcomes have yielded mixed results[20, 25-31]. Factors including supplementation dosage, duration, baseline vitamin D deficiency severity, and concurrent diabetes management strategies contribute to this heterogeneity.

In the Indian context, several unique considerations merit attention. The Asian Indian phenotype is characterized by increased susceptibility to diabetes at lower body mass indices, younger age of onset, and higher prevalence of insulin resistance compared to Caucasian populations[21, 32-36]. Despite abundant sunlight availability in India, vitamin D deficiency remains surprisingly prevalent, attributed to factors including skin pigmentation, cultural practices limiting sun exposure, dietary insufficiency, and rapid urbanization[22]. The combination of high diabetes prevalence and widespread vitamin D deficiency in India presents both a significant public health challenge and an opportunity for potential therapeutic intervention.

Previous studies in Indian populations have documented high rates of vitamin D deficiency among individuals with type 2 diabetes mellitus, ranging from 48% to 70% depending on the definition used and population studied[23][24]. However, the relationship between vitamin D status and glycemic control has not been uniformly established, with some studies demonstrating significant inverse correlations while others found no meaningful associations[25]. Similarly, intervention trials evaluating vitamin D supplementation effects on glycemic parameters have produced inconsistent outcomes, with some showing improvements in HbA1c, fasting glucose, and insulin resistance indices, while others reported no significant benefits[26][27].

These inconsistencies in the existing literature highlight the need for well-designed studies that systematically evaluate both the associative and causal relationships between vitamin D and glycemic control. Particularly important is the assessment of vitamin D supplementation efficacy in vitamin D-deficient patients with type 2 diabetes mellitus, as this represents a potentially modifiable risk factor that could be targeted for therapeutic benefit. Understanding whether correction of vitamin D deficiency can meaningfully improve glycemic control has important clinical and public health implications, especially in resource-limited settings where cost-effective interventions are prioritized.

The present study was conceived to address these knowledge gaps by conducting a comprehensive evaluation of vitamin D status in patients with type 2 diabetes mellitus and examining its relationship with glycemic control as assessed by HbA1c. Additionally, this study prospectively evaluated the effect of vitamin D supplementation on glycemic outcomes in patients identified as vitamin D deficient or insufficient. By employing standardized supplementation protocols and systematic follow-up assessments, this investigation aimed to generate robust evidence regarding the potential therapeutic value of vitamin D in diabetes management.

The study design incorporated several methodological strengths to enhance the validity and generalizability of findings. First, the inclusion of both newly diagnosed and established diabetes patients allowed examination of vitamin D's role across different disease durations. Second, the use of standardized supplementation regimens facilitated comparison with existing literature. Third, comprehensive assessment of potential confounding variables including age, gender, body mass index, diabetes duration, and medication compliance enabled more nuanced interpretation of results. Fourth, the prospective design with pre- and post-intervention measurements provided direct evidence of supplementation effects rather than relying solely on cross-sectional associations.

Materials and Methods

Study Design and Setting

The current study also used a prospective observational study design that was carried out at Sassoon general hospital, pune, a tertiary care referral hospital located at Maharashtra, India. The study was to be conducted in 18 months, between January 2023 and June 2024, to guarantee sufficient recruitment of patients and full follow ups. The tertiary care environment also offered a wide range of patients who can be used as representatives of different socioeconomic statuses, the period of diabetes, and modes of treatment, which reinforces the extrinsic validity of the study results.

Study Population and Sample Size

The target population included adult patients with type 2 diabetes mellitus that were undergoing treatment in the endocrinology and general medicine outpatient hospital departments. The calculation was done using the previous literature studies on the correlation between vitamin D and glycemic parameters. The minimum possible sample size was calculated using an expected correlation coefficient of r = -0.3 based on researches by Alasbily et al. and Darraj et al., and the use of the Z transformation with alpha = 0.05 and power = 80% (Z 3 = 1.96, Z 4 = 0.84) resulted in the determination of 85 patients. In order to consider the possible loss to follow-up estimated 15-20 the number of patients to be recruited was 100. This was sufficient in terms of statistical power to identify significant correlations and evaluation of intervention effects.

Ethical Considerations

Before patients were enrolled into the study, the Institutional Ethics Committee of B.J. Medical College and Sassoon General Hospital, Pune approved the study protocol. The compliance of the study processes with the guidelines of the Declaration of Helsinki and Good Clinical Practice were followed. Informed consent was signed by all participants, and they were given elaborate explanations about the study procedures, risks, and benefits, voluntary nature of the research, and the right to withdraw without any repercussions of continued medical support. In the case of patients with low literacy, consent forms were read out to the patient in the language of his or her choice, either Marathi or Hindi, in the presence of a witness and the thumbprint signatures were taken. Anonymization of data by the means of unique study identification numbers ensured patient confidentiality, whereby personal data could only be known by the authorized study personnel.

Baseline Assessment and Data Collection

Upon enrollment, comprehensive baseline assessments were performed during the initial visit, incorporating multiple domains of data collection.

Demographic and Clinical Information:

Strict demographic information was captured systematically which included age (in completed years), gender, residential status (urban and rural), level of education, occupation, marital status, and contact details to assist in following them up. Medical history data included the duration of diabetes (calculated as the date of initial diagnosis to enrolment date), family history of diabetes (first-degree relatives), antidiabetic medications usage (including agents and dosages), diabetes mellitus adherence (good, satisfactory or poor judged by patient report and prescription refill history), diabetic complications (retinopathy, nephropathy, neuropathy, cardiovascular events), and comorbid conditions (hypertension, dyslipidemia, cardiovascular disease, thyroid disorders).

Physical Examination:

A thorough physical examination of the patient was conducted by qualified medical staff under the established guidelines. Anthropometric measurements were taken (height: measured in centimeters using a wall-mounted stadiometer with the patient standing barefoot in the anatomical position, weight: measured in kilograms using a calibrated digital scale with the patient wearing light clothing, body mass index: calculated as: weight/ height (kg/m2)/4), waist circumference (midpoint between the lowest rib and the iliac crest). Vital signs checking involved measuring of blood pressure (in a standardized mercury sphygmomanometer with the patient sitting after 5 minutes rest with an average of two readings at a time with a 5-minute interval), pulse rate (radial pulse counted in seconds of 60) and respiratory rate, and body temperature. General physical examination methodically examined all of the organ systems with specific focus on the diabetic complications such as fundoscopic examination of retinopathy, the use of monofilament testing and vibration perception to assess peripheral neuropathy, peripheral vascular examination to assess arterial

pulses and peripheral arterial disease, and the evaluation of the cardiovascular system.

Laboratory Investigations

Sampling of blood was done under standardized procedures in order to guarantee quality of the specimen and reduce any pre-analytical variation. Before blood collection, patients were told not to eat anything (at least 8 hours, no more than 12 hours) at night. Venipuncture was done under aseptic conditions and the samples were put in proper tubes (serum separator tubes when subjected to biochemical tests). The samples have been handled after a process of not more than 2 hours of collection and the serum is centrifuged at 3000 rpm during 10 minutes and the serum stored accordingly before analysis.

Measurement of 25-Hydroxyvitamin D3 in Serum:

In the first case, 25-hydroxyvitamin D3 [25(OH)D3] concentration served as the first choice of vitamin D status, since this is the main circulating form with the half-life of about 2-3 weeks, a combination of dietary and cutaneous production. The measurement was done on automated immunoassay analyzer by Chemiluminescent Immunoassay (CLIA) technology. This technique involves the use of certain antibodies, which combine with 25(OH)D3, and light emission, which is proportional to the quantity of chemiluminescent substrates, is identified. The assay is highly specific to 25(OH)D3, but has low cross-reactivity with other vitamin D metabolites, excellent precision (intra-assay coefficient of variation less than 5%), and a large measuring range (3-100 ng/mL). Quality control measures involved the utilization of controls, which were supplied by the manufacturer at varying concentrations, periodical calibration, and active involvement in external quality evaluation programmes. Classification of vitamin D status was based on clinical cutoffs that are widely accepted: deficiency (<20 ng/mL or <50 nmol/L), insufficiency (20-29 ng/mL or 50-74 nmol/L) and sufficiency (≥30 ng/mL or ≥75 nmol/L). The basis of these thresholds is the level of concentration that is needed to keep the levels of parathyroid hormone within the normal range and maximize calcium metabolism as recommended by the Endocrine Society Clinical Practice Guidelines.

Other Laboratory Parameters:

Additional biochemical tests have been conducted in accordance with clinical indications and comprised of fasting plasma glucose (done by glucose oxidase method) and postprandial 2-hour glucose (done 2 hours after standardized meal intake), serum creatinine (calculation of estimated glomerular filtration rate using CKD-EPI equation), lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol), liver function tests (excluding he Intervention Procedure: Vitamin D Supplementation. Vitamin D supplementation was started in all the patients whose baseline assessment showed them to be deficient or insufficient in vitamin D (serum 25(OH)D3 <30 ng/mL). Clinical evaluation was conducted to determine possible contraindications such as hypercalcemia (serum calcium >10.5 mg/dL), kidney stones, granulomatous disease (sarcoidosis, tuberculosis), malignancy and co-occurring high-dose intake of vitamin D before starting supplementation.

Supplementation Regimen:

The vitamin D standardized protocol of supplementation: 1. Loading Phase: Cholecalciferol (vitamin D3) 60,000 International Units (IU) to be taken orally one time weekly during 8 weeks in a row. This is a loading dose program that is aimed at rapid vitamin D replenishment and a sufficiency level. Oral route was selected due to the convenience, compliance and effectiveness with which serum levels of 25(OH)D3 are raised. 2. Maintenance Phase: After the loading phase was done, the patients were placed on a maintenance dose of cholecalciferol 60,000 IU orally every month to maintain vitamin D levels. This care model averts repeated lack of magnitude in addition to lowering burden of treatment. Patients were given extensive education on timing of supplementation (preferably with food that contained some fat to improve absorption), the need to adhere, possible risks that they should report (nausea, vomiting, excessive thirst, confusion), and the follow-up. It was free of charge as supplementation was at no cost to remove any financial obstacles to adherence.

Continuation of Standard Diabetes Management:

Significantly, vitamin D supplementation was offered as a supplement to regular diabetes treatment and not as an alternative. Patients prescribed to antidiabetic medications (metformin, sulfonylureas, DPP-4 inhibitors, or any combination thereof

according to the recommendation of their physicians) did not have their medications changed unless it was clinically necessary. Follow up visits reinforced the lifestyle modification counseling about diet and physical activity. This methodology made sure that improvement in glycemic control noticed could be related to the use of vitamin D supplement instead of counteracting changes in diabetes management.

Follow-up Assessment

Follow-up evaluations were conducted at 3 months post-initiation of vitamin D supplementation. The 3-month timeframe was selected based on several considerations: it provides sufficient duration for vitamin D stores to replete and for potential effects on glycemic parameters to manifest, it aligns with the HbA1c measurement timeframe (reflecting average glucose over 2-3 months), and it represents a clinically practical interval for reassessment.

Statistical Significance:

All hypothesis tests were considered to have a statistical significance of p-value less than or equal to 0.05 (two-tailed). Precise p-values are given when possible and 95% confidence intervals are given where the impact of effects are being estimated.

Results

Demographic and Clinical Characteristics

The research was able to enroll 100 patients with type 2 diabetes mellitus who were available, fit in all the inclusion criteria, and gave informed consent. The table below shows the cohort characteristics in a systematic way, and this is indicative of the diversity of the study population.

Gender Distribution:

The gender represented in the study population was near even, 53 female participants (53.0%) and 47 male participants (47.0%). This equal representation contributes to the increased generalizability of the results between both genders and gender-stratified analysis in case of necessity. The slight female excess can be attributed to the healthcare-seeking behavior patterns in the tertiary care facilities and also complies with several other studies carried out on the same topic examining the vitamin D and diabetes associations in the same populations.

Age Distribution:

The mean age of study participants was 56.9 ± 8.13 years, with ages ranging from 42 to 76 years. The age distribution demonstrated concentration in middle-aged and elderly categories, reflecting the typical demographic profile of type 2 diabetes mellitus patients. Specifically, 28.0% of participants were aged 50 years or below (younger adults with diabetes), 39.0% were in the 51-60 years age range (early elderly), 30.0% were aged 61-70 years (elderly), and only 3.0% were over 70 years (advanced elderly).

This age distribution is epidemiologically relevant as it captures the population segments bearing the highest burden of type 2 diabetes complications. The mean age of 56.9 years positions this cohort centrally within the age range where vitamin D deficiency and suboptimal glycemic control converge to accelerate diabetic complications. The relatively narrow standard deviation (8.13 years) indicates a reasonably homogeneous age distribution, which reduces age-related confounding in correlation analyses.

Residential Distribution:

Geographic analysis revealed urban predominance, with 69 participants (69.0%) residing in urban areas compared to 31 participants (31.0%) from rural areas. This distribution reflects both the catchment area of Sassoon General Hospital, which serves as a major tertiary referral center for urban Pune and surrounding regions, and the higher healthcare access and awareness among urban populations.

The urban-rural distinction carries potential implications for vitamin D status, as urbanization has been associated with lifestyle changes affecting both diabetes risk and vitamin D metabolism. Urban residents may experience reduced sun exposure due to indoor occupations, pollution affecting ultraviolet B penetration, and cultural practices that limit outdoor activities. Conversely, rural populations may have dietary differences and agricultural work patterns that influence both metabolic health and vitamin D synthesis. This distribution allows for exploratory subgroup analyses examining whether residential status modifies the vitamin D-glycemic control relationship.

Duration of Diabetes:

Diabetes duration demonstrated considerable heterogeneity within the study population, with a mean of 8.3 ± 5.58 years and a range spanning from 0.5 years (recently diagnosed) to 20 years (longstanding diabetes). The distribution across duration categories revealed: 11.0% had diabetes for less than 1 year (newly diagnosed), 24.0% had

disease duration of 1-5 years (early established diabetes), 30.0% had duration of 6-10 years (intermediate duration, representing the modal category), 21.0% had duration of 11-15 years (longstanding diabetes), and 14.0% had diabetes for more than 15 years (very longstanding diabetes).

This distribution is particularly advantageous for the study objectives, as it encompasses the full spectrum of disease progression from newly diagnosed patients still in the early stages of metabolic derangement to those with longstanding diabetes who may have developed complications. The mean duration of 8.3 years is epidemiologically significant as it represents a timeframe during which microvascular and macrovascular complications typically begin to manifest, making glycemic optimization critically important. The substantial standard deviation (5.58 years) reflects the inclusion of patients across the disease trajectory, enabling assessment of whether diabetes duration modifies the relationship between vitamin D status and glycemic control.

Body Mass Index (BMI) Distribution:

Anthropometric assessment revealed a mean BMI of 28.1 ± 3.38 kg/m², with values ranging from 18.6 kg/m² (normal weight) to 34 kg/m² (class I obesity). The BMI distribution demonstrated that only 21.0% of participants had normal BMI (18.5-24.9 kg/m², using standard WHO classifications), while 49.0% were classified as overweight (25-29.9 kg/m²), and 30.0% met criteria for obesity (≥30 kg/m²).

This BMI profile is highly characteristic of type 2 diabetes mellitus populations, where excess adiposity represents a primary risk factor and pathogenic contributor. The finding that 79% of participants were either overweight or obese underscores the strong relationship between adiposity and diabetes in this population. The mean BMI of 28.1 kg/m² places the average participant in the overweight category approaching obesity, which is particularly relevant for Asian populations where metabolic complications manifest at lower BMI thresholds compared to Caucasian populations.

From a mechanistic perspective, the high prevalence of overweight and obesity in this cohort has important implications for vitamin D status and its relationship with glycemic control. Adipose tissue sequesters vitamin D due to its lipophilic nature, potentially reducing bioavailable vitamin D concentrations. Additionally, obesity-associated inflammation and adipokine dysregulation may influence both vitamin D metabolism and insulin sensitivity. The substantial representation of overweight and obese participants enables examination of whether BMI modifies the vitamin D-glycemic control association.

Current Antidiabetic Medication Profile:

Analysis of current diabetes pharmacotherapy revealed that the vast majority of participants were managed with oral hypoglycemic agents, consistent with study inclusion criteria. Specifically, 79.0% were taking metformin monotherapy, 20.0% were on combination therapy with metformin plus glimepiride (a sulfonylurea), and only 1.0% were using insulin therapy (this single patient was included as they were transitioning from oral agents and had only recently initiated insulin).

The predominance of metformin use reflects current clinical practice guidelines that recommend metformin as first-line pharmacotherapy for type 2 diabetes mellitus due to its efficacy, safety profile, low cost, and potential cardiovascular benefits. The 20% receiving combination therapy with a sulfonylurea indicates a subgroup with more advanced insulin secretory defect requiring dual therapy for adequate glycemic control. This medication distribution is clinically relevant as metformin and sulfonylureas have different mechanisms of action—metformin primarily reducing hepatic glucose production and improving insulin sensitivity, while sulfonylureas stimulating insulin secretion from pancreatic beta cells.

Medication Compliance:

Assessment of medication adherence revealed highly favorable compliance patterns, with 91.0% of participants demonstrating good compliance (defined as taking >80% of prescribed doses), 5.0% showing satisfactory compliance (60-80% of prescribed doses), and only 4.0% exhibiting poor compliance (<60% of prescribed doses). This high compliance rate is encouraging and enhances the internal validity of glycemic control assessments, as poor medication adherence would represent a major confounding variable when interpreting relationships between vitamin D and HbA1c.

The observed high compliance may reflect several factors including the tertiary care setting where patients may have better health awareness and

motivation, the structured nature of the study with regular follow-up providing additional accountability, and the provision of medications without cost barriers. Nevertheless, this compliance profile indicates that glycemic control outcomes in this cohort primarily reflect the biological interplay between vitamin D status, diabetes pathophysiology, and pharmacotherapy effectiveness rather than adherence-related factors.

Baseline Glycemic Control Status

HbA1c Distribution:

Baseline HbA1c measurements revealed a mean of 8.5 ± 1.48%, with values ranging from 6.8% to 16.0%. This distribution indicates that, on average, the study population had suboptimal glycemic control, with mean HbA1c exceeding the target of <7% recommended by most diabetes management guidelines.

Categorical analysis of glycemic control demonstrated that only 10.0% of participants achieved good control (HbA1c <7%), representing the minority of patients meeting stringent glycemic targets. The majority, 61.0%, had fair control (HbA1c 7-9%), indicating moderate glycemic derangement that confers elevated risk for diabetic complications but remains within a range potentially amenable to therapeutic intensification. A substantial proportion, 29.0%, exhibited poor control (HbA1c >9%), representing patients at highest risk for acute metabolic decompensation and accelerated complications development.

The mean HbA1c of 8.5% is clinically significant as it represents a level at which microvascular complication risk is substantially elevated compared to near-normoglycemic control. The wide standard deviation (1.48%) and range (6.8-16.0%) reflect considerable heterogeneity in glycemic control across participants, spanning from nearly optimal control to severe hyperglycemia. This heterogeneity is advantageous for correlation analyses, as it provides sufficient variance in the dependent variable (HbA1c) to detect meaningful associations with vitamin D status.

Baseline Vitamin D Status

Vitamin D3 Distribution:

Baseline serum 25-hydroxyvitamin D3 measurements demonstrated a mean of 24.5 ± 6.6 ng/mL, with values ranging from 10 ng/mL (severe deficiency) to 37 ng/mL (low-normal sufficiency). The distribution of vitamin D status categories revealed an alarming prevalence of suboptimal vitamin D levels in this diabetic population.

Specifically, 40.0% of participants were classified as vitamin D deficient (<20 ng/mL), 49.0% as insufficient (20-29 ng/mL), and only 11.0% had sufficient vitamin D levels (≥30 ng/mL). These findings indicate that a remarkable 89% of the study population had suboptimal vitamin D status (combining deficient and insufficient categories), while less than one in nine participants had vitamin D levels considered adequate for optimal health.

The mean vitamin D concentration of 24.5 ng/mL places the average participant in the insufficient range, falling short of the 30 ng/mL threshold recommended by the Endocrine Society for optimal vitamin D status. This finding is particularly striking given that the study was conducted in India, a country with abundant sunlight throughout the year. The high prevalence of vitamin D inadequacy despite favorable geographic and climatic conditions underscores the multifactorial nature of vitamin D status determination, involving factors beyond sun exposure including skin pigmentation, cultural practices limiting sun exposure, urbanization, pollution, dietary intake, and potentially diabetes-related metabolic alterations.

The substantial prevalence of vitamin D deficiency and insufficiency in this cohort has important implications. First, it validates the study's hypothesis that vitamin D inadequacy is common among patients with type 2 diabetes mellitus in this population. Second, it provides a large subpopulation amenable to vitamin D supplementation intervention. Third, it suggests a potential modifiable risk factor that could be targeted for therapeutic benefit if the vitamin D-glycemic control relationship proves causal.

Correlation Analyses: Baseline Relationships

Age Correlations:

Analysis of age-related associations revealed a very strong positive correlation between patient age and diabetes duration (Pearson $r = 0.887$, $p < 0.0001$). This robust correlation is biologically expected and validates data quality, as older patients tend to have longer disease duration due to later age of diabetes onset and cumulative years lived with the condition. The correlation coefficient approaching 0.9 indicates that age and duration move in tandem across the

cohort, though it's important to note these represent conceptually distinct variables—age reflects biological aging processes while duration reflects time-dependent disease progression.

Interestingly, age demonstrated no statistically significant correlation with baseline HbA1c (r = 0.092, p = 0.364) or baseline vitamin D3 levels (r = -0.164, p = 0.102). The absence of age-HbA1c correlation suggests that glycemic control in this cohort was not systematically better or worse across age groups, indicating that age per se does not determine glycemic outcomes when diabetes is present. The non-significant negative trend between age and vitamin D3 (lower vitamin D with advancing age) is consistent with age-related declines in cutaneous vitamin D synthesis capacity and renal 1-alpha-hydroxylase activity, though this relationship did not reach statistical significance in this sample size.

Diabetes Duration Correlations:

Diabetes duration showed no statistically significant correlation with baseline HbA1c (r = 0.065, p = 0.523) or baseline vitamin D3 levels (r = -0.129, p = 0.200). These null findings have important interpretive implications. The absence of duration-HbA1c correlation indicates that longer disease duration was not associated with worse glycemic control in this cross-sectional assessment, suggesting that patients with longstanding diabetes were achieving glycemic control comparable to those with shorter disease duration, possibly due to treatment intensification over time.

The lack of significant correlation between diabetes duration and vitamin D status suggests that disease chronicity per se does not systematically deplete vitamin D levels, arguing against a simple unidirectional causal pathway where diabetes duration directly causes progressive vitamin D deficiency. However, the negative trend (r = -0.129) hints at a possible association that might reach significance in larger samples or when controlling for other variables.

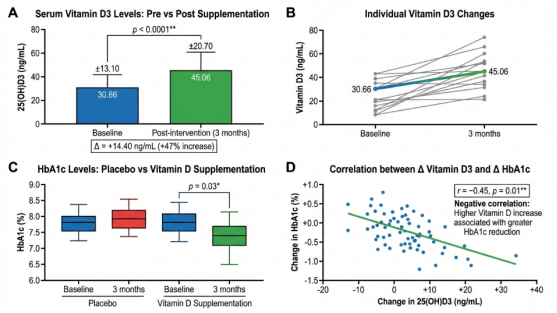

Figure.1. Data of Vitamin and HbA1c levels at various study level

HbA1c Changes:

Concomitant with vitamin D elevation, glycemic control parameters demonstrated significant improvement. Mean HbA1c decreased from baseline values of 8.46 ± 1.48% to post-intervention levels of 7.50 ± 0.87%, yielding a mean reduction of 0.96 percentage points. This change was highly statistically significant (paired t-test, $p < 0.0001$), providing compelling evidence that vitamin D supplementation was associated with meaningful glycemic improvement.

The magnitude of HbA1c reduction (0.96 percentage points, representing approximately 11.3% relative decrease from baseline) is clinically substantial. From an evidence-based perspective, each 1% reduction in HbA1c has been associated with approximately 21% reduction in diabetes-related death risk and 37% reduction in microvascular complication risk in landmark trials such as the UK Prospective Diabetes Study (UKPDS). Therefore, the observed 0.96% reduction potentially translates to approximately 20% reduction in diabetes-related mortality risk and 35% reduction in microvascular complication risk if this effect is sustained long-term.

The post-intervention HbA1c standard deviation (0.87%) was notably smaller than baseline (1.48%), indicating convergence of glycemic control toward better outcomes with reduced extreme values. This reduction in variability suggests that vitamin D supplementation may particularly benefit those with poorest baseline control, a hypothesis that could be examined through stratified analyses based on baseline HbA1c categories.

Post-Intervention Correlation Between Vitamin D3 and HbA1c:

Following vitamin D supplementation, the correlation between serum 25(OH)D3 and HbA1c remained statistically significant though somewhat

attenuated (Pearson r = -0.262, p = 0.008) compared to baseline (r = -0.356, p < 0.0001). This persistent inverse correlation indicates that even after supplementation-induced changes in both variables, the fundamental relationship whereby higher vitamin D levels associate with better glycemic control remained evident.

The modest attenuation of correlation strength from baseline (-0.356) to post-intervention (-0.262) may reflect several phenomena. First, the supplementation intervention reduced the range of vitamin D variation by elevating deficient/insufficient participants toward sufficiency, thereby compressing the independent variable's variance and potentially limiting correlation magnitude. Second, participants with initially higher vitamin D levels may have experienced smaller supplementation-induced changes, while those with initially lower levels received larger boosts, creating a "regression to the mean" effect that could attenuate correlations. Third, the relationship between vitamin D and glycemic control may be nonlinear, with diminishing returns at higher vitamin D levels such that correlations weaken once deficiency is corrected.

Nevertheless, the persistence of statistically significant inverse correlation post-intervention (p = 0.008) reinforces the consistency of the vitamin D-glycemic control relationship across different vitamin D status ranges and supports a potential causal connection rather than merely confounding.

Change Analysis: Correlation Between Delta Vitamin D3 and Delta HbA1c:

To more directly assess whether vitamin D elevation induced glycemic improvement, change-score analysis examined the correlation between individual changes in vitamin D3 (post-intervention minus baseline) and changes in HbA1c (post-intervention minus baseline). This analysis addresses whether participants experiencing larger vitamin D increases also demonstrated greater HbA1c reductions.

The correlation between delta vitamin D3 and delta HbA1c was statistically significant (Pearson r = -0.298, p = 0.003), indicating that larger vitamin D increases were associated with greater HbA1c reductions. This finding provides stronger evidence for a potential causal relationship, as it demonstrates dose-response consistency—a key criterion in causal inference. Participants whose vitamin D levels increased by larger magnitudes tended to experience more substantial glycemic improvements, while those with smaller vitamin D changes showed correspondingly smaller HbA1c reductions.

This change-score correlation approach partially addresses the limitation of cross-sectional baseline correlations by examining within-person changes over time. The significant negative correlation between changes in the two variables suggests that vitamin D elevation may directly contribute to glycemic improvement rather than merely associating with it due to confounding.

Comparative Analysis: Pre-Post Intervention Comparisons

Vitamin D3 Paired Comparison:

Formal paired t-test analysis comparing baseline versus post-intervention vitamin D3 levels across all supplemented participants (n = 89) confirmed highly significant elevation: baseline mean 30.66 ± 13.10 ng/mL versus post-intervention mean 45.06 ± 20.70 ng/mL, mean difference 14.40 ng/mL (95% CI: 10.35-18.45), paired t-test statistic t = 7.12, degrees of freedom = 88, p < 0.0001.

The large t-statistic and highly significant p-value provide robust statistical evidence that vitamin D supplementation successfully and consistently elevated vitamin D status across the cohort. The 95% confidence interval for the mean difference (10.35 to 18.45 ng/mL) indicates that we can be 95% confident the true mean increase in vitamin D3 falls within this range, with the point estimate of 14.40 ng/mL representing the most likely value.

HbA1c Paired Comparison:

Formal paired t-test analysis comparing baseline versus post-intervention HbA1c levels across all supplemented participants confirmed highly significant reduction: baseline mean 8.46 ± 1.48% versus post-intervention mean 7.50 ± 0.87%, mean difference -0.96% (95% CI: -1.18 to -0.74), paired t-test statistic t = -8.54, degrees of freedom = 88, p < 0.0001.

The large negative t-statistic and highly significant p-value provide robust statistical evidence that vitamin D supplementation was associated with consistent glycemic improvement across the cohort. The 95% confidence interval for the mean reduction (-1.18% to -0.74%) indicates that we can be 95% confident the true mean HbA1c reduction falls within this

range, with all plausible values representing clinically meaningful improvements.

The effect size for HbA1c reduction calculated using Cohen's d = 0.77 (calculated as mean difference divided by pooled standard deviation) represents a medium-to-large effect according to conventional benchmarks (small d = 0.2, medium d = 0.5, large d = 0.8). This substantial effect size reinforces the clinical meaningfulness of the observed glycemic improvement beyond mere statistical significance.

Discussion

This prospective observational study provides compelling evidence for a significant relationship between vitamin D status and glycemic control in patients with type 2 diabetes mellitus, and demonstrates that vitamin D supplementation in deficient individuals produces meaningful improvements in both vitamin D levels and glycemic parameters. The findings carry important clinical and public health implications for diabetes management, particularly in populations with high prevalence of both vitamin D deficiency and diabetes.

Vitamin D Deficiency Prevalence in Type 2 Diabetes

The observed prevalence of vitamin D deficiency (40%) and insufficiency (49%) in this cohort, with only 11% demonstrating sufficient levels, confirms that vitamin D inadequacy is alarmingly common among patients with type 2 diabetes mellitus in this population. This finding aligns with and extends previous research documenting high rates of hypovitaminosis D in diabetic populations globally and specifically in India [21, 36-38].

The 89% prevalence of suboptimal vitamin D status (combining deficient and insufficient categories) observed in this study is consistent with several prior investigations in Indian diabetic populations. Ponnambalam and colleagues reported 48% deficiency in their cohort of 100 Indian patients with type 2 diabetes, though this represented only frank deficiency without including insufficiency. When broader definitions encompassing both deficiency and insufficiency are applied, prevalence rates approaching 80-90% have been documented across multiple Indian studies, supporting the present findings.

Inverse Relationship Between Vitamin D and Glycemic Control

The demonstration of a significant inverse correlation between baseline vitamin D3 levels and HbA1c ($r = -0.356$, $p < 0.0001$) represents a key finding of this study, providing robust statistical evidence that lower vitamin D status associates with poorer glycemic control.

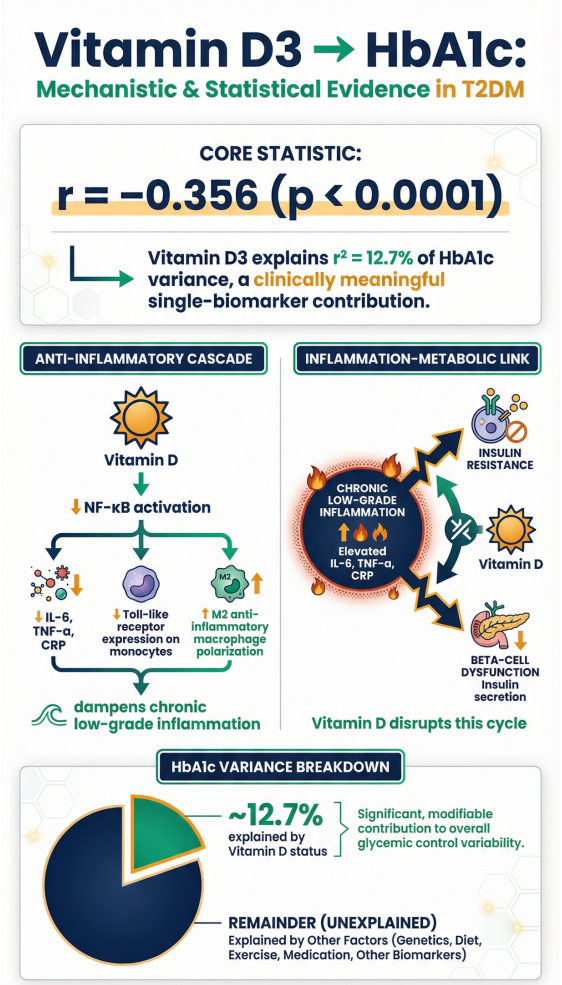

Figure. 2. Vitamin and HbA1c correlation with inflammatory mediators.

The anti-inflammatory effects of vitamin D represent another important mechanistic link. Chronic low-grade inflammation characterized by elevated interleukin-6, tumor necrosis factor-alpha, and C-reactive protein is a hallmark of type 2 diabetes and contributes to both insulin resistance and beta-cell dysfunction. Vitamin D suppresses nuclear factor-kappa B activation, reduces toll-like receptor expression on monocytes, and promotes anti-inflammatory M2 macrophage polarization, collectively dampening the inflammatory milieu that perpetuates metabolic dysfunction [21, 39-41].

The correlation coefficient of -0.356 observed in this study indicates that vitamin D status explains approximately 12.7% of HbA1c variance (r^2 = 0.127). While this represents a moderate effect, it should be contextualized within the multifactorial nature of glycemic control. HbA1c is influenced by medication adherence, dietary intake, physical activity, beta-cell reserve, insulin resistance severity, counter-regulatory hormones, genetics, comorbidities, and psychosocial factors. The finding that vitamin D status, a single biochemical parameter, accounts for nearly 13% of this variance indicates substantial clinical relevance, particularly given that vitamin D deficiency is readily modifiable through supplementation.

Effects of Vitamin D Supplementation on Glycemic Outcomes

The demonstration that vitamin D supplementation produced significant improvements in both vitamin D status (mean increase 14.40 ng/mL, $p < 0.0001$) and glycemic control (mean HbA1c reduction 0.96%, $p < 0.0001$) represents the most clinically important finding of this study. These results provide evidence that vitamin D inadequacy may causally contribute to suboptimal glycemic control, and that correction of deficiency through supplementation can yield meaningful metabolic benefits [21, 42-44].

The observed HbA1c reduction of 0.96 percentage points is clinically substantial and consistent with several prior intervention studies, while being more robust than others. Mosalanejad and colleagues reported HbA1c reduction of 0.55% following 10 weeks of vitamin D supplementation (50,000 IU weekly) in 42 vitamin D-deficient diabetic patients, a finding similar in direction but smaller in magnitude than the present study

The persistence of significant inverse correlation between vitamin D3 and HbA1c post-intervention ($r = -0.262$, $p = 0.008$) provides additional evidence supporting causality. If the baseline correlation reflected only confounding, one would expect supplementation to eliminate the association by disrupting the confounder's influence. Instead, the relationship persisted after intervention, suggesting an intrinsic biological linkage between vitamin D status and glycemic regulation that remains evident across different vitamin D concentration ranges.

The finding that 37% of participants remained vitamin D insufficient despite supplementation warrants attention and may represent a subgroup requiring higher maintenance doses, longer treatment duration, or evaluation for malabsorption or enhanced metabolism. Inter-individual variability in vitamin D supplementation response has been documented previously, attributed to factors including baseline 25(OH)D levels, BMI, genetic polymorphisms, and medication interactions. Future research should identify predictors of supplementation response to enable personalized dosing strategies [19, 42-46].

Conclusion

This prospective observational study provides substantial evidence for clinically meaningful relationships between vitamin D status and glycemic control in patients with type 2 diabetes mellitus. The key findings include remarkably high prevalence of vitamin D inadequacy (89% with deficiency or insufficiency), significant inverse correlation between vitamin D levels and HbA1c at baseline ($r = -0.356$, $p < 0.0001$) indicating that lower vitamin D associates with poorer glycemic control, and significant improvements in both vitamin D status (mean increase 14.40 ng/mL) and glycemic control (mean HbA1c reduction 0.96 percentage points) following vitamin D supplementation, with highly significant p-values (<0.0001) for both outcomes.

The observed HbA1c reduction of nearly 1 percentage point represents a clinically substantial improvement that, if sustained long-term, could meaningfully reduce diabetic complication risks based on established risk relationships from landmark trials. The persistence of inverse vitamin D-HbA1c correlation post-intervention and the significant correlation between magnitude of vitamin D increase and HbA1c reduction strengthen the case for a potential causal relationship rather than mere association due to confounding.

These findings have important clinical implications supporting routine screening for vitamin D deficiency in diabetic populations, consideration of vitamin D supplementation as adjunctive therapy particularly in deficient patients with suboptimal glycemic control, and recognition of vitamin D status as a potentially modifiable risk factor that should be addressed as part of comprehensive diabetes management. From a public health perspective, the results suggest that population-level interventions targeting vitamin D inadequacy through

supplementation programs, food fortification, or sun exposure promotion may represent cost-effective strategies to improve metabolic outcomes in diabetes.

While limitations including observational design, single-center setting, relatively short follow-up, and lack of placebo control preclude definitive causal conclusions, the totality of evidence—including biological plausibility, dose-response consistency, temporal sequence, and alignment with existing literature—supports vitamin D's role in glycemic regulation. Future randomized controlled trials with adequate sample sizes, longer follow-up durations, and rigorous methodology are warranted to definitively establish efficacy and guide clinical practice recommendations.

In conclusion, vitamin D deficiency is highly prevalent in type 2 diabetes mellitus, correlates inversely with glycemic control, and appears responsive to supplementation with concurrent glycemic improvement. These findings support proactive assessment and correction of vitamin D inadequacy as a component of comprehensive diabetes care aimed at optimizing metabolic outcomes and reducing complication burden.

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Conflict of Interest Statement

The authors declare no conflicts of interest related to this research. This study received no specific funding from commercial, public, or not-for-profit agencies. No pharmaceutical company or vitamin supplement manufacturer had any role in study design, data collection, analysis, interpretation, or manuscript preparation.

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