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Original Article

Impact of Vitamin D Supplementation on HbA1c Levels in Type 2 Diabetes Mellitus Patients with Asymptomatic Vitamin D Deficiency: A Prospective Study.

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ABSTRACT

Background: Vitamin D deficiency is highly prevalent among patients with type 2 diabetes mellitus (T2DM) and has been associated with impaired insulin secretion, increased insulin resistance, and poor glycemic control. Emerging evidence suggests that vitamin D supplementation may improve metabolic outcomes in diabetic patients; however, findings remain inconsistent across different populations and study settings.

Objective: To evaluate the effect of vitamin D supplementation on glycated hemoglobin (HbA1c) levels in patients with T2DM and asymptomatic vitamin D deficiency.

Methods: This prospective interventional study was conducted at the Department of Diabetes, Endocrinology and Metabolic Diseases, Hayatabad Medical Complex, Peshawar, Pakistan, from January 2023 to January 2024. A total of 250 patients with T2DM and serum vitamin D levels below 20 ng/mL were enrolled, of whom 128 completed follow-ups. Participants were allocated into two groups: Group A received metformin therapy alone, while Group B received metformin plus oral vitamin D supplementation (200,000 IU monthly for three months). HbA1c and serum vitamin D levels were measured at baseline and after three months. Data were analyzed using SPSS version 24.0, and a p-value <0.05 was considered statistically significant.

Results: Among the 128 participants analyzed, baseline characteristics were comparable between groups. Patients receiving vitamin D supplementation demonstrated a significantly greater reduction in HbA1c levels compared with those receiving metformin alone ($p<0.05$). Serum vitamin D concentrations increased significantly in the intervention group, whereas no meaningful changes were observed in the control group.

Conclusion: Vitamin D supplementation significantly improves glycemic control in T2DM patients with asymptomatic vitamin D deficiency and may serve as a beneficial adjunct to standard antidiabetic therapy.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, resulting in persistent hyperglycemia. It represents a major global public health challenge, with a steadily increasing prevalence in both developed and developing countries. Poor glycemic control is associated with serious long-term complications, including cardiovascular disease, nephropathy, neuropathy, and retinopathy, leading to increased morbidity and mortality [1,2]. Vitamin D deficiency is frequently observed among patients with T2DM and has emerged as a potential factor influencing glucose metabolism. Beyond its established role in calcium homeostasis and bone health, vitamin D is involved in pancreatic β-cell function and insulin sensitivity. The presence of vitamin D receptors in pancreatic tissue and insulin-responsive peripheral tissues suggests a possible role in maintaining glucose homeostasis [3,4]. Several studies have demonstrated an association between low serum vitamin D levels and poor glycemic control in patients with T2DM. Vitamin D deficiency may impair insulin secretion, increase insulin resistance, and promote inflammatory pathways that contribute to metabolic dysfunction [5,6]. Consequently, vitamin D supplementation has attracted considerable attention as a potential adjunctive therapy in diabetes management. Recent interventional studies have reported improvements in HbA1c levels and insulin sensitivity following vitamin D supplementation, although findings remain inconsistent across different populations and study designs [7,8]. Given the high prevalence of both T2DM and vitamin D deficiency in Pakistan, further investigation is warranted. Therefore, this study aimed to evaluate the effect of vitamin D supplementation on glycemic control, measured by HbA1c levels, in patients with type 2 diabetes mellitus and asymptomatic vitamin D deficiency.

MATERIALS AND METHODS

Study Design and Setting

This prospective interventional comparative study was conducted at the Department of Diabetes, Endocrinology and Metabolic Diseases, Hayatabad Medical Complex, Peshawar, Pakistan, from January 2023 to January 2024.

Sample Size

The sample size was calculated using OpenEpi version 3.01 at a 95% confidence level and 80% study power, considering an expected difference in HbA1c reduction between the intervention and control groups based on previously published studies. The minimum required sample size was estimated to be 120 participants. To compensate for possible dropouts and loss to follow-up, 250 patients with type 2 diabetes mellitus (T2DM) were initially enrolled. After applying the eligibility criteria and accounting for attrition during follow-up, 128 participants completed the study and were included in the final analysis.

Inclusion Criteria

Patients aged 30–60 years with a confirmed diagnosis of T2DM, HbA1c levels between 7.0% and 9.5%, serum vitamin D levels below 20 ng/mL, and receiving stable metformin therapy for at least three months were included. Written informed consent was obtained from all participants.

Exclusion Criteria

Patients with type 1 diabetes mellitus, chronic kidney disease, chronic liver disease, malabsorption syndromes, pregnancy, endocrine disorders affecting calcium metabolism, severe systemic illness, or current vitamin D supplementation were excluded. Individuals unwilling to participate or unable to complete follow-up were also excluded.

Data Collection Procedure

Eligible participants were allocated into two groups. Group A received metformin therapy (1000 mg daily), while Group B received metformin therapy along with oral vitamin D supplementation (200,000 IU monthly for three months). Baseline demographic characteristics, HbA1c levels, and serum vitamin D concentrations were recorded at enrollment. Follow-up assessments were performed after three months using standardized laboratory methods.

Ethical Approval

Ethical approval was obtained from the Hospital Ethics Committee and Postgraduate Studies Committee, Hayatabad Medical Complex, Peshawar (**Ref No. 799/HEC/B&PSC/04/2022**). The study was conducted in accordance with the principles of the Declaration of Helsinki.

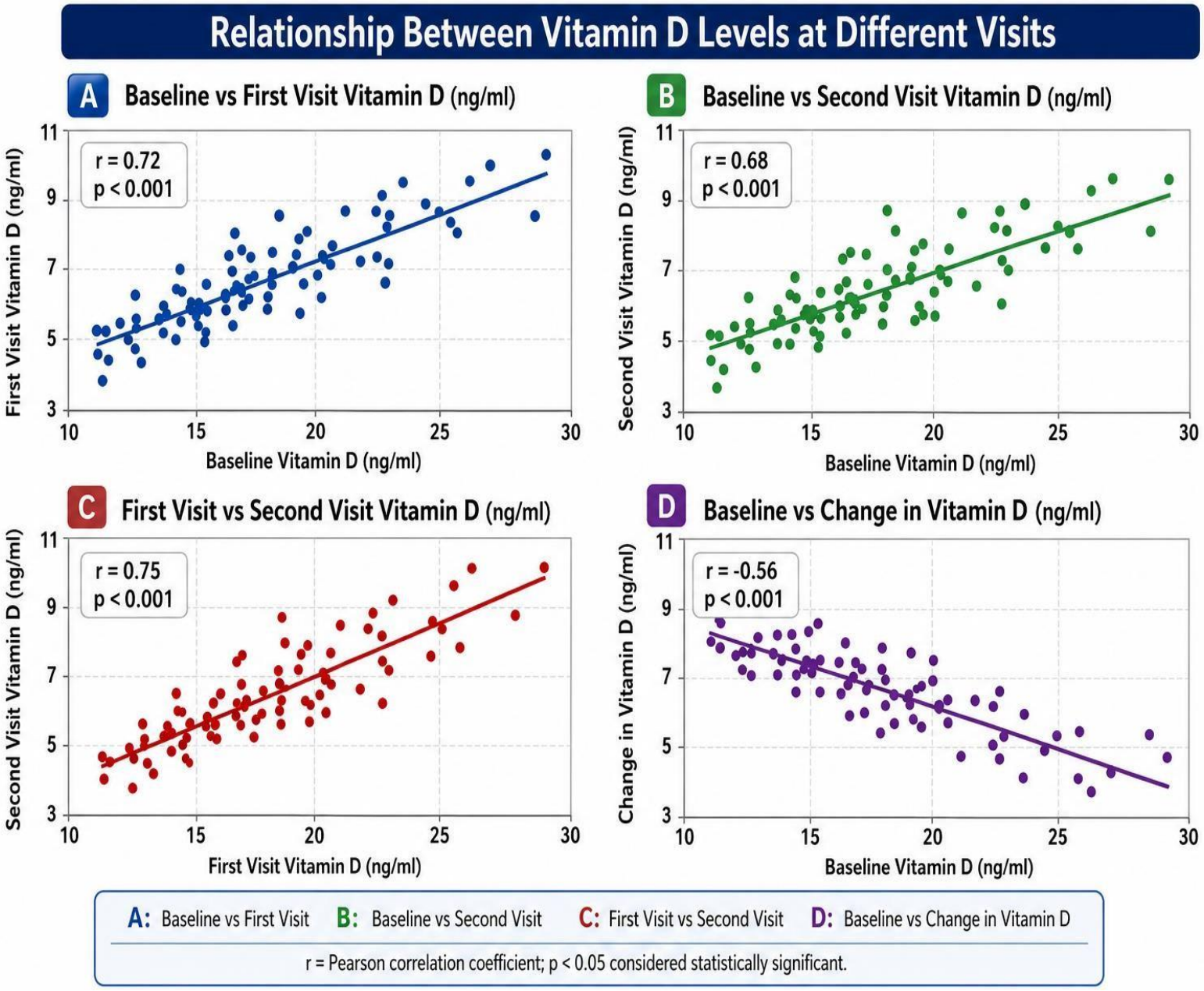
Statistical Analysis

Data were analyzed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Independent-sample t-tests and paired t-tests were applied where appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 128 participants completed the study and were included in the final analysis, with 64 patients in each study group. Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences observed (Table 1). Following the three-month intervention period, patients receiving metformin plus vitamin D supplementation (Group B) demonstrated a significantly greater reduction in HbA1c levels compared with those receiving metformin alone (Group A). The mean HbA1c level decreased from 7.30 ± 0.65% to 6.62 ± 0.71% in Group B, whereas only a modest reduction was observed in Group A (Table 2). Serum vitamin D concentrations increased significantly among patients receiving vitamin D supplementation, while only minimal changes were observed in the control group. Similarly, random blood sugar levels improved in the intervention group compared with Group A (Table 3). Correlation analysis revealed significant associations between vitamin D levels measured at different follow-up visits. Strong positive correlations were observed between baseline and first-visit vitamin D levels, baseline and second-visit vitamin D levels, and first-visit and second-visit vitamin D levels. A significant negative correlation was observed between baseline vitamin D levels and the magnitude of change in vitamin D concentration during follow-up (Figure 1). Overall, vitamin D supplementation was associated with improved glycemic control and increased serum vitamin D levels, supporting its potential role as an adjunctive therapy in the management of type 2 diabetes mellitus.

Figure 1. Relationship Between Vitamin D Levels at Different Visits



A. Baseline vs First Visit Vitamin D (ng/mL): Demonstrates a strong positive correlation between baseline serum vitamin D levels and first-visit vitamin D levels ($r = 0.72$, $p < 0.001$).

B. Baseline vs Second Visit Vitamin D (ng/mL): Shows a significant positive correlation between baseline vitamin D levels and second-visit vitamin D levels ($r = 0.68$, $p < 0.001$).

C. First Visit Vs Second Visit Vitamin D (ng/mL): Illustrates a strong positive relationship between first-visit and second-visit vitamin D concentrations ($r = 0.75$, $p < 0.001$).

D. Baseline vs Change in Vitamin D (ng/mL): Demonstrates a significant negative correlation between baseline vitamin D levels and the magnitude of change in vitamin D levels during follow-up ($r = -0.56$, $p < 0.001$), indicating that participants with lower baseline vitamin D levels experienced greater increases following supplementation.

Table 1. Baseline Characteristics of Study Participants

Variable	Group A (Metformin) (n=64)	Group B (Metformin + Vitamin D) (n=64)	p-value*
Age (years), Mean ± SD	43.2 ± 5.8	44.1 ± 6.1	0.391
Male, n (%)	33 (51.6)	32 (50.0)	0.857
Female, n (%)	31 (48.4)	32 (50.0)	0.857
Baseline HbA1c (%), Mean ± SD	7.45 ± 0.72	7.30 ± 0.65	0.218
Baseline Vitamin D (ng/mL), Mean ± SD	17.2 ± 2.5	18.1 ± 2.7	0.057

*Independent-samples t-test for continuous variables and Chi-square test for categorical variables.

Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences observed.

Table 2. Changes in HbA1c Levels Following Intervention

Group	Baseline HbA1c (%) Mean ± SD	Final HbA1c (%) Mean ± SD	Mean Difference	95% CI	p-value†
Group A (Metformin)	7.45 ± 0.72	7.10 ± 0.68	−0.35	**−0.72 to 0.02**	0.061
Group B (Metformin + Vitamin D)	7.30 ± 0.65	6.62 ± 0.71	−0.68	−0.89 to −0.47	<0.001

†Paired t-test used for within-group comparison.

Patients receiving vitamin D supplementation demonstrated a significantly greater reduction in HbA1c levels compared with the metformin-only group.

Table 3. Changes in Serum Vitamin D and Random Blood Sugar (RBS) Levels

Parameter	Group A (Metformin) Mean ± SD	Group B (Metformin + Vitamin D) Mean ± SD	p-value‡
Baseline Vitamin D (ng/mL)	17.2 ± 2.5	18.1 ± 2.7	0.057
Final Vitamin D (ng/mL)	17.5 ± 2.6	21.8 ± 3.2	<0.001
Baseline RBS (mg/dL)	219 ± 12	221 ± 10	0.317
Final RBS (mg/dL)	200 ± 10	196 ± 8	0.018

‡Independent-samples t-test used for between-group comparisons.

Vitamin D supplementation significantly increased serum vitamin D levels and was associated with improved glycemic parameters compared with metformin therapy alone.

DISCUSSION

The present study evaluated the effect of vitamin D supplementation on glycemic control among patients with type 2 diabetes mellitus (T2DM) and asymptomatic vitamin D deficiency. The findings demonstrated that supplementation with vitamin D in addition to standard metformin therapy resulted in a significant reduction in HbA1c levels compared with metformin therapy alone. Furthermore, serum vitamin D concentrations increased significantly after supplementation, suggesting that correcting vitamin D deficiency may improve metabolic control in patients with T2DM. Vitamin D deficiency was highly prevalent among the study participants, which is consistent with previous reports indicating a substantial burden of hypovitaminosis D among individuals with diabetes mellitus [12,13]. Several epidemiological studies have demonstrated an inverse relationship between serum vitamin D levels and glycemic indices, supporting the hypothesis that vitamin D status may influence glucose metabolism. In the present study, lower baseline vitamin D levels were associated with poorer glycemic control, as reflected by higher HbA1c values. Similar findings have been reported by Omidian et al. and Penckofer et al., who observed significant associations between vitamin D deficiency and adverse metabolic outcomes in diabetic populations [14,15]. The biological plausibility of these findings is supported by the presence of vitamin D receptors in pancreatic β-cells and peripheral insulin-responsive tissues. Vitamin D plays an important role in regulating insulin secretion, enhancing insulin sensitivity, and maintaining intracellular calcium homeostasis, all of which are essential for normal glucose metabolism [16]. In addition, vitamin D possesses anti-inflammatory and immunomodulatory properties that may reduce cytokine-mediated insulin resistance, a key contributor to the pathogenesis of T2DM. The results of the current study are consistent with several interventional studies demonstrating beneficial effects of vitamin D supplementation on glycemic parameters. Bhatt et al. reported significant improvements in glycemic measures following vitamin D supplementation, while Cojic et al. observed favorable effects on metabolic markers among patients with T2DM [8,9]. Similarly, recent clinical investigations have shown that correction of vitamin D deficiency may improve insulin sensitivity and metabolic regulation, supporting its role as an adjunctive therapeutic strategy in diabetes management [17,18]. However, the available literature remains heterogeneous. Some studies have reported minimal or non-significant effects of vitamin D supplementation on HbA1c and other metabolic outcomes [10,11]. Differences in study design, duration of treatment, dosage regimens, baseline vitamin D status, ethnicity, and sample size may account for these inconsistencies. In the present study, vitamin D was administered as a monthly high-dose regimen, which was associated with significant improvement in serum vitamin D concentrations and glycemic control. Nevertheless, the magnitude of HbA1c reduction was modest, suggesting that vitamin D supplementation should be viewed as an adjunct rather than a replacement for established antidiabetic therapies [19]. Beyond glycemic control, vitamin D deficiency has been associated with an increased risk of cardiovascular disease, metabolic syndrome, diabetic neuropathy, and other chronic complications commonly observed in patients with T2DM [20,21]. Therefore, correction of vitamin D deficiency may provide broader clinical benefits extending beyond glucose regulation. Emerging evidence also suggests that vitamin D influences gene expression and oxidative stress.

pathways, and pancreatic β-cell function, potentially contributing to preservation of β-cell activity and improved long-term metabolic outcomes [22,23].Overall, the findings of this study support the growing body of evidence indicating that vitamin D supplementation may improve glycemic control in patients with T2DM and vitamin D deficiency. However, due to variations in study methodologies and patient populations, caution is warranted when generalizing these findings. Large multicenter randomized controlled trials with standardized supplementation protocols and longer follow-up periods are required to establish definitive clinical recommendations regarding the routine use of vitamin D supplementation in diabetes management.

LIMITATIONS

This study has several limitations. First, the sample size was relatively small, and only patients completing follow-up were analyzed, which may introduce selection bias. Second, all participants were receiving a similar treatment regimen, which limited comparisons with other therapeutic approaches. Third, vitamin D was administered monthly, and variations in absorption were not assessed. Additionally, factors such as diet, sun exposure, and physical activity were not controlled. Finally, long-term outcomes were not evaluated.

CONCLUSION

Vitamin D supplementation significantly improved HbA1c levels in patients with type 2 diabetes mellitus and vitamin D deficiency. These findings suggest that vitamin D may serve as a useful adjunct to standard antidiabetic therapy. However, due to variability in existing evidence, further large-scale, long-term studies are required to confirm its clinical effectiveness and establish clear treatment guidelines.

Authors' Contributions (ICMJE)

Aftab Khattak: Conceptualization, study design, supervision, manuscript review.

Ziaullah Khan: Data collection, statistical analysis, manuscript drafting.

Khalid Usman: Methodology development, interpretation of results, critical revision.

Tahir Ghaffar: Data validation, literature review, final manuscript editing.

All authors: Reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest: Not applicable.

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Ethical Statement

Ethical approval was obtained from the Hospital Ethics Committee, Hayatabad Medical Complex, Peshawar **(Ref. No:799/HEC/B&PSC/04/2022).**

Data Availability Statement

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

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