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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 common in patients with type 2 diabetes mellitus (T2DM) and may influence glycemic control.

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

Methods: A total of 250 patients were enrolled, of which 128 completed the study. Participants were divided into two groups: Group A (metformin only) and Group B (metformin plus vitamin D supplementation 200,000 IU/month for 3 months). HbA1c and vitamin D levels were assessed at baseline and follow-up. Statistical analysis was performed using SPSS version 20, with $p<0.05$ considered significant.

Results: A total of 128 patients were analyzed. Group B showed a significant reduction in HbA1c levels compared to Group A ($p<0.05$). Vitamin D levels increased significantly in the intervention group.

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

Keywords: Type 2 diabetes mellitus; vitamin D; HbA1c; metformin; glycemic control

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a long-term metabolic condition that is caused by insulin resistance and impaired insulin release, which results in chronic hyperglycemia. It is a significant health burden in the world and its prevalence is on the rise in both the developed and the developing world [1]. Long-term complications linked to poor glycemic control are cardiovascular disease, nephropathy, neuropathy, and retinopathy, which have a significant impact on morbidity and mortality [2].Vitamin D deficiency is becoming well-known as a comorbidity that may be found in T2DM patients. In addition to its conventional effects in the calcium homeostasis and bone metabolism, vitamin D has been observed to have an effect on glucose metabolism by modulating the functioning of the β-cells and the insulin sensitivity [3]. The fact that there are vitamin D receptors in pancreatic tissue and peripheral insulin-responsive tissues indicates a possible role in glycemic regulation [4].A number of studies have shown a correlation between poor glycemic control and low serum vitamin D levels in patients with T2DM [5]. Deficiency in Vitamin D can hinder the secretion of insulin and enhance insulin resistance and thus contribute to the exacerbation of hyperglycemia [6]. Moreover, vitamin D is known to modulate the inflammatory mechanisms that have an important contribution to the pathogenesis of insulin resistance and metabolic dysfunction [7].There has been a rise in clinical interest in the use of vitamin D supplementation as an adjunctive treatment in the management of diabetes in recent years. Improved HbA1c levels and insulin sensitivity after administering vitamin D have been reported in some interventional studies [8]. But the evidence is not consistent and other studies indicate little or no significant benefit [9]. These inconsistencies can be explained by variations in the study design, dosage, supplementation period, the baseline vitamin D status, and patient groups [10].Vitamin D deficiency is very common in some areas like Pakistan because of the lack of sun exposure, dietary habits and cultural behavior and thus is a significant health issue of public concern [11].This shortcoming could be of great importance in enhancing the glycemic control and the alleviation of diabetes-related complications.With the increasing T2DM burden and the possible effect of vitamin D on glucose metabolism, more research on the therapeutic effect of vitamin D is necessary. Thus, the purpose of this study was to determine the effect of vitamin D supplementation on the glycemic control, assessed by the level of HbA1c in patients with type 2 diabetes mellitus and asymptomatic vitamin D deficiency.

MATERIALS AND METHODS

This prospective study was conducted from January 2023 to January 2024 at Department of Diabetes, Endocrinology & Metabolic diseases, Hayat Abad Medical Complex, Peshawar, Pakistan. A total of 250 patients diagnosed with type 2 diabetes mellitus were enrolled, of which 128 completed the study. Eligible participants were adults aged 30–60 years with HbA1c levels between 7% and 9.5% and serum vitamin D levels below 20 ng/mL. Patients were divided into two groups: Group A received metformin (1000 mg daily), while Group B received metformin along with oral vitamin D supplementation (200,000 IU monthly for three months).Baseline and follow-up measurements included HbA1c and serum vitamin D levels. Patients were monitored over the study period, and outcomes were compared between the two groups to assess the effect of vitamin D supplementation on glycemic control.

INCLUSION CRITERIA

Participants aged 30–60 years with a confirmed diagnosis of type 2 diabetes mellitus, HbA1c levels between 7% and 9.5%, and serum vitamin D levels <20 ng/mL were included. Patients receiving stable metformin therapy and willing to participate with informed consent were eligible for enrollment.

EXCLUSION CRITERIA

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

DATA COLLECTION

Data were collected using a structured proforma. Baseline demographic characteristics, HbA1c levels, and serum vitamin D levels were recorded at enrollment and after three months of follow-up. All laboratory investigations were performed using standardized procedures in hospital laboratories to ensure accuracy and consistency of results.

ETHICAL APPROVAL STATEMENT

Ethical approval was obtained from the Hospital Ethics Committee/Board & Postgraduate Studies Committee, Hayatabad Medical Complex, Peshawar (**Ref. No. 799/HEC/B&PSC/04/2022, granted to Dr. Khalid Usman).**

STATISTICAL ANALYSIS

Data were analyzed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation. Paired and independent t-tests were used to compare within-group and between-group differences. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 128 patients completed the study and were included in the final analysis. The study population included both male and female participants, with a mean age ranging from 42 to 45 years. Baseline characteristics were comparable between the two groups. In Group A (metformin only), a slight reduction in HbA1c levels was observed; however, the change was not statistically significant. In contrast, Group B (metformin plus vitamin D supplementation) demonstrated a significant reduction in HbA1c levels after three months of treatment ($p<0.05$). Mean HbA1c levels decreased from 7.52% to 6.44% in male patients and from 7.01% to 6.80% in female patients in Group B.Serum vitamin D levels showed a significant increase in the intervention group following supplementation, whereas no significant change was observed in the control group.No significant differences were noted in serum calcium, phosphorus, or alkaline phosphatase levels between the two groups. Overall, vitamin D supplementation was associated with improved glycemic control, suggesting its potential role as an adjunct therapy in the management of type 2 diabetes mellitus.

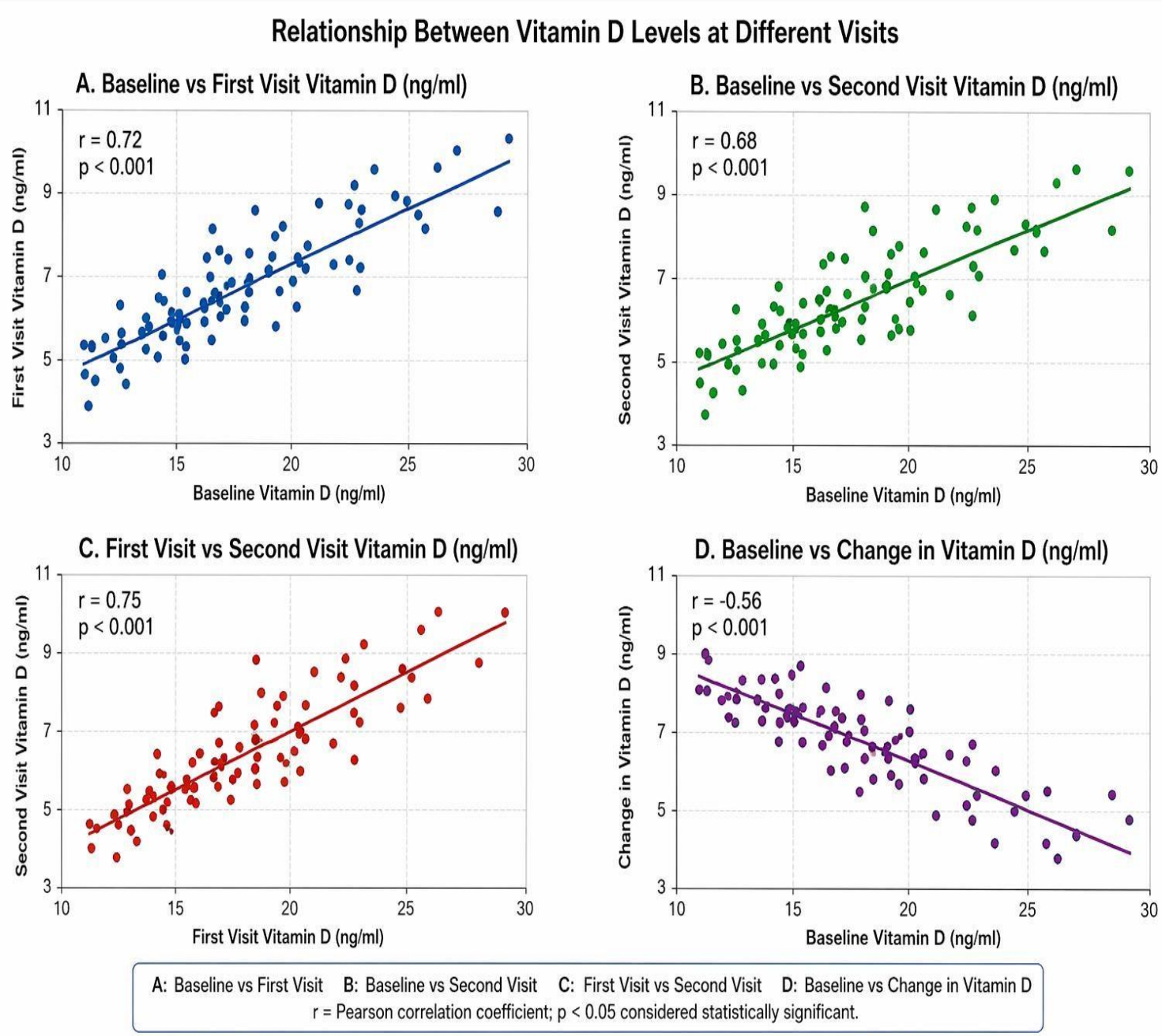
Relationship Between Vitamin D Levels at Different Visits
A. Baseline vs First Visit Vitamin D (ng/ml)
r = 0.72
p < 0.001
First Visit Vitamin D (ng/ml)
Baseline Vitamin D (ng/ml)
B. Baseline vs Second Visit Vitamin D (ng/ml)
r = 0.68
p < 0.001
Second Visit Vitamin D (ng/ml)
Baseline Vitamin D (ng/ml)
C. First Visit vs Second Visit Vitamin D (ng/ml)
r = 0.75
p < 0.001
Second Visit Vitamin D (ng/ml)
First Visit Vitamin D (ng/ml)
D. Baseline vs Change in Vitamin D (ng/ml)
r = -0.56
p < 0.001
Change in Vitamin D (ng/ml)
Baseline Vitamin D (ng/ml)
A: Baseline vs First Visit B: Baseline vs Second Visit C: First Visit vs Second Visit D: Baseline vs Change in Vitamin D
r = Pearson correlation coefficient; p < 0.05 considered statistically significant.

Table 1. Baseline characteristics of study participants.

Variable	Group A (Metformin)	Group B (Metformin + Vitamin D)
Total participants (n)	64	64
Age (years, mean ± SD)	43.2 ± 5.8	44.1 ± 6.1
Male (%)	52%	50%
Female (%)	48%	50%
Baseline HbA1c (%)	7.4 ± 0.7	7.3 ± 0.6
Baseline Vitamin D (ng/mL)	17.2 ± 2.5	18.1 ± 2.7

This table presents the baseline demographic and clinical characteristics of participants in both study groups.

Table 2. Changes in HbA1c levels after intervention

Group	Baseline HbA1c (%)	Final HbA1c (%)	Mean Change	p-value
Group A (Metformin)	7.45 ± 0.72	7.10 ± 0.68	-0.35	>0.05
Group B (Metformin + Vitamin D)	7.30 ± 0.65	6.62 ± 0.71	-0.68	<0.05

This table shows the change in HbA1c levels before and after intervention. A statistically significant reduction was observed in the vitamin D supplementation group.

Table 3. Changes in vitamin D and random blood sugar levels

Parameter	Group A	Group B
Vitamin D (ng/mL) Baseline	17.2 ± 2.5	18.1 ± 2.7
Vitamin D (ng/mL) Final	17.5 ± 2.6	21.8 ± 3.2
RBS Baseline (mg/dL)	219 ± 12	221 ± 10
RBS Final (mg/dL)	200 ± 10	196 ± 8

This table summarizes secondary outcomes, including serum vitamin D levels and random blood sugar (RBS). A significant improvement in vitamin D and RBS was observed in the intervention group.

DISCUSSION

This study assessed the effectiveness of vitamin D supplementation in enhancing glycemic control in type 2 diabetes mellitus (T2DM) patients with vitamin D deficiency [12]. The results showed that vitamin D supplementation in combination with metformin standard dose regime showed a significant decrease in the level of HbA1c as compared to metformin itself. These findings are in line with the hypothesis that vitamin D could have a contributory role in glucose metabolism and glycemic control. Both male and female participants had vitamin D deficiency, which is in agreement with the existing literature, which shows that hypovitaminosis D is prevalent among people with T2DM[13]. A negative correlation was also found between vitamin D levels and HbA1c, which indicates that decreased concentration of vitamin D could be related to the worse glycemic control. The observation is in line with observational studies which have indicated reduced serum 25-hydroxyvitamin D levels are associated with the development of insulin resistance and poor glucose tolerance[14,15].The biological feasibility of these results is backed by the fact that vitamin D plays a role in the functioning of the pancreatic β-cells as well as insulin sensitivity. Vitamin D receptors are also present in the pancreatic tissue and peripheral insulin-responsive cells, which means that it plays a role in glucose homeostasis [16].Vitamin D increases insulin secretion and raises insulin sensitivity through mechanisms of regulating calcium influx and intracellular signal transduction. Moreover, it has anti-inflammatory properties, decreasing the insulin resistance caused by cytokines, which is one of the main factors of the pathogenesis of T2DM.Although these results are promising, the literature evidence is not consistent [17,18].Other interventional studies have also documented massive changes in glycemic parameters due to vitamin D supplementation, whereas, others have shown insignificant or no changes. The differences can be explained by the differences in the study design, dosage, supplementation time, vitamin D status at baseline, and population factors[19].Specifically, variations in

supplementation protocols, including daily versus monthly supplementation, can affect the therapeutic results.In the current research, vitamin D supplementation was done monthly, which could have influenced absorption and bioavailability. Also, the change in HbA1c was statistically significant but rather small, which would indicate that vitamin D would be regarded as an addition to the therapy and not a primary mode of glycemic control[20]. The results also suggest that vitamin D supplementation can be effective to improve metabolic parameters but it might not be enough as a single intervention. Vitamin D has more than a glycemic control association with diabetes. Epidemiological research has attributed vitamin D deficiency to the high risk of cardiovascular disease, metabolic syndrome, and other chronic diseases. Since vitamin D deficiency is extremely common in the world and especially in developing countries, the treatment of this deficiency can have wider implications on the health of the population[21]. The preventative effect of vitamin D supplementation against diabetes or any meaningful modulation of the course of the disease, however, is still not clear.The other factor that should be considered is the part played by vitamin D in cellular and molecular processes in diabetes. Vitamin D has demonstrated the ability to control gene expression via epigenetic regulation, to minimize oxidative stress and calcium homeostasis of pancreatic 0-cells[22]. The effects can assist in maintaining the β-cell functions and slowing down the disease. Nevertheless, these processes are complicated and not completely comprehended, which means that additional studies are necessary. On the whole, the results of the proposed research are consistent with the existing body of research on the possible advantages of taking vitamin D supplementation in T2DM. Nonetheless, due to the inconsistency in the current literature, one should be cautious when making generalizations of such findings. Bigger, properly planned randomized controlled trials that include standard dosing schedules and extended follow-up are required to draw conclusive clinical guidelines [23].

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, limiting comparison 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 Contribution

Concept & Design of Study: Aftab Khattak

Drafting: Ziaullah Khan

Data Collection & Critical Review:Khalid Usman,Tahir Ghaffar

Final Approval of Version: All Authors

CONFLICT OF INTEREST: Not applicable.

FUNDING DISCLOSURE: No external funding was received for this study.

ETHICAL STATEMENT

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

AI USAGE STATEMENT

AI tools (**e.g., ChatGPT**) were used for language editing and structuring of the manuscript. The authors take full responsibility for the content and accuracy of the manuscript.

COPYRIGHT STATEMENT

DATA AVAILABILITY STATEMENT

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

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