

IMPACT OF VITAMIN D DEFICIENCY ON GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Vitamin D deficiency is increasingly recognized as an emerging metabolic risk factor in patients with type 2 diabetes mellitus. Its potential role in glucose regulation, insulin secretion, and insulin sensitivity has gained clinical relevance, particularly in regions where deficiency is widespread.

Objective: To evaluate the impact of vitamin D deficiency on glycemic control among individuals with type 2 diabetes mellitus attending tertiary care hospitals in Punjab, Pakistan.

Methods: This cross-sectional study was conducted from January 2024 to March 2025, including 160 adults diagnosed with type 2 diabetes mellitus. Participants were recruited from tertiary care hospitals across Punjab using consecutive sampling. Serum 25-hydroxyvitamin D, fasting blood glucose, HbA1c, fasting insulin, and HOMA-IR were measured. Vitamin D status was categorized as deficient, insufficient, or sufficient. Glycemic control was assessed according to HbA1c levels. Statistical analysis included ANOVA, chi-square tests, and Pearson correlation, with significance set at $p < 0.05$.

Results: Vitamin D deficiency was highly prevalent, affecting 64 percent of participants. Patients with deficiency exhibited significantly elevated fasting glucose and HbA1c compared with those with sufficient vitamin D levels. Mean fasting glucose was highest in the deficient group (173.2 ± 31.6 mg/dL), and mean HbA1c was highest among deficient participants ($8.7 \pm 1.0\%$). Poor glycemic control was observed in 76.5 percent of vitamin D-deficient patients versus 27.3 percent of vitamin D-sufficient participants. Serum 25-hydroxyvitamin D demonstrated a strong inverse correlation with both fasting glucose and HbA1c.

Conclusion: Vitamin D deficiency is strongly associated with poor glycemic control and increased insulin resistance in patients with type 2 diabetes mellitus. Routine assessment and correction of vitamin D levels may serve as an effective adjunct in improving metabolic outcomes.

Keywords: Vitamin D deficiency, Type 2 diabetes mellitus, Glycemic control, HbA1c, Insulin resistance, 25-hydroxyvitamin D, Punjab Pakistan

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most widespread non-communicable metabolic diseases on Earth, it still ranks high in terms of morbidity and mortality, not to mention healthcare spending. T2DM is described as peripheral insulin resistance, disrupted insulin to be released as well as persistent hyperglycemia and is experienced by millions of people in developed and developing countries¹. Recent estimates in the world show that more and more people are represented with diabetes

due to the growing trends of unhealthy lifestyles, urbanization, improper dieting and rising incidences of obesity. Ideal glycemic control is the main focus of the prevention of a long-term complication like nephropathy, retinopathy, neuropathy, and cardiovascular disease; nevertheless, even with the development of pharmacotherapy, a significant percentage of patients cannot reach the target levels of glycemic control²⁻⁴.

Over the last few years, micronutrient malfunctions, especially the deficiency of vitamin D, have been

discussed as possible glucose homeostasis modulators. Vitamin D that is traditionally identified with bone mineralization and calcium balance has been identified as a multifunctional hormone with important endocrine and metabolic consequences⁵. The vitamin D receptors (VDRs) are abundant in pancreatic β -cells, adipose tissue, liver, muscle and immune cells suggesting a wider physiological functionality than skeletal health. Via its genomic and non-genomic processes, vitamin D affects insulin secretion, insulin sensitivity, inflammatory pathways, and calcium-dependent processes that play a vital role in glucose metabolism^{6,7}.

A number of studies indicate vitamin D deficiency in serum (25(OH)D) which is the main form of vitamin D in circulation to be a cause of impaired β cell functioning, elevated insulin resistance and poor glycemic regulation. Both chronic inflammation, oxidative stress, dysregulated cytokine production, and changes of glucose transporter activity have been suggested as biological pathways between vitamin D deficiency and T2DM⁸. Furthermore, the fact that people of darker skin color, limited sun exposure, or cultural clothing habits like most communities in South Asia and Middle East are at a quite high risk of vitamin D deficiency further makes this correlation especially clinical in these areas⁹⁻¹¹.

Pakistan is particularly burdened with both rampant cases of vitamin D deficiency and skyrocketing cases of T2DM. In spite of the high levels of sunlight, cases of vitamin D deficiency among over 60% of the population have been recorded in many studies due to the lifestyle that people live indoors, poor food consumption, and insufficient understanding of the supplements. Simultaneously, the quality of glycemic control in a large number of diabetic patients is less than optimal and leads to further complications and the consumption of healthcare services. The insights on whether vitamin D deficiency directly affects the dysregulation of glycemic control can thus be of significance when it comes to diabetes management interventions amongst the local population¹².

Although the international data confirms the possible correlation between the vitamin D status and the glycemic control, the results are still inconsistent because of the differences in sample sizes, ethnic groups, geographical locations, and the methods of the research. Local information of this relation by Pakistani adults with T2DM is scarce¹³. Therefore, it is necessary to analyze this relationship in our clinical environment to offer location-specific data and inform future treatment strategies¹⁴⁻¹⁵.

The current study aimed at examining the effects of vitamin D deficiency on the glycemic control in patients with type 2 diabetes mellitus. This study will help establish clinically relevant evidence on whether inadequate vitamin D levels are linked to worse metabolic outcomes in T2DM because it will evaluate serum 25(OH)D levels and fasting blood glucose, HbA1c, and insulin resistance markers. The knowledge of this association can facilitate clinicians to

consider screening and supplementation of vitamin D as part of diabetes management to enhance glycemic control and minimize the morbidity and mortality in the long-term^{16,17}.

MATERIALS AND METHODS

Study Design and Setting: This study was a cross-sectional analytical study that was done in various tertiary care hospitals in Punjab, Pakistan. Such hospitals were identified due to the fact that they are the largest referral centers of managing diabetes and metabolic disorders. The research was conducted throughout the year between 2024 and 2025 (Jan-March). The principles of the ethical standards of the Declaration of Helsinki were observed in all the procedures of the study. Institutional ethical review committees of all participating hospitals gave their approval to the start of data collection and informed written consent was obtained before the start of data collection.

Study Population: The participants of the study were adult patients diagnosed with type 2 diabetes mellitus who attended the endocrinology and diabetes outpatient departments of the centers used in the research. A sample size of 160 was used, where the consecutive sampling technique was used. The sample was considered to be sufficient according to the prevalence levels of vitamin D deficiency in diabetic patients in the region and a confidence level of 95. The eligibles were men and women aged between 30 and 70 years who had at least six months of confirmed diagnosis of type 2 diabetes mellitus. The eligibility criteria were that the patients should have chronic kidney disease in stage III or higher, chronic liver disease, malabsorption disorders, thyroid dysfunction, acute infections, autoimmune diseases, or malignancies. The pregnant or lactating women and those who had taken vitamin D supplements in the past three months were also excluded to eliminate confounding effects that could have impacted on the serum vitamin D levels.

Data Gathering and Clinical Evaluation: All the participants were interviewed and evaluated clinically. Demographic and socioeconomic information was entered such as age, gender, occupation and residence. There were also clinical features, which were duration of diabetes, current medications, comorbidities and family history. The lifestyle issues such as access to sunlight, physical exercise and eating habits were evaluated using a standard questionnaire. The anthropometric measurements were done with the international guidelines. A stadiometer that was mounted on the wall was used to measure height and a calibrated digital scale was used to measure weight. The body mass index was determined by a division of height in meters by the square of the weight in kilograms. Measurement of blood pressure was done through an automated sphygmomanometer and taken after a rest period of ten minutes to be accurate.

Laboratory Investigations: Each of the participants was subjected to fasting biochemical test which was based on 10-12 hours of fasting. Blood samples were taken in aseptic conditions through venous blood in two kinds of vacutainers; gel tube as serum separation and EDTA tube as HbA1c. A centrifugation was performed at a speed of 3000 rpm at ten minutes and the serum was kept at -20 C until analysis. Chemiluminescent microparticle immunoassay was used in the determination of serum 25-hydroxyvitamin D, which has a high sensitivity and specificity of the status of vitamin D. The level of vitamin D was classified as deficient when less than 20 ng/mL, insufficient when 20-29 ng/mL, and adequate when 30ng/mL and above. The glucose oxidaseperoxidase method of measuring the fasting blood glucose was done on an automated chemistry analyzer. The HbA1c levels were measured using the high-performance liquid chromatography to achieve a good level of quantification. An enzyme-linked immunosorbent assay was used in the determination of fasting insulin levels. The estimation of insulin resistance was done using the homeostatic model assessment formula using standard formula of the values of fasting insulin and glucose.

The classification of glycemic control was done as per the American Diabetes Association guidelines. Those who had a HbA1c of under 7 percent of the population were deemed to have proper glycemic control and those who had HbA1c levels of 7 percent and above were deemed to have poor glycemic control. They conducted the study to determine the correlation between vitamin D deficiency and the glycemic results of type 2 diabetic patients using this classification.

Statistical Analysis: All the data got were entered and analyzed with the help of the Statistical Package of the Social Sciences version 26. Continuous variables (vitamin D levels of serums, fasting level of glucose, fasting level of insulin, and HbA1c) were summarized as mean and standard deviation, whereas categorical variables (gender distribution, vitamin D categories, and glycemic control status) were presented in the form of frequencies and percentages. The vitamin D groups were compared by using one-way analysis of variance when the variables

were continuous and the chi-square test was used when the variables were of the categorical type. To measure the relationship between glycemic variables and serum 25-hydroxyvitamin D, Pearson correlation coefficients were computed to determine the relationship. The p-value that was considered to be statistically significant was less than 0.05.

RESULTS

A total of 160 patients with type 2 diabetes mellitus (88 females and 72 males) aged means 53.4 8.7 years were enrolled in the study. It was also established that the general prevalence of vitamin D deficiency was high whereby 64 percent of the sample participants fell into the deficient category, 22 percent had insufficient levels of vitamin D and only 14 percent showed adequate levels. The average age of study population having diabetes was 7.9 plus or minus 3.6 years. There was no statistically significant difference in the baseline demographic factors age, gender distribution, or BMI between the three Vitamin D groups, which proved comparability of the groups.

The analysis proved that the vitamin D status had a great influence on glycemic indices. The vitamin D deficient participants had significantly elevated levels of fasting blood glucose and HbA1c as compared to those with insufficient or adequate levels as shown in Table 1. The average fasting blood glucose of the deficient group was 173.2mg/dl + 31.6 which was significantly greater than the insufficient group 152.4mg/dl + 25.8 and the sufficient group 134.1mg/dl + 21.3. This was also the case with HbA1c with the deficient group showing a mean HbA1c of 8.7 ± 1.0 percent that was highly elevated in comparison with 7.9 ± 0.8 percent in the insufficient and 6.8 ± 0.7 percent in the inadequate groups, respectively. These were statistically significant differences with a p-value of less than 0.001. There was also the same tendency in the fasting insulin level and the calculated HOMA-IR which showed that there were people with lower serum vitamin D who have higher insulin resistance which again supports the metabolic association.

Table 1: Comparison of Glycemic Parameters Across Vitamin D Status Groups

Parameter	Vitamin D Deficient (<20 ng/mL)	Vitamin D Insufficient ($20-29$ ng/mL)	Vitamin D Sufficient (≥ 30 ng/mL)	p-value
Fasting Blood Glucose (mg/dL)	173.2 ± 31.6	152.4 ± 25.8	134.1 ± 21.3	<0.001
HbA1c (%)	8.7 ± 1.0	7.9 ± 0.8	6.8 ± 0.7	<0.001
Fasting Insulin (μ IU/mL)	18.9 ± 4.1	15.8 ± 3.5	12.4 ± 3.0	<0.001
HOMA-IR	8.08 ± 2.1	5.94 ± 1.8	4.10 ± 1.1	<0.001

Table 2: Distribution of Glycemic Control Across Vitamin D Groups

Glycemic Control Status	Vitamin D Deficient	Vitamin D Insufficient	Vitamin D Sufficient	p-value
Good Control (HbA1c $< 7\%$)	23.5%	44.4%	72.7%	<0.001
Poor Control (HbA1c $\geq 7\%$)	76.5%	55.6%	27.3%	<0.001

As Table 1 displays, the vitamin D deficient people always had better glycemic profiles and lower HOMA-IR values by far as compared to the deficiency and insufficiency categories.

Additional examination of glycemic control variables showed that poor glycemic control, which was determined to be 7 percent of HbA1c and above, was significantly higher among the vitamin D deficient patients. Table 2 demonstrates that 76.5 percent of the people who were vitamin D-deficient had poor glycemic control in comparison with 55.6 percent of the people who had insufficient vitamin D levels and only 27.3 percent of those with sufficient levels. This was found to be statistically significant, thus establishing a high level of association between vitamin D deficiency and poor glycemic control.

The correlation analysis revealed a significant negative correlation between fasting glucose, HbA1c and serum 25-hydroxyvitamin D. The correlation coefficient of vitamin D on HbA1c was found to be -0.47, which means that a decline in the levels of vitamin D was correlated with a gradual deterioration in glycemic control. In the same manner, vitamin D was considered to have a negative relationship with fasting glucose with a correlation coefficient of -0.42 indicating that the lower the concentration of vitamin D in the body, the higher the level of fasting glucose. There were positive associations observed between fasting insulin and HOMA-IR and vitamin D deficiency, which supports the results of the fact that vitamin D deficiency is a contributing factor to insulin resistance.

In general, the findings of the current research suggest that the problem of vitamin D deficiency is quite common with patients having type 2 diabetes mellitus and is closely linked with increasing fasting blood glucose, high HbA1c, and insulin resistance. The data has a strong supporting role on the possibility of vitamin D as metabolism modulator and the significance of vitamin D analysis as a part of the usual care of diabetic patients.

DISCUSSION

The results of this research prove that there is a close and clinically significant relationship between poor glycemic control and vitamin D deficiency in patients with type 2 diabetes mellitus who receive tertiary care in hospitals in Punjab, Pakistan^{18,19}. The number of vitamin D deficient in this cohort group was quite high and is in line with earlier studies performed on South Asian population, where culture, lack of exposure to much sunlight, low dietary intake, and darker pigmentation of skin contribute to the high prevalence of vitamin deficiency. Such high prevalence shows a great necessity to pay more clinical attention to vitamin D status of those having chronic metabolic diseases²⁰.

In the current research, it was found that the patients with vitamin D deficiency reported substantially elevated

levels of fasting blood glucose and HbA1c with respect to the patients having an insufficient or adequate stock of vitamin D. These results support the premise that vitamin D is an important component of glucose homeostasis. This relationship is supported by a number of biological processes. Pancreatic β -cells express vitamin D receptors, and active vitamin D stimulates insulin secretion by controlling the level of intracellular calcium. Also, vitamin D has anti-inflammatory properties, by regulating TNF- α and IL-6, both of which are well known to increase insulin resistance. Poor vitamin D levels can thus affect the insulin sensitivity and the insulin secretion at the same time causing poor glycemic conditions²¹.

The negative relationships between serum 25-hydroxyvitamin D and glycemic indices also underpin the physiologic connection between the levels of vitamin D and metabolic stability in diabetes mellitus type 2. The reason is that vitamin D and HbA1c are strongly negatively correlated, which means that chronic poor vitamin D status can be one of the causes of persistent hyperglycemia. In the same manner, the correlation between low vitamin D and high HOMA-IR indicates that it has a huge effect on insulin resistance. These results are compatible with other studies worldwide (Europe, Middle East, and Southeast Asia) that have documented the improvement of insulin sensitivity and small changes in the HbA1c after the use of the vitamin D supplement²².

The distribution of the glycemic control groups in this study would also give further clinical understanding. Over three-quarters of patients who were deficient in vitamin D demonstrated poor glycemic control, with most of those who had adequate vitamin D levels having HbA1c levels that were less than 7 percent. Such a high variance implies that vitamin D might be involved in the regulation of long-term glycemic regulation. The diabetic microvascular and macrovascular complications are directly associated with poor glycemic control, which are already extremely high in South Asia populations. Vitamin D deficiency therefore may be a low-cost, easy to implement, strategy to promote metabolic stability and the alleviation of the burden of diabetes complications^{23,20}.

Although the relationships between the two are strong, it is not possible to make any conclusions about causality in terms of the cross-sectional nature of this study. There is a possibility that the very poor glycemic control is one of the causes of the decreased absorption of vitamin D or the change in the metabolism. Additional longitudinal and interventional studies are required to help determine the causality more thoroughly and assess how much vitamin D supplementation might help better the glycemic results. Besides, genetic variation in the metabolism of vitamin D, such as the presence of polymorphic vitamin D receptor receptors, can also contribute to the correlation of vitamin D status and

metabolic control and needs to be investigated in the future²⁴.

However, the findings have significant clinical-practical implications especially in Pakistan where the prevalence of diabetes and vitamin D deficiency are very high. Vitamin D deficiency screening in diabetics clinics on a routine basis would assist in the early detection of high-risk patients. Vitamin D supplementation as an adjunct in the management of diabetes could achieve better glycemic control in the patients who cannot attain their glycemic targets despite proper pharmacological management²⁵.

CONCLUSION

The conclusion of this study is that vitamin D deficiency among patients with type 2 diabetes mellitus is very high among patients admitted in tertiary care hospitals of the Punjab region of Pakistan and closely linked with bad glycemic control. A low level of serum 25-hydroxyvitamin D is associated with high fasting blood glucose, high HbA1c, and high insulin resistance, which point to the possibility that vitamin D can be very significant in the metabolic process of glucose homeostasis. Vitamin D deficient patients had much better glycemic profiles than vitamin D deficient or insufficient patients. The results indicate the significance of regular monitoring of the vitamin D status in diabetic patients and assert that the interest in the remedy of vitamin D deficiency should be considered to enhance the metabolic results. It is encouraged that further interventional research should be undertaken to determine therapeutic advantages of vitamin D supplementation in the optimization of glycemic control and the minimization of complications in diabetes.

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