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Association of vitamin D deficiency with insulin resistance among type 2 diabetes mellitus patients - A case-control study

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Abstract:
The association between vitamin D deficiency and insulin resistance **is of interest. Hence,** 140 participants-70 type 2 diabetes mellitus (T2DM) patients and 70 age- and sex-matched healthy controls **were** evaluate**d**. Serum 25(OH) vitamin D levels and HOMA-IR scores were measured and compared. Vitamin D levels were significantly lower and HOMA-IR significantly higher in T2DM patients compared to controls. An inverse correlation was observed between vitamin D levels and insulin resistance. Thus, we show a potential role of vitamin D deficiency in the pathophysiology of insulin resistance in T2DM.

Keywords: Vitamin D deficiency, type 2 diabetes mellitus, insulin resistance, HOMA-IR, case-control study

Background:
Type 2 diabetes mellitus (T2DM), a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency **[1]**. It is a major public health concern globally, contributing to significant morbidity and mortality **[2]**. While the pathogenesis of T2DM is multifactorial, emerging evidence has identified a possible link between micronutrient deficiencies-particularly vitamin D deficiency and insulin resistance **[3]**. Vitamin D is known to play a role in glucose metabolism through its effects on pancreatic β-cell function and insulin sensitivity **[4]**. Hypovitaminosis D has been widely reported in individuals with T2DM, but whether this relationship is causal or associative remains debated **[5]**. Several observational studies have suggested that lower levels of 25-hydroxyvitamin D [25(OH) D] may be associated with increased insulin resistance **[6]**. The vitamin D–endocrine system plays a major role in physiological processes that modulate mineral metabolism and immune function with probable link to several chronic and infectious conditions **[7]**. Therefore, it is of interest to evaluate the association between serum vitamin D levels and insulin resistance in patients with T2DM through a case-control design, comparing them with age- and sex-matched non-diabetic individuals.

Materials and Methods:
This case-control study was conducted at the Department of Endocrinology of a tertiary care teaching hospital between January 2023 and December 2023. A total of 140 participants were enrolled, comprising 70 patients diagnosed with type 2 diabetes mellitus (T2DM) and 70 age- and sex-matched healthy controls. The T2DM group included individuals aged between 30 and 65 years who had been diagnosed with diabetes for at least one year, based on ADA criteria. The control group consisted of healthy individuals with no history of diabetes, metabolic syndrome, or any chronic systemic illness. Participants with chronic kidney disease, hepatic disorders, malabsorption syndromes, endocrine abnormalities other than diabetes, or those who were on vitamin D supplementation or medications affecting glucose metabolism (other than anti-diabetic agents in cases) were excluded. After obtaining informed consent, fasting venous blood samples were collected from all participants for biochemical analysis. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using chemiluminescence immunoassay. Vitamin D deficiency was defined as serum 25(OH)D levels below 20 ng/mL. Data were statistically analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using the unpaired t-test. Pearson's correlation coefficient was used to analyze the relationship between vitamin D levels and HOMA-IR, with a p-value of less than 0.05 considered statistically significant.

Results:
A total of 140 participants were analyzed, including 70 T2DM patients and 70 healthy controls. The two groups were comparable in age and gender distribution. T2DM patients showed significantly lower serum 25(OH) vitamin D levels and higher HOMA-IR values, indicating a clear association between vitamin D deficiency and insulin resistance. An inverse correlation between vitamin D levels and HOMA-IR was observed in the diabetic group. **Table 1** shows the age and gender distribution between the T2DM and control groups were statistically similar, eliminating demographic bias. **Table 2** shows Mean serum vitamin D levels were significantly lower in T2DM patients compared to controls. **Table 3** shows the prevalence of vitamin D deficiency was markedly higher in the diabetic group. **Table 4** shows Fasting insulin levels were significantly elevated in the T2DM group, reflecting increased insulin resistance. **Table 5** shows Fasting blood glucose levels were significantly higher in diabetic patients, consistent with their diagnosis. **Table 6** shows HOMA-IR values were significantly higher in the T2DM group, confirming greater insulin resistance. **Table 7** shows an inverse correlation was observed between serum vitamin D levels and HOMA-IR in the diabetic group. **Table 8** shows Vitamin D deficiency was associated with significantly higher insulin resistance in diabetic patients. **Table 9** shows a larger proportion of vitamin D–deficient diabetics had poorly controlled glucose levels. **Table 10**

shows Body Mass Index (BMI) was slightly higher in T2DM patients but not statistically significant between groups.

Table 1: Demographic characteristics of study participants

Characteristic	T2DM Group (n=70)	Control Group (n=70)	p-value
Mean Age (years)	52.4 ± 7.2	51.8 ± 6.9	0.62
Male (%)	38 (54.3%)	36 (51.4%)	0.72
Female (%)	32 (45.7%)	34 (48.6%)	

Table 2: Comparison of Serum 25(OH) Vitamin D Levels

Group	Mean Vitamin D (ng/mL) ± SD	p-value
T2DM	16.3 ± 5.4	
Control	24.7 ± 6.1	<0.001

Table 3: Prevalence of Vitamin D Deficiency

Vitamin D Status	T2DM Group (n=70)	Control Group (n=70)	p-value
Deficient (<20 ng/mL)	54 (77.1%)	22 (31.4%)	<0.001
Sufficient (≥20 ng/mL)	16 (22.9%)	48 (68.6%)	

Table 4: Fasting insulin levels

Group	Mean Fasting Insulin (μU/mL) ± SD	p-value
T2DM	18.6 ± 4.7	
Control	11.2 ± 3.9	<0.001

Table 5: Fasting plasma glucose levels

Group	Mean Fasting Glucose (mg/dL) ± SD	p-value
T2DM	154.3 ± 23.1	
Control	91.6 ± 12.4	<0.001

Table 6: HOMA-IR Comparison between Groups

Group	Mean HOMA-IR ± SD	p-value
T2DM	7.08 ± 2.14	
Control	2.53 ± 1.02	<0.001

Table 7: Correlation between Vitamin D Levels and HOMA-IR (T2DM Group)

Parameter Pair	Correlation Coefficient (r)	p-value
Vitamin D vs HOMA-IR	-0.68	<0.001

Table 8: HOMA-IR in Diabetics Based on Vitamin D Status

Vitamin D Status	Mean HOMA-IR ± SD	p-value
Deficient (<20 ng/mL)	7.62 ± 1.83	
Sufficient (≥20 ng/mL)	5.21 ± 1.14	<0.001

Table 9: Glycemic Control and Vitamin D Status in T2DM

HbA1c > 7%	T2DM with Deficiency (n=54)	T2DM without Deficiency (n=16)	p-value
Poor Control (%)	42 (77.8%)	6 (37.5%)	0.004

Table 10: Body mass index comparison

Group	Mean BMI (kg/m²) ± SD	p-value
T2DM	27.9 ± 2.8	
Control	26.8 ± 2.6	0.07

Discussion:

This case-control study demonstrates a significant association between vitamin D deficiency and insulin resistance among patients with type 2 diabetes mellitus (T2DM). The findings reveal that T2DM patients had markedly lower serum 25(OH) vitamin D levels and significantly higher HOMA-IR scores compared to age- and sex-matched healthy controls. This supports previous evidence suggesting that vitamin D may play an essential role in maintaining insulin sensitivity and glucose metabolism **[8]**. The inverse correlation found between vitamin D levels and insulin resistance in the diabetic group reinforces the hypothesis that vitamin D deficiency contributes to the pathophysiology of insulin resistance **[9]**. Vitamin D is believed to enhance insulin receptor expression and improve insulin responsiveness in peripheral tissues. It may also influence calcium homeostasis in pancreatic β-cells, affecting insulin secretion **[10]**. Deficiency in vitamin D might, therefore, impair both insulin production and its action, contributing to the development and worsening of T2DM **[11]**. Furthermore, the significantly higher prevalence of vitamin D deficiency in T2DM patients underscores the need for routine screening and potential correction of this modifiable risk factor. Diabetics with vitamin D deficiency also had poorer glycemic control, as indicated by higher HbA1c levels, which could suggest an added burden on disease management **[12]**. Although BMI was marginally higher in the diabetic group, it was not statistically significant, ruling out obesity as a major confounder in this cohort. Despite the compelling associations observed, this study has limitations. Being observational and retrospective, it cannot establish a causal relationship **[13]**. Other factors such as sun exposure, dietary intake and physical activity were not controlled, which might have influenced vitamin D levels. Nevertheless, the consistency of findings with existing literature suggests that vitamin D status should not be overlooked in the clinical management of diabetes **[14,15]**. These results support the potential role of vitamin D supplementation as an adjunct in managing insulin resistance and improving metabolic control in T2DM patients. Future large-scale randomized controlled trials are necessary to determine whether vitamin D supplementation can lead to meaningful improvements in insulin sensitivity and long-term diabetic outcomes.

Conclusion:

A strong inverse association between vitamin D deficiency and insulin resistance in patients with type 2 diabetes mellitus. Diabetic individuals with lower vitamin D levels exhibited significantly higher HOMA-IR scores and poorer glycemic control. These findings emphasize the potential role of vitamin D in glucose metabolism and support the consideration of routine vitamin D assessment and correction as part of comprehensive diabetes management.

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