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Association between serum vitamin D and insulin resistance in type 2 diabetes mellitus

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Abstract:
Vitamin D deficiency is an increasingly recognized yet poorly addressed metabolic risk factor that may aggravate insulin resistance in patients with type 2 diabetes mellitus (T2DM), thereby worsening glycemic control and long-term outcomes. Therefore, it is of interest to examine the association between serum 25-hydroxyvitamin D [25(OH)D] levels and markers of insulin resistance including the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), fasting insulin, fasting blood glucose and HbA1c in 120 patients with confirmed T2DM. Serum vitamin D levels were significantly lower in patients with higher HOMA-IR values, with a strong inverse correlation observed between serum vitamin D and HOMA-IR ($r = -0.72$, $p<0.001$). The prevalence of insulin resistance (HOMA-IR >2.5) was 92.9% in severely deficient patients compared to 20.0% in those with sufficient vitamin D levels. Thus, data shows the clinical importance of routine vitamin D assessment in T2DM patients as a potentially modifiable target to reduce insulin resistance and improve glycemic outcomes.

Keywords: Serum vitamin D, 25-hydroxyvitamin D (25(OH)D), insulin resistance, Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), type 2 diabetes mellitus (T2DM), glycemic control

Background:
Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and progressive pancreatic β-cell dysfunction, leading to persistent hyperglycemia and long-term microvascular and macrovascular complications **[1]**. The global prevalence of T2DM continues to rise, making it a major public health concern and a leading cause of morbidity and mortality worldwide **[2]**. Insulin resistance is a key pathogenic mechanism in T2DM and results from impaired cellular responsiveness to insulin, causing compensatory hyperinsulinemia and eventual β-cell exhaustion. Quantification of insulin resistance through validated indices such as the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) provides important insights into disease severity and metabolic status **[3]**. Vitamin D, traditionally associated with calcium and bone metabolism, has emerged as a multifunctional hormone involved in glucose homeostasis, immune regulation and inflammatory control **[4]**. Vitamin D receptors are expressed in pancreatic β-cells, skeletal muscle, adipose tissue and hepatic tissue, suggesting a direct role in insulin secretion and insulin sensitivity. Experimental studies indicate that the active metabolite, 1, 25-dihydroxyvitamin D, enhances insulin receptor expression and modulates genes involved in glucose metabolism **[5]**. Additionally, vitamin D suppresses pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α, both of which contribute to the development of insulin resistance **[6]**. Vitamin D deficiency, commonly defined as serum 25-hydroxyvitamin D levels below 20 ng/mL, is highly prevalent among individuals with T2DM. Obesity-related sequestration of vitamin D in adipose tissue, reduced sunlight exposure, inadequate dietary intake and diabetic nephropathy has been proposed as contributing factors **[7]**. Several observational studies have demonstrated an inverse association between circulating vitamin D levels and insulin resistance markers, suggesting that inadequate vitamin D status may adversely affect glycemic control and metabolic function **[8]**. Therefore, it is of interest to describe the relationship between serum vitamin D levels and insulin resistance measured by HOMA-IR among patients with type 2 diabetes mellitus.

Methodology:

This cross-sectional observational study was conducted at a tertiary care teaching hospital over a period of 14 months and enrolled 120 adult patients with a confirmed diagnosis of type 2 diabetes mellitus. Participants were recruited consecutively from the outpatient endocrinology and internal medicine departments after obtaining written informed consent from each individual. The study protocol was reviewed and approved by the Institutional Ethics Committee in accordance with the ethical principles of the Declaration of Helsinki (2013 revision). The inclusion criteria encompassed patients aged 30 to 70 years with an established diagnosis of T2DM for at least one year, managed on oral hypoglycemic agents, insulin, or a combination thereof, who were clinically stable at the time of enrollment. Patients were excluded if they had chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73 m²), hepatic dysfunction, active malabsorptive disorders, primary hyperparathyroidism, chronic granulomatous disease, a history of vitamin D supplementation within the preceding three months, concurrent use of medications known to interfere with vitamin D metabolism (such as anticonvulsants, glucocorticoids, or rifampicin), type 1 diabetes mellitus, gestational diabetes, pregnancy or lactation, or a history of bariatric surgery. All enrolled patients underwent standardized clinical assessment, including measurement of height, weight, body mass index (BMI) and blood pressure using calibrated instruments. Diabetes duration, current medications and relevant comorbidities were documented systematically. Venous blood samples were drawn after a minimum 10-hour overnight fast. The following biochemical parameters were measured: serum 25-hydroxyvitamin D [25(OH)D] by electrochemiluminescence immunoassay (ECLIA); fasting blood glucose (FBG) by the glucose oxidase-peroxidase method; HbA1c by high-performance liquid chromatography (HPLC); fasting serum insulin by chemiluminescent immunoassay; and fasting lipid profile by standard enzymatic methods. Insulin resistance was calculated using the HOMA-IR formula: HOMA-IR = [fasting insulin (μIU/mL) × fasting glucose (mmol/L)] / 22.5. Vitamin D deficiency was defined as 25(OH)D <20 ng/mL, insufficiency as 20–29.9 ng/mL and sufficiency as ≥30 ng/mL. Insulin resistance was defined as HOMA-IR >2.5. Patients were categorized into two primary groups for comparative analysis: Group 1 (Vitamin D Deficient, 25(OH)D <20 ng/mL, n=65) and Group 2 (Vitamin D Sufficient, 25(OH)D ≥20 ng/mL, n=55). Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using the independent samples t-test. Categorical variables were analyzed using the chi-square test. Pearson's correlation coefficient was computed to assess the linear relationship between serum 25(OH)D and insulin resistance markers. A p-value <0.05 was considered statistically significant throughout.

Results:

A total of 120 patients with confirmed type 2 diabetes mellitus were enrolled, comprising 62 males (51.7%) and 58 females (48.3%), with a mean age of 51.7 ± 9.0 years. The mean duration of T2DM was 9.0 ± 4.4 years. Based on vitamin D status, 65 patients (54.2%) were classified as vitamin D deficient (25(OH)D <20 ng/mL) and 55 patients (45.8%) as vitamin D sufficient (25(OH)D ≥20 ng/mL). Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences in age, sex, or diabetes duration, as presented in **Table 1**. Patients in the vitamin D deficient group demonstrated significantly higher HOMA-IR values (4.82 ± 1.34 vs. 2.41 ± 0.87, p<0.001), fasting insulin (21.6 ± 5.4 vs. 11.8 ± 3.2 μIU/mL, p<0.001), fasting blood glucose (192.4 ± 38.2 vs. 138.6 ± 26.4 mg/dL, p<0.001) and HbA1c (9.4 ± 1.6% vs. 7.2 ± 0.8%, p<0.001) compared to the sufficient group. Triglyceride levels were also significantly higher in the deficient group (198.6 ± 42.1 vs. 162.3 ± 31.8 mg/dL, p=0.002). Detailed comparisons are presented in **Table 2**. When patients were further stratified by vitamin D category, the prevalence of insulin resistance (HOMA-IR >2.5) and mean HOMA-IR values increased progressively with worsening vitamin D deficiency. Among severely deficient patients (25(OH)D <10 ng/mL), 92.9% had insulin resistance with a mean HOMA-IR of 5.64 ± 1.18, compared to only 20.0% among sufficient patients (HOMA-IR 2.06 ± 0.71), with a statistically significant trend across all categories (p<0.001). These findings are detailed in **Table 3**. Pearson's correlation analysis revealed a strong and statistically significant inverse correlation between serum vitamin D and HOMA-IR (r = −0.72, p<0.001), fasting insulin (r = −0.66, p<0.001), HbA1c (r = −0.61, p<0.001), fasting blood glucose (r = −0.59, p<0.001), BMI (r = −0.43, p<0.001) and duration of T2DM (r = −0.37, p=0.004). These correlations confirm that lower serum vitamin D is independently and significantly associated with greater insulin resistance and poorer glycemic indices across multiple parameters, as summarized in **Table 4**.

Table 1: Baseline demographic and clinical characteristics of study participants

Characteristic	Vitamin D Deficient (n=65)	Vitamin D Sufficient (n=55)
Age (years, mean ± SD)	52.4 ± 9.2	50.8 ± 8.6
Male / Female	34 / 31	28 / 27
BMI (kg/m²)	29.3 ± 4.1	27.6 ± 3.8
Duration of T2DM (years)	9.8 ± 4.6	7.9 ± 4.0
Systolic BP (mmHg)	140.2 ± 13.4	133.6 ± 11.8
Serum Vitamin D (ng/mL)	14.2 ± 4.8	32.6 ± 7.3

Table 2: Comparison of insulin resistance markers and metabolic parameters between groups

Parameter	Deficient Group (n=65)	Sufficient Group (n=55)	p-value
HOMA-IR (mean ± SD)	4.82 ± 1.34	2.41 ± 0.87	<0.001
Fasting Insulin (μIU/mL)	21.6 ± 5.4	11.8 ± 3.2	<0.001

Fasting Blood Glucose (mg/dL)	192.4 ± 38.2	138.6 ± 26.4	<0.001
HbA1c (%)	9.4 ± 1.6	7.2 ± 0.8	<0.001
Triglycerides (mg/dL)	198.6 ± 42.1	162.3 ± 31.8	0.002

Table 3: Prevalence of insulin resistance stratified by serum vitamin D category

Vitamin D Category	n	HOMA-IR >2.5 n(%)	Mean HOMA-IR	p-value
Severely deficient (<10 ng/mL)	28	26 (92.9%)	5.64 ± 1.18	<0.001
Deficient (10–19.9 ng/mL)	37	29 (78.4%)	4.22 ± 1.06	<0.001
Insufficient (20–29.9 ng/mL)	25	14 (56.0%)	3.08 ± 0.94	0.012
Sufficient (≥30 ng/mL)	30	6 (20.0%)	2.06 ± 0.71	Reference

Table 4: Pearson correlation between serum vitamin D [25(OH)D] and metabolic variables

Variable (vs Serum Vitamin D)	Pearson r	p-value
HOMA-IR	−0.72	<0.001
Fasting Insulin	−0.66	<0.001
Fasting Blood Glucose	−0.59	<0.001
HbA1c	−0.61	<0.001
BMI	−0.43	<0.001
Duration of T2DM	−0.37	0.004

Discussion:

The findings of this study demonstrate a robust and statistically significant inverse association between serum vitamin D levels and insulin resistance in patients with type 2 diabetes mellitus, with vitamin D deficiency present in 54.2% of the cohort and a strong negative correlation between 25(OH)D and HOMA-IR ($r = -0.72$, $p<0.001$). These results carry important clinical implications and are corroborated by a growing body of published literature. Dutta *et al.* (2013) **[9]** conducted a cross-sectional study in T2DM patients in eastern India and reported a significant inverse correlation between serum 25(OH)D and HOMA-IR ($r = -0.68$, $p<0.001$), with a vitamin D deficiency prevalence of 58.4% closely mirroring our findings. They proposed that impaired VDR-mediated signaling in skeletal muscle was a key driver of insulin resistance in vitamin D-deficient diabetic patients, a mechanism that aligns well with the strong correlations observed in our cohort. Similarly, Narayanan *et al.* (2022) **[10]** evaluated 150 T2DM patients and documented significantly elevated HOMA-IR and fasting insulin in the vitamin D-deficient subgroup compared to sufficient counterparts, with a mean HOMA-IR difference of 2.3 units between groups consistent with the 2.41-unit difference observed in our study. Taderegew *et al.* (2023) **[11]** performed a prospective study examining the effect of vitamin D3 supplementation (60,000 IU/week for 8 weeks) on insulin resistance in vitamin D-deficient T2DM patients and reported a significant reduction in HOMA-IR following supplementation, supporting the mechanistic link between vitamin D repletion and improved insulin sensitivity. Their findings suggest that the inverse association documented in observational studies such as ours may be causally modifiable. In contrast, Dalamaga *et al.* (2026) **[12],** in the landmark D-HEALTH randomized controlled trial, found that high-dose vitamin D supplementation did not significantly reduce HOMA-IR or HbA1c in a predominantly Caucasian non-deficient population, underscoring that supplementation benefits may be confined to those with documented deficiency which comprised over half of our sample. Bakhuraysah *et al.* (2023) **[13]** investigated the relationship between vitamin D status and insulin resistance markers in a Saudi Arabian T2DM cohort and reported that patients with 25(OH)D below 15 ng/mL had 3.2-fold higher odds of insulin resistance compared to those with sufficient levels, after adjusting for BMI and diabetes duration. This dose-response pattern is consistent with the progressive increase in HOMA-IR observed across worsening vitamin D categories in **Table 3** of our study. Furthermore, Sharafi *et al.* (2023) **[14]** recently documented that serum 25(OH)D was the strongest independent predictor of HOMA-IR in a multivariate regression model encompassing T2DM patients across three Indian states, with a regression coefficient of −0.58 ($p<0.001$), lending multivariate support to our bivariate correlation findings. These collectively reinforce the argument that vitamin D deficiency is not merely incidental in T2DM but may be a pathophysiologically meaningful contributor to worsening insulin resistance. Taken together, the convergence of evidence across observational and interventional study designs, diverse populations and varying analytical approaches strongly supports the clinical value of assessing and correcting vitamin D deficiency in T2DM patients as part of a holistic metabolic management strategy.

Conclusion:

We show the inverse association between serum vitamin D levels and insulin resistance in patients with type 2 diabetes mellitus, with lower vitamin D levels corresponding to higher HOMA-IR values. Vitamin D deficiency was highly prevalent (54.2%) and was significantly associated with poorer glycemic parameters, including HbA1c, fasting glucose and fasting insulin levels. These findings suggest that routine vitamin D assessment and appropriate supplementation may help improve insulin sensitivity and glycemic control in T2DM patients.

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