ORIGINAL ARTICLE

To Study the Correlation of Low Vitamin D Levels with Insulin Resistance

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Received: 04 August 2025; *Accepted:* 02 July 2026

Abstract

Background: Vitamin D deficiency has been increasingly linked to various nonskeletal conditions, including type 2 diabetes mellitus (T2DM). Despite evidence suggesting an association between vitamin D levels and metabolic parameters, such as insulin sensitivity and glucose metabolism, randomized controlled trials have yielded inconsistent results regarding the efficacy of vitamin D supplementation in diabetes management.

Introduction: Vitamin D insufficiency is associated with insulin resistance, impaired glucose tolerance, and an increased risk of T2DM. This study aims to explore the relationship between vitamin D status and metabolic parameters in T2DM patients, particularly focusing on fasting plasma glucose, glycated hemoglobin (HbA1c), and insulin resistance. The study also examines the impact of vitamin D status on lipid profiles and other biochemical markers.

Materials and methods: This prospective study was conducted at Lala Lajpat Rai Memorial Medical College, Meerut, with 84 T2DM patients. Participants were categorized into vitamin D deficiency, insufficiency, and sufficiency groups based on serum 25(OH)D levels. Demographic data, clinical history, and metabolic parameters [fasting plasma glucose, HbA1c, insulin, homeostatic model assessment for insulin resistance (HOMA-IR), and lipid profiles] were collected and analyzed. Statistical analyses, including analysis of variance (ANOVA) and Chi-squared tests, were used to assess differences between groups.

Results: The study revealed significant associations between vitamin D levels and various metabolic parameters. Patients with vitamin D deficiency had higher fasting plasma glucose, HbA1c, and insulin levels than those with sufficient vitamin D. Insulin resistance, as measured by HOMA-IR, was highest in the deficiency group. Lipid profiles showed higher triglycerides, lower high-density lipoprotein (HDL), and higher low-density lipoprotein (LDL) levels in the deficiency group. No significant differences were found in serum creatinine, total cholesterol, or liver function tests among the vitamin D status groups.

Conclusion: Vitamin D deficiency is prevalent among older T2DM patients and those with a longer duration of diabetes. Lower vitamin D levels are strongly associated with poor glycemic control, increased insulin resistance, and adverse lipid profiles. These findings suggest that addressing vitamin D deficiency could improve metabolic control in T2DM patients. Further research is needed to validate these associations and explore the potential benefits of vitamin D supplementation as a complementary treatment for T2DM.

Keywords: Glycemic control, Insulin resistance, Lipid profile, Type 2 diabetes mellitus, Vitamin D.

Journal of The Association of Physicians of India (2026): 10.59556/japi.74.1671

Introduction

Vitamin D insufficiency has been linked to nonskeletal conditions, such as type 2 diabetes mellitus (T2DM), in recent years.[1] Both conditions share common risk factors, such as aging, obesity, African American ethnicity, and low physical activity. Vitamin D deficiency is also associated with osteoporosis, cardiovascular disease, and metabolic syndrome.[2]

Studies suggest a link between vitamin D insufficiency and T2DM, as vitamin D may affect insulin sensitivity and secretion, thereby influencing glucose tolerance.[3] Subjects with T2DM have lower circulating levels of 25(OH)D than healthy individuals. Additionally, older men with vitamin D deficiency secrete more insulin after glucose intake, and women with T2DM are more likely to have vitamin D deficiency.[4] Vitamin D decreases insulin resistance, presumably by upregulating the insulin receptor gene and by affecting calcium and phosphorus metabolism.[5] In one trial, vitamin D treatment enhanced insulin sensitivity by 54% in 5,677 patients with impaired glucose tolerance.[5,6] It is believed that elevated insulin resistance and β-cell dysfunction lead to the development of T2DM.[6]

A low serum 25(OH)D level has been associated with a higher risk of T2DM and insulin resistance in prospective observational studies.[7,8] The widespread prevalence of vitamin D deficiency has sparked interest in its potential role in improving glucose homeostasis.[9] However, randomized controlled trials (RCTs) have shown inconsistent effects of vitamin D supplementation on β-cell activity, insulin sensitivity, and insulin secretion.

Research has demonstrated a clear link between vitamin D insufficiency and insulin resistance (IR). Insulin resistance plays a key role in the development of cardiovascular risk factors, such as obesity, metabolic syndrome, hypertension, T2DM, and nonalcoholic fatty liver disease (NAFLD). Moreover, insulin resistance has been linked to the development of asymptomatic organ damage, such as atherosclerosis, chronic kidney disease (CKD), and left ventricular hypertrophy (LVH),[10,11] as well as cardiovascular disease outcomes.[12] Insulin resistance occurs because of defects in the insulin receptor or postreceptor signaling. The insulin receptor is widely expressed, and insulin regulates various biological processes, including the cell cycle, neurohormonal balance, vascular function, platelet aggregation, ion exchange, and metabolism.[13] Insulin resistance can be organ specific and affects multiple physiological processes, not just metabolism. Vitamin D receptors (VDRs), which are part of the steroid/thyroid receptor family, function similarly to insulin receptors and are widely expressed. After vitamin D binds to its receptor, the VDR complex moves to the nucleus, where it interacts with retinoid X receptors (RXRs) to regulate target gene transcription through the vitamin D response element (VDRE).[14] Vitamin D affects almost 200 genes, or >3% of the human genome, by upregulating or downregulating their expression.[15] Vitamin D regulates not only mineral and bone metabolism but also immune responses, the cell cycle, neurohormonal activity, and other physiological processes. Vitamin D receptors are also found on cell membranes, where

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How to cite this article: Gupta A, Sharma S, *et al.* To Study the Correlation of Low Vitamin D Levels with Insulin Resistance. J Assoc Physicians India 2026;74(8):e18–e23.

ligand binding activates second messengers, influencing kinases such as protein kinase A (PKA), protein kinase B (PKB), and mitogen-activated protein kinase (MAPK). These nongenomic effects highlight vitamin D's role as a pleiotropic hormone, similar to insulin.[16]

A meta-analysis suggests that the inconsistent results observed in RCTs evaluating vitamin D and insulin sensitivity may be due to differences in surrogate measures, vitamin D dosage and treatment duration, and variations in study populations regarding ethnicity, glucose tolerance, and vitamin D status.[17,18] Nevertheless, in five trials, the hyperinsulinemic-euglycemic clamp, the gold standard method for determining insulin sensitivity, showed no effect of vitamin D supplementation on insulin sensitivity.[19,20] Three of these investigations, however, were limited by small sample sizes (n = 12–18).[18,19] The two additional trials also showed no effect of vitamin D in metabolically healthy overweight or obese subjects or in individuals with long-term T2DM, despite using a rigorous approach and an adequate sample size (n = 62–65).[20,21]

The association between vitamin D insufficiency and insulin resistance in T2DM is important for clinical practice and public health. Insulin resistance and reduced β-cell activity, which are key features of T2DM, lead to chronic hyperglycemia. Research suggests that vitamin D may influence insulin sensitivity and glucose metabolism. Understanding this relationship could provide new insights into the pathogenesis of T2DM and potential therapeutic approaches, such as vitamin D supplementation, which may improve glucose tolerance and insulin sensitivity. Addressing vitamin D deficiency could enhance current treatment strategies and help reduce the global burden of T2DM.

Materials and Methods

This prospective study was conducted in the Department of General Medicine at Lala Lajpat Rai Memorial Medical College, Meerut, with a sample size of 84 participants. The sample size was calculated using a 95% confidence interval and an estimated 32% prevalence of vitamin D deficiency among T2DM patients, with a 10% margin of error. Considering a 10% noncompliance rate, the final sample size was rounded to 100. The inclusion criteria encompassed patients aged 18 years or older diagnosed with T2DM, excluding those with renal, hepatic, or bone diseases, malignancies, or a history of insulin use. Ethical clearance and informed consent were obtained from all participants. Data collected included demographic profiles, family history, weight, height, body mass index (BMI), fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), serum creatinine, lipid profiles [total cholesterol (TC), triacylglycerol (TAG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL)], insulin, calcium, phosphorus, alkaline phosphatase, and serum 25(OH)D, all measured according to institutional standard procedures.

Patients were classified into three groups based on vitamin D status: deficiency, insufficiency, and sufficiency. Insulin resistance was determined using the homeostatic model assessment for insulin resistance (HOMA-IR), calculated by multiplying fasting blood glucose by insulin and dividing by 22.5. Those with HOMA-IR values greater than or equal to three-quarters digits were classified as insulin resistant. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 26. Continuous variables were presented as means and standard deviations, whereas dichotomous variables were analyzed using the Chi-squared test. Analysis of variance (ANOVA) was used to compare means across groups, with a p-value of <0.05 or <0.001 considered statistically significant.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, IL, USA) for Windows (version 26.0) was used for statistical analysis.

Results

The prospective study conducted in the Department of General Medicine at Lala Lajpat Rai Memorial Medical College, Meerut, investigated T2DM among 84 participants who were selected based on specific inclusion criteria, excluding those with renal, hepatic, or bone diseases, malignancies, or current drug therapy. The analysis revealed that the majority of individuals with vitamin D deficiency were aged 60 years or older (50%), whereas those with insufficiency were predominantly in the 30–39 years age-group (40%). The sufficiency group also had the highest proportion of individuals aged 60 years or older (57.14%). However, statistical analysis showed no significant difference in age distribution or mean age across the groups, indicating that age was not a key factor in vitamin D status. Gender did not significantly affect vitamin D status, with the deficiency group comprising 51.56% males and 48.44% females, the insufficiency group comprising 60% males and 40% females, and the sufficiency group comprising 52.38% males and 47.62% females. Statistical analysis confirmed no significant differences in gender distribution among the groups. Body mass index (BMI) was significantly associated with vitamin D status, as a higher percentage of individuals with deficiency had a BMI of 30 or above than those with insufficiency and sufficiency. The mean BMI was highest in the deficiency group and lowest in the sufficiency group, with a significant difference in mean BMI (Table 1).

A borderline significant association was observed between past medical history and vitamin D status, with individuals having no past medical history being more prevalent in the sufficiency group, whereas those with hypertension, dyslipidemia, and cardiovascular disease were more common in the deficiency group, although the differences were not statistically significant (Fig. 1). The duration of T2DM showed a significant association with vitamin D status, as the mean

Table 1: Demographic distribution of the enrolled individuals among groups

Demographics		*Deficiency (n = 64)*	*Insufficiency (n = 15)*	*Sufficiency (n = 21)*	*p-value*
Age	18–29 years	9 (14.06%)	1 (6.67%)	4 (19.05%)	$\chi = 11.16$
	30–39 years	10 (15.63%)	6 (40.00%)	2 (9.52%)	$p = 0.1930$
	40–49 years	7 (10.94%)	2 (13.33%)	2 (9.52%)	
	50–59 years	6 (9.38%)	3 (20.00%)	1 (4.76%)	
	≥60 years	32 (50.00%)	3 (20.00%)	12 (57.14%)	
	Age mean ± SD	54.60 ± 18.68	46.46 ± 12.57	52.13 ± 17.55	$F = 1.309$
					$p = 0.2748$
Gender	Male	33 (51.56%)	9 (60.00%)	11 (52.38%)	$\chi = 0.3514$
	Female	31 (48.44%)	6 (40.00%)	10 (47.62%)	$p = 0.8389$
BMI	18.5–24.9	17 (26.56%)	3 (20.00%)	12 (57.14%)	$\chi = 7.976$
	25–29.9	20 (31.25%)	5 (33.33%)	4 (19.05%)	$p = 0.0924$
	≥30	27 (42.19%)	7 (46.67%)	5 (23.81%)	
	BMI mean ± SD	29.72 ± 4.65	27.67 ± 4.14	26.60 ± 4.85	$F = 4.090$
					$p = 0.0197$*

*Statistically significant of difference in mean BMI among the three vitamin D groups $p < 0.05$

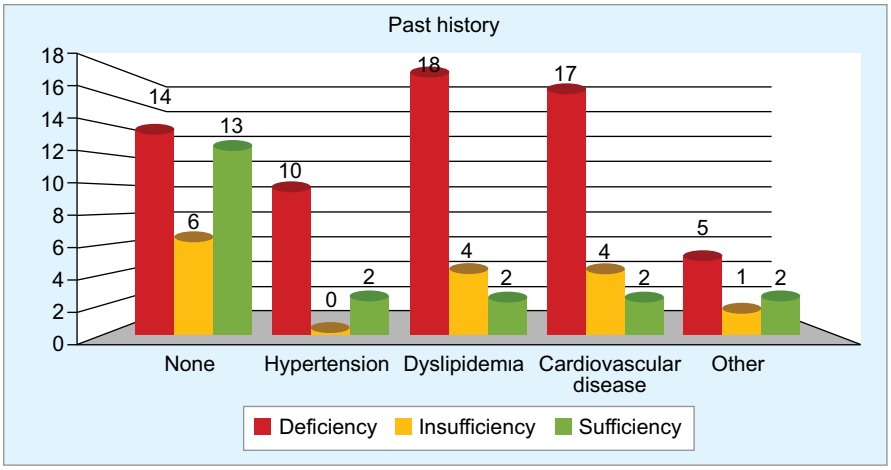

Fig. 1: Graphical representation of past medical history among groups

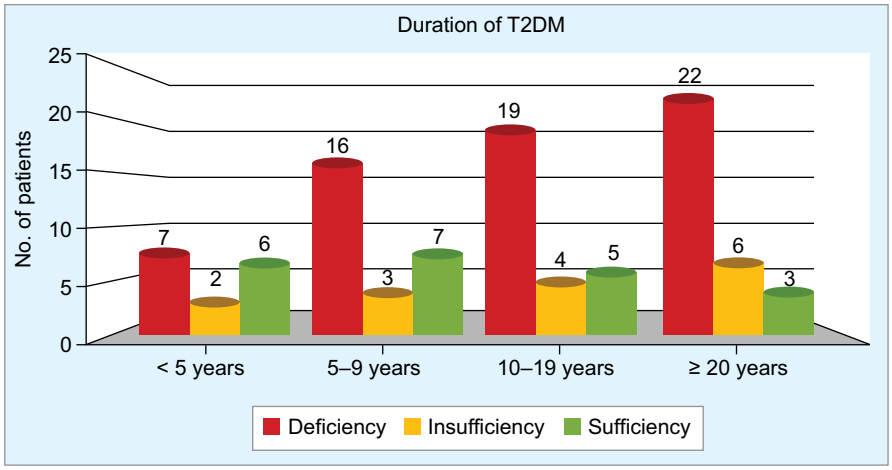

Fig. 2: Graphical representation of the duration of T2DM among groups

duration was highest in the deficiency group and lowest in the sufficiency group (Fig. 2).

Higher fasting plasma glucose levels were significantly associated with vitamin D deficiency, with the deficiency group having the highest mean fasting plasma glucose level compared with the insufficiency and sufficiency groups. Serum fasting insulin levels varied significantly across the groups, with the deficiency group having the highest mean insulin level and the sufficiency group having the lowest. HOMA-IR values were also significantly associated with vitamin D deficiency, with higher values in the deficiency group. HbA1c levels were significantly different among the groups, with the deficiency group having the highest mean HbA1c level and the sufficiency group having the lowest. No significant differences in serum creatinine levels were found among the groups. Total cholesterol levels showed no significant variation, whereas triglyceride levels were significantly associated with vitamin D deficiency, with the deficiency group having the highest mean triglyceride level. HDL cholesterol levels were significantly different among the groups, with the deficiency group having the lowest mean HDL cholesterol level and the sufficiency group having the highest. LDL cholesterol levels also varied significantly, with the deficiency group having the highest mean LDL cholesterol level and the sufficiency group having the lowest. Liver function tests and other biochemical markers showed no significant differences among the groups, indicating that these markers did not vary significantly with vitamin D status. This study highlights significant associations between vitamin D status and various metabolic and biochemical parameters in T2DM, particularly emphasizing the effects of BMI, duration of diabetes, and glucose metabolism (Table 2).

Discussion

The study findings indicate that vitamin D levels are not significantly affected by age or gender. Although older individuals were predominant in the deficiency and sufficiency groups and younger individuals in the insufficiency group, statistical analysis showed no significant age-related differences across the vitamin D status groups. Gender distribution also did not significantly influence vitamin D status, as evidenced by a Chi-square value of 0.3514 and a *p*-value of 0.8389. Similarly, in the study by Talaei et al.,[6] which included 100 patients with a mean age of 54.1 ± 11 years, the mean weight remained stable from 70 ± 12 kg to 71 ± 05 kg, with only 8% of patients on diet alone and 92% controlled with oral hypoglycemic medications, such as glibenclamide, metformin, and repaglinide.

The study showed a link between vitamin D levels and BMI, with higher BMIs associated with increased deficiency and insufficiency, whereas a BMI of 18.5–24.9 was associated with higher sufficiency. Despite this trend, the overall distribution of BMI categories across the vitamin D status groups was not significantly different, although there was a notable variation in mean BMI among the groups. This suggests that a higher BMI is substantially associated with lower vitamin D levels. BMI was identified as an independent risk factor for insulin resistance (IR) in T2DM patients in a study by Sun et al.[22] An increased BMI was associated with an increased risk of

Table 2: Distribution of fasting plasma glucose (FPG) levels among groups

		Deficiency (n = 64)	*Insufficiency (n = 15)*	*Sufficiency (n = 21)*	*p-value*
FPG	<100 mg/dL	5 (7.81%)	2 (13.33%)	10 (47.62%)	$\chi = 22.05$
	100–125 mg/dL	24 (37.50%)	8 (53.33%)	8 (38.10%)	$p = 0.0002$*
	>125 mg/dL	35 (54.69%)	5 (33.33%)	3 (14.29%)	
	FPG (mg/dL) Mean ± SD	154.00 ± 31.90	146.00 ± 42.30	131.00 ± 34.60	$F = 3.616$ $p = 0.0306$*
Serum fasting insulin	<5 µU/L	10 (15.62%)	2 (13.33%)	6 (28.57%)	$\chi = 14.06$
	5–15 µU/L	16 (25.00%)	7 (46.67%)	12 (57.14%)	$p = 0.0071$*
	>15 µU/L	38 (59.38%)	6 (40.00%)	3 (14.29%)	
	Insulin (µU/L) Mean ± SD	11.80 ± 6.80	9.16 ± 5.20	7.70 ± 3.10	$F = 4.170$ $p = 0.0183$*
HOMA-IR	<1	7 (10.94%)	1 (6.67%)	9 (42.86%)	$\chi = 20.34$
	1–2.9	24 (37.50%)	6 (40.00%)	5 (23.81%)	$p = 0.0004$*
	≥3	33 (51.56%)	4 (26.67%)	2 (9.52%)	
	HOMA-IR Mean ± SD	3.60 ± 1.20	2.23 ± 1.05	1.61 ± 0.95	$F = 28.29$ $p < 0.0001$*
HbA1c	<5.7%	3 (4.69%)	1 (6.67%)	0 (0.00%)	$\chi = 11.12$
	5.7–6.4%	7 (10.94%)	5 (33.33%)	0 (0.00%)	$p = 0.0252$*
	≥6.5%	54 (84.38%)	9 (60.00%)	21 (100.00%)	
	HbA1c Mean ± SD	6.98 ± 0.72	6.54 ± 0.64	5.84 ± 0.65	$F = 21.61$ $p < 0.0001$*
Serum creatinine	<0.6 mg/dL	3 (4.69%)	1 (6.67%)	2 (9.52%)	$\chi = 4.053$
	0.6–1.2 mg/dL	23 (35.94%)	8 (53.33%)	11 (52.38%)	$p = 0.3989$
	>1.2 mg/dL	38 (59.38%)	6 (40.00%)	8 (38.10%)	
	Serum creatinine (mg/dL)	1.08 ± 0.27	0.97 ± 0.26	0.94 ± 0.32	$F = 2.445$ $p = 0.0921$
Total cholesterol	<200 mg/dL	37 (57.81%)	10 (66.67%)	14 (66.67%)	$\chi = 0.7592$
	200–239 mg/dL	27 (42.19%)	5 (33.33%)	7 (33.33%)	$p = 0.6841$
	Total cholesterol Mean ± SD (mg/dL)	192.74 ± 2.61	189.35 ± 29.46	191.04 ± 19.41	$F = 0.3814$ $p = 0.6840$
Triglyceride	<150 mg/dL	17 (26.56%)	1 (6.67%)	3 (14.29%)	$\chi = 12.72$
	150–199 mg/dL	17 (26.56%)	0 (0.00%)	3 (14.29%)	$p = 0.0127$*
	≥200 mg/dL	30 (46.88%)	14 (93.33%)	15 (71.43%)	
	Triglyceride Mean ± SD (mg/dL)	246.28 ± 41.13	227.11 ± 53.98	196.84 ± 59.00	$F = 8.776$ $p = 0.0003$*
HDL	<40 mg/dL	45 (70.31%)	8 (53.33%)	6 (28.57%)	$\chi = 11.62$
	40–59 mg/dL	19 (29.69%)	7 (46.67%)	15 (71.43%)	$p = 0.0030$*
	HDL Mean ± SD (mg/dL)	40.78 ± 8.65	43.49 ± 5.80	46.87 ± 9.50	$F = 3.489$ $p = 0.0344$*
LDL	<100 mg/dL	16 (25.00%)	1 (6.67%)	9 (42.86%)	$\chi = 6.049$
	100–159 mg/dL	48 (75.00%)	14 (93.33%)	12 (57.14%)	$p = 0.0486$*
	LDL Mean ± SD (mg/dL)	135.08 ± 16.89	115.53 ± 22.09	114.29 ± 23.08	$F = 12.97$ $p = 0.0060$*
LFT and other tests Mean ± SD	AST (U/L)	23.68 ± 8.99	26.61 ± 6.62	21.95 ± 8.82	$F = 1.276$ $p = 0.2838$
	ALT (U/L)	24.95 ± 9.34	25.75 ± 7.63	26.49 ± 7.50	$F = 0.2592$ $p = 0.7722$
	ALP (U/L)	77.88 ± 22.27	70.13 ± 20.07	78.42 ± 22.20	$F = 0.8270$ $p = 0.4404$
	Serum calcium (mg/dL)	8.97 ± 0.62	8.74 ± 0.54	8.99 ± 0.50	$F = 1.034$ $p = 0.3594$
	Serum phosphorous (mg/dL)	3.51 ± 0.57	3.25 ± 0.58	3.46 ± 0.47	$F = 1.346$ $p = 0.2651$
Serum 25(OH)D	<20 ng/mL	64 (100.00%)	0 (0%)	0 (0%)	$\chi = 200.0$
	20–29 ng/mL	0 (0%)	15 (100.00%)	0 (0%)	$p < 0.0001$*
	≥30 ng/mL	0 (0%)	0 (0%)	21 (100.00%)	
	Serum 25(OH)D (ng/mL)	14.30 ± 3.21	24.26 ± 1.68	34.73 ± 2.97	$F = 387.2$ $p < 0.0001$*

*Statistically significant at p<0.05. 25(OH)D, 25-hydroxyvitamin D; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; LDL, low-density lipoprotein

IR, particularly among overweight or obese individuals, according to a previous study by Deng et al.[23] Visceral fat, indicated by a high BMI, releases hormones and proinflammatory substances that can disrupt insulin signaling and cause insulin resistance.[22]

The study revealed a strong association between vitamin D levels and medical history, with individuals without prior medical conditions having higher vitamin D levels. Vitamin D deficiency was associated with higher rates of hypertension, dyslipidemia, and cardiovascular disease, suggesting that a greater burden of comorbidities may correlate with lower vitamin D levels. Additionally, vitamin D insufficiency and deficiency increased with the duration of T2DM, with significant differences noted among those with T2DM for 20 years or longer. However, serum creatinine levels remained similar across the vitamin D status groups, showing no significant variation.

Vitamin D status was significantly correlated with fasting plasma glucose (FPG) levels, with only 14.29% of individuals with FPG >125 mg/dL having sufficient vitamin D, compared with 47.62% of those with FPG <100 mg/dL. Significant differences were noted, as indicated by an *F*-value of 3.616 ($p = 0.0306$) and a Chi-square value of 22.05 ($p = 0.0002$). However, the statement that "higher FPG levels (were) associated with better vitamin D sufficiency and lower FPG levels with increased vitamin D deficiency" is inconsistent with the preceding results. Based on the presented findings, higher FPG levels were associated with greater vitamin D deficiency, whereas lower FPG levels were associated with better vitamin D sufficiency. Talaei et al.[6] found that vitamin D_3 supplementation significantly reduced FPG and insulin levels, with a 30% reduction in FPG. They used paired *t*-tests for normally distributed FPG data and the Wilcoxon test for nonnormally distributed HOMA-IR and insulin data and recommended linear regression for predicting FPG changes after treatment. According to Pittas et al.,[24] monthly supplementation with 1,20,000 units of vitamin D significantly improved insulin sensitivity. Sun et al.[22] found that vitamin D supplementation significantly reduced 2-hour plasma glucose (2hPG), fasting blood glucose (FBG), and HbA1c levels in patients with T2DM and IR, with the combination therapy group experiencing more pronounced reductions than the conventional treatment group.

The study found a strong correlation between vitamin D status and insulin levels, with lower insulin levels associated with greater vitamin D sufficiency. Significant differences in insulin levels were observed, indicating that greater vitamin D sufficiency corresponded to lower insulin levels. According to Talaei et al.,[6] higher baseline 25(OH)D levels were inversely associated with final FPG, suggesting that vitamin D supplementation is more effective in lowering FPG when baseline vitamin D levels are higher. The study also noted that vitamin D concentrations between 40 and 60 ng/mL have a significant effect on insulin resistance, with less effect at lower or higher concentrations.

The study revealed a significant correlation between vitamin D status and HbA1c levels. Individuals with vitamin D deficiency had the highest HbA1c levels, with 84.38% having HbA1c ≥6.5%, compared with 60% in the insufficiency group. The deficiency group also had significantly higher mean HbA1c values (6.98 ± 0.72) than the sufficiency group (5.84 ± 0.65), suggesting that vitamin D deficiency is associated with increased HbA1c levels. Recent studies by Pieńkowska et al.[25] and Fong et al.[26] showed that vitamin D insufficiency affects insulin secretion, sensitivity, and resistance, affecting approximately 50% of T2DM patients. After vitamin D supplementation, the combination therapy group showed greater reductions in 2hPG, FBG, and HbA1c, along with greater increases in 25(OH)D_3 than the conventional treatment group. Vitamin D also improves insulin resistance by decreasing inflammatory substances produced by adipocytes.

The study found distinct lipid profile patterns among the vitamin D status groups. Total cholesterol levels were similar across the groups, with no significant differences. However, significant variations were noted in triglyceride, HDL, and LDL levels. The deficiency group had the highest mean triglyceride level (246.28 mg/dL) and the lowest mean HDL level (40.78 mg/dL), while also showing the highest mean LDL level (135.08 mg/dL). These differences indicate that vitamin D deficiency is associated with a more adverse lipid profile, including elevated triglyceride levels, reduced HDL levels, and increased LDL levels. According to Talaei et al.,[6] the mean serum concentrations of total cholesterol (TC), triglycerides (TG), HDL, and LDL cholesterol did not change after 8 weeks of vitamin D administration compared with baseline. Sun et al.[22] examined changes in lipid metabolism before and after treatment to determine the effect of vitamin D supplementation on lipid metabolism in T2DM patients with IR. Following treatment, both groups showed improved HDL cholesterol and reduced TG and TC levels, with the combination therapy group exhibiting significantly higher HDL cholesterol and lower TG and TC levels than the conventional treatment group. LDL cholesterol levels remained similar between the groups. These results suggest that vitamin D supplementation improves glucose and lipid metabolism in T2DM patients with IR. No significant differences were observed in aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), serum calcium, or phosphorus levels among the vitamin D status groups, indicating that these markers are not influenced by vitamin D levels.

The study significantly differentiated the vitamin D status groups based on serum 25(OH)D levels: deficiency (<20 ng/mL), insufficiency (20–29 ng/mL), and sufficiency (≥30 ng/mL). The deficiency group had the lowest mean level (14.30 ± 3.21 ng/mL), the insufficiency group had an intermediate mean level (24.26 ± 1.68 ng/mL), and the sufficiency group had the highest mean level (34.73 ± 2.97 ng/mL). Statistical analysis (F-value = 387.2, $p < 0.0001$) confirmed a significant gradient in vitamin D levels among the groups. According to Talaei et al.,[6] the mean 25(OH)D concentration was 43.03 ± 19.28 ng/mL (107.5 ± 48.2 nmol/L) at baseline. Based on a 25(OH)D level of <20 ng/mL (50 nmol/L), 24% of individuals were vitamin D deficient at baseline. Numerous studies have demonstrated the effects of vitamin D supplementation on glucose homeostasis. For instance, Inzucchi et al.[27] demonstrated a 60% improvement in insulin sensitivity by increasing the serum 25(OH) D concentration from 10 to 30 ng/mL (25 to 75 nmol/L), with 54 and 13% of patients receiving metformin and troglitazone, respectively. Vitamin D supplementation was shown by Von Hurst et al.[28] to significantly improve insulin resistance and insulin sensitivity. According to Chiu and Audrey,[29] insulin sensitivity is directly correlated with vitamin D concentration and inversely correlated with FPG.

The participants in the deficiency group showed the highest mean HOMA-IR value (3.60 ± 1.20), whereas those in the sufficiency group showed the lowest mean value (1.61 ± 0.95). With a Chi-square value of 20.34 and a p-value of 0.0004, the distribution of HOMA-IR values differed significantly among the groups, suggesting a strong association. According to Talaei et al.,[6] there was a significant difference in mean HOMA-IR values between the groups, as indicated by an F-value of 28.29 and a p-value of <0.0001. The association between low vitamin D levels and poor insulin sensitivity was highlighted by Talaei et al.,[6] who suggested that the deficiency group had significantly higher HOMA-IR levels, a marker of insulin resistance. A significant decrease in mean HOMA-IR was observed

after vitamin D administration compared with pretreatment values. A baseline serum 25(OH)D stratification technique was used, and changes in each variable were plotted to reflect the changes for each stratum. Witham et al.[30] discovered that vitamin D supplementation, at different dosages, had no effect on insulin resistance or HbA1c, despite the significant reduction in HOMA-IR reported in some studies, including that by Lind et al.[31] According to Nagpal et al.,[32] 2 years of vitamin D administration improved HOMA-IR but had no effect on mean insulin sensitivity.

This study underscores the important relationship between vitamin D status and T2DM management by demonstrating significant associations with FPG, HbA1c, and insulin resistance. It suggests that addressing vitamin D deficiency may be important for improving diabetes management and outcomes. The findings support further research to determine whether vitamin D supplementation could complement standard treatment, potentially leading to more effective and comprehensive approaches to T2DM management and improved patient quality of life.

Conclusion

In conclusion, this study revealed a high prevalence of vitamin D deficiency among older T2DM patients and those with a longer duration of diabetes. Although age and gender did not significantly affect vitamin D status, poor glycemic control, elevated FPG, and increased insulin resistance were strongly associated with lower vitamin D levels. Additionally, higher triglyceride and LDL cholesterol levels, along with lower HDL levels, were more prevalent among individuals with vitamin D deficiency. No significant differences were observed in serum creatinine, total cholesterol, or liver function tests across the vitamin D status groups. These findings suggest a complex relationship between vitamin D levels and metabolic control in T2DM patients, highlighting the potential benefits of vitamin D supplementation in improving glycemic and metabolic parameters. Further longitudinal studies are needed to validate these associations and explore therapeutic interventions.

Consent

Written informed consent was obtained from all participants in accordance with international or university standards and is maintained by the authors.

Ethical Approval

Ethical approval was granted in compliance with international or university standards, and the written approval is preserved by the authors.

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