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Original Article

Association between vitamin D deficiency and insulin resistance assessed by the triglyceride-glucose index in type 2 diabetes mellitus adults in Northwest Algeria

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Abstract

Vitamin D plays a role in glucose metabolism and insulin regulation. This study aimed to assess the association between vitamin D levels and the triglyceride-glucose (TyG) index, a surrogate marker of insulin resistance (IR), in Algerian adults with type 2 diabetes mellitus (T2DM). In this cross-sectional study, 105 patients with type 2 diabetes mellitus (T2DM) were evaluated. Clinical and biochemical data were collected, including fasting glucose, lipid profile, glycated hemoglobin (HbA1c), and 25-hydroxyvitamin D [25(OH)D] levels. The TyG index was calculated. Associations were analyzed using Spearman correlation and binary logistic regression. Patients with vitamin D deficiency exhibited significantly higher levels of fasting glucose and glycated hemoglobin, with P values of 0.015 and 0.013, respectively. A negative correlation was observed between vitamin D and the TyG index (r=–0.237; P=0.015). Vitamin D >20 ng/mL was associated with a lower risk of elevated TyG index (OR=0.246; 95% CI: 0.080–0.752; P=0.014). Low vitamin D levels were significantly associated with higher TyG index values in T2D patients, suggesting a potential link between vitamin D deficiency and IR in this population.

Keywords: type 2 diabetes mellitus, vitamin D, index triglyceride–glucose, insulin resistance, Algeria

Introduction

Vitamin D, also known as the D-hormone, plays a crucial role in calcium metabolism and affects several physiological systems. Low vitamin D levels have been associated with an increased risk of insulin resistance (IR) in individuals with type 2 diabetes mellitus (T2DM) and metabolic syndrome [1]. This hormone exerts its biological effects by binding to the vitamin D receptor (VDR), a nuclear receptor expressed in various tissues, including pancreatic β-cells. Upon activation, VDR regulates gene expression involved in glucose transport and insulin secretion. This process is indirectly regulated through the modulation of intracellular calcium concentrations, which, in turn, affect the expression of voltage-gated calcium channels, thereby facilitating the mobilization and exocytosis of insulin vesicles [2, 3].

Insulin resistance is most commonly assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index [4]. A study conducted in patients with type 2 diabetes mellitus reported an inverse association between vitamin D deficiency and the HOMA-IR values, suggesting a potential link between vitamin D status and insulin sensitivity [5]. Most recently, the triglyceride-glucose (TyG) index has emerged as a novel surrogate marker for evaluating IR in diabetic populations [6, 7]. Compared to the HOMA-IR index, the TyG index has demonstrated a stronger ability to predict the prevalence and incidence of T2DM [8]. Interestingly, a high TyG index has also been identified as a potential risk factor for VDD, particularly among men [9].

The association between the TyG index and vitamin D has been studied in diverse populations, including cohorts from China, India and Europe [10]. However, this relationship has yet to be studied in North African populations, where ethnicity, dietary habits, sun exposure, and cultural clothing practices may influence vitamin D status [11]. In Algeria, a large proportion of adults have either developed the disease or are at high risk, due in part to high rates of obesity and sedentary lifestyles [12]. In this context, the present study aims to explore, for the first time, the association between vitamin D levels and the TyG index in individuals with type 2 diabetes mellitus (T2DM) from the Tlemcen region in northwest Algeria.

Material and methods

Study design and patients

This observational cross-sectional study included 105 adult patients with confirmed type 2 diabetes (T2DM), recruited between January and June 2024 from Dr. Tidjani Damerdji University Hospital in Tlemcen, Algeria. A healthcare provider made the diagnosis of T2DM according to the American Diabetes Association criteria [13].

Patients were excluded if they had major comorbidities, type 1 diabetes mellitus or other types of diabetes mellitus, pregnancy, malignant tumor, autoimmune disease, a body mass index (BMI) >35 kg/m^2, or advanced diabetes-related complications. Ethical approval was obtained from the scientific council of the faculty and the university ethics and deontology committee. The study was conducted in accordance with the Declaration of Helsinki, and all participants provided written informed consent.

Sociodemographic and clinical data were obtained from standardized questionnaires and medical records. These included age, sex, weight, height, medical history, and current antidiabetic treatment history of patients receiving oral agents (metformin), insulin or a combination of insulin and metformin (mixed). However, detailed information on drug dosage, treatment duration, and adherence was not available.

BMI was subsequently calculated as weight (kg) divided by the square of height (m^2) and classified into normal (BMI <25 kg/m^2), overweight (25 kg/m^2 ≤BMI <30 kg/m^2), and obesity (30 kg/m^2 ≤BMI <35 kg/m^2) categories.

Blood Samples

Fasting blood samples were drawn in the morning after 12 12-hour overnight fast. Serum separation was performed within 30 minutes of collection to minimize glycolysis, although the tubes used did not contain glycolysis inhibitors. The serum collected in plain tubes was used to measure fasting blood glucose (FBG), urea, creatinine, cholesterol, High-Density Lipoproteins Cholesterol (HDL-C), Low-Density Lipoproteins Cholesterol (LDL-C), and triglycerides (TG) using standard enzymatic assays (Roche Cobas 6000 c 501, Mannheim, Germany).

Vitamin D levels were measured in plasma obtained from heparinized blood, which was then centrifuged at 3000 rpm for 5 to 10 minutes. A radioimmunoassay using monoclonal antibodies specific to 25(OH)D_2/D_3 was performed (Wizard 2480 Gamma Counter). VDD was defined as plasma 25(OH)D <20 ng/mL, while values ≥20 ng/mL were considered non-deficient [14]. HbA1c was measured in whole blood collected in EDTA tubes using the Tosoh HLC-723GX automated glycohemoglobin analyzer.

The TyG index was calculated using the following formula [7]:

$$TyG\ indice = \ln\left[\, fasting\ TG\ (mg/dL) \times\ FBG (mg/dL)/2\right]$$

TG – Triglyceride; FBG– fasting Blood Glucose.

Statistical analysis

Statistical analysis was performed using SPSS software (Statistical Package for the Social Sciences) version 26 (IBM Corporation, USA) and GraphPad Prism 8 (CA, USA). For continuous variables, normality of the data was assessed using the Kolmogorov-Smirnov test. Data following a normal distribution were expressed as mean±Standard Deviation (SD) ($\bar{X}$±σ), and non-normally distributed data were presented as median (Q1–Q3). Categorical variables were expressed as percentages. Student's t-test or the Mann–Whitney U test was used for comparing two continuous variables, and the chi-square test was applied for categorical data.

As there is no universally accepted threshold for the TyG index to define IR [15], the TyG index values

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were categorized into quartiles. Q1 was defined as the reference category. Analysis of variance (ANOVA) was used to compare mean vitamin D levels across TyG quartiles, followed by Tukey's post hoc test for pairwise comparisons. Correlations between variables were assessed using Spearman's rank correlation for non-normally distributed data, and Pearson's correlation for normally distributed variables. To identify independent predictors of a high TyG index, binary logistic regression analysis was performed. The TyG index was dichotomized into two groups: <Q1 (reference group) and ≥Q1. Variables with a p-value <0.2 in univariate analysis were included in the multivariate model [15]. Results were presented as odds ratios (OR) with 95% confidence intervals (CI). Model adequacy was assessed using a goodness-of-fit test.

A p-value<0.05 was considered statistically significant. Significance levels were reported as follows: * – P<0.05; ** – P<0.01; *** – P<0.001.

Results

Sociodemographic and clinical characteristics

The study included 105 patients with type 2 diabetes mellitus (T2DM) from northwest Algeria. The mean

Table 1: Anthropometric, clinical and biochemical characteristics of the study population based on vitamin D levels.

Variables	All (n=105)	No VDD (n=62)	VDD (n=43)	P-value
Age (years) [a]	58.50±14.25	60.35±15.23	55.81±12.39	0.096
Gender female, n (%)	71 (67.61)	42 (67.7)	29 (67.4)	0.974
BMI (kg/m²) [a]	25.26±4.44	25.47±4.30	24.95±4.66	0.561
BMI groups n (%)				
Normal	51 (48.60)	30 (48.40)	21 (48.80)	
Overweight	38 (36.20)	22 (35.50)	16 (37.20)	0.856
Obesity	16 (15.20)	10 (16.10)	6 (14)	
Treatment n (%)				
Metformin	52 (49.5)	31 (50)	21 (48.8)	
Insulin	17 (16.2)	10 (16.1)	7 (16.3)	0.993
Mixed	36 (34.3)	21 (33.9)	15 (34.9)	
VitD (ng/mL) [b]	23.24 (12.15–34.70)	32.07 (25.87–39.57)	10.90 (8.43–15.40)	0.0001
FBG (g/L) [b]	1.48 (1.07–2.43)	1.37 (1.04–1.90)	1.89 (1.16–2.78)	0.015
HbA1c (%) [b]	6.60 (6.02–7.28)	6.30 (5.97–7.02)	6.9 (6.3–7.5)	0.013
Hypertension, n (%)	30 (28.6)	14 (22.6)	16 (37.2)	0.103
Index TyG [a]	9.22±0.70	9.14±0.69	9.34±0.69	0.149
Cholesterol (g/L) [b]	1.86 (1.65–2.13)	1.88±0.43	1.98±0.50	0.284
TG (g/L) [b]	1.23 (0.93–1.76)	1.26 (0.95–1.75)	1.26 (0.95–1.75)	0.779
HDL-C (g/L) [b]	0.52 (0.40–0.70)	052 (0.43–0.80)	0.49 (0.35–0.61)	0.131
LDL-C (g/L) [b]	0.82 (0.50–1.07)	0.89 (0.48–1.09)	0.73 (0.50–1.02)	0.388
Urea (g/L) [b]	0.30 (0.22–0.37)	0.28 (0.22–0.36)	0.31 (0.22–0.39)	0.836
Creatinine (mg/L) [a]	8.70±2.49	8.79±2.51	8.64±2.49	0.689

Note: VDD – hypovitaminosis D; VitD – vitamin D; FBG – fasting blood glucose. [a] – Values following a normal distribution were expressed as mean±standard deviation; [b] – The non-parametric values were expressed as median (Q1–Q3). Comparisons of quantitative variables between the VitD<20 ng/ml and ≥20 ng/ml groups were analysed using the Student (t) test or the Mann-Whitney test for a non-normal distribution. Qualitative variables were analyzed using the Chi-square test.

age was 58.5±14.25 years, and 67.6% of participants were female. The average BMI was 25.26±4.44 kg/m^2, corresponding to the overweight category. The median vitamin D concentration was within the reference range, while the mean TyG index was 9.22±0.70. Biochemical markers such as fasting blood glucose (FBG) and HbA1c exceeded recommended thresholds. Similarly, elevated triglycerides and total cholesterol levels were observed in the overall population, while other parameters remained within normal limits (Table 1).

Patients with VDD showed significantly higher FBG and HbA1c values compared to those without deficiency (P=0.015 and P=0.013, respectively). Median 25(OH)D levels were markedly lower in the VDD group (10.90 *vs.* 32.07 ng/mL, P<0.0001). No significant differences were observed between the two groups in terms of age, gender distribution, BMI, TyG index, lipid profile (cholesterol, triglycerides, HDL-C, LDL-C), kidney function markers (urea, creatinine), or prevalence of hypertension. The distribution of antidiabetic treatments was also comparable (P=0.993) (Table 1).

TyG index analysis

The TyG index was analyzed across relevant subgroups. Female participants exhibited significantly higher TyG index values compared to males (9.43±0.65 *vs.* 9.12±0.69; P=0.027). A significant difference in TyG values was also observed across BMI categories (P=0.039), with the highest index recorded among individuals classified as obese (Figure 1).

To further explore the relationship between the TyG index and vitamin D status, patients were stratified into quartiles based on TyG index values. The analysis of variance (ANOVA) showed a significant difference in plasma 25(OH)D levels across TyG quartiles (P=0.007) (Table 2).

Post-hoc Tukey test classified Q1 into a distinct statistical subgroup A, while Q2, Q3, and Q4 formed subgroup B. Participants in Q1 (lowest TyG values) had the highest mean vitamin D levels ([VitD]=31.52±12.80 ng/mL).

Association analysis

Correlation results are presented in Table 3. This revealed a significant inverse association between vitamin D levels and the TyG index (r=-0.237; P=0.015). Vitamin D levels were also negatively correlated with both fasting blood glucose (r=-0.327; P<0.001) and HbA1c (r=-0.260; P=0.007). In contrast, the TyG index was positively associated with BMI (r=0.255, P=0.009), HbA1c (r=0.422), and cholesterol (r=0.369), with P values ≤ 0.0001. No significant correlations were observed

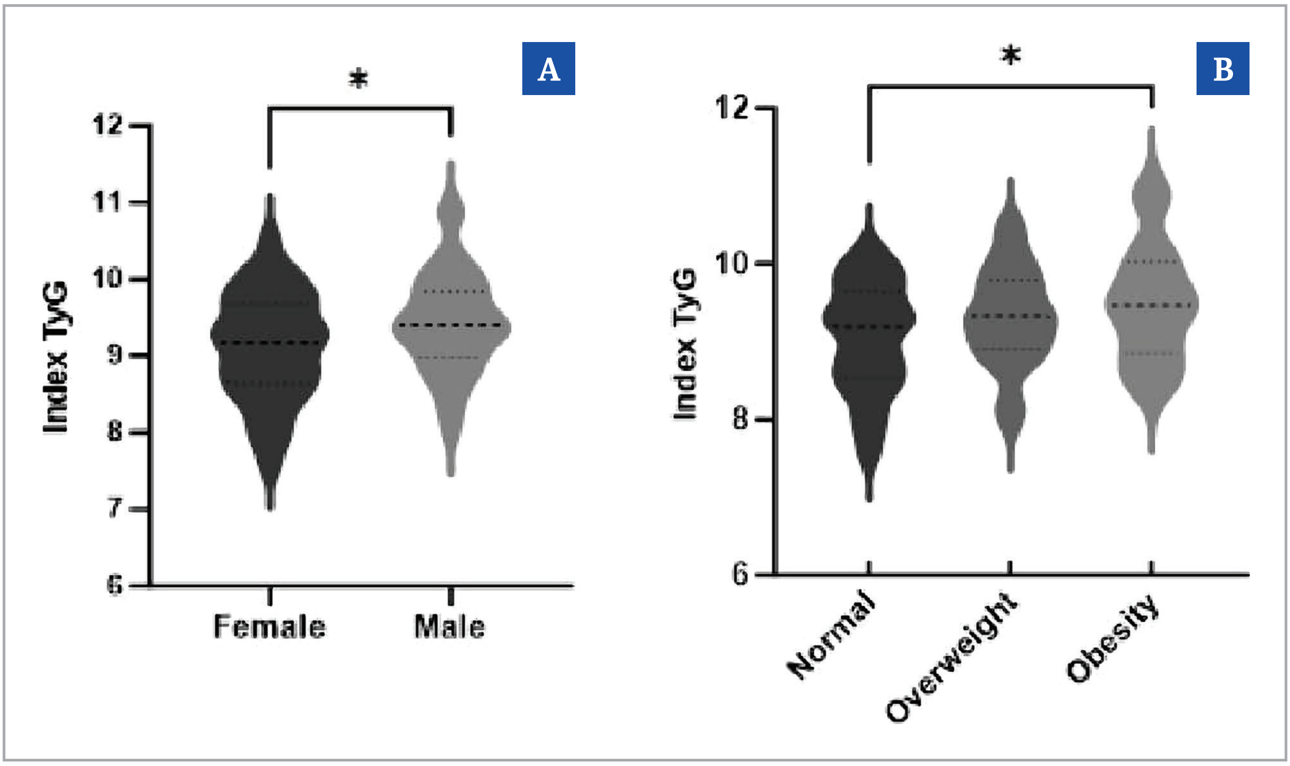

Figure 1: Comparison of mean TyG index according to gender (a) and BMI status (b). Student's t-test and ANOVA were performed, respectively (* – P<0.05).

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Table 2: Distribution of vitamin D levels according to TyG Index quartiles.

Index TyG quartile	Q1 (≤8.74)	Q2 [8.75–9.26]	Q3 [9.27–9.72]	Q4 (≥9.73)	P-value
Vit D (ng/mL)	31.52±12.80	21.70±12.40	21.67±10.46	22.74±12.38	0.007

between vitamin D and other lipid parameters (HDL-C, LDL-C, and TG).

Gender-stratified correlation between vitamin D and TYG index

Among female participants, vitamin D levels were significantly and inversely correlated with the TyG index (r=-0.281; P=0.013). No significant association was observed in male participants (r=-0.147; P=0.408) (Figure 2).

Multivariate analysis

Table 4 presents the results of the binary logistic regression, using Q1 (the lowest TyG quartile) as the reference category. The unadjusted results showed that patients with vitamin D levels <20 ng/mL had a higher risk of having a TyG index ≥Q1, with an OR=3.159; 95% CI (1.150 – 8.675; P=0.026). This association remained significant after adjusting for potential confounders, including gender, cholesterol, creatinine, and BMI, with an OR of 4.065 (95% CI, 1.329 –12.520; P=0.014).

Table 3: Correlation matrix between clinical and biochemical variables.

Variables		Age	Cholesterol	HDL-C	LDL-C	TG	FBG	HbalC	TyG index	Vit D
Age	r									
	P									
Cholesterol	r	-0.147								
	P	0.139								
HDL-C	r	-0.150	-0.050							
	P	0.137	0.624							
LDL-C	r	-0.137	0.319**	-0.107						
	P	0.177	0.001	0.290						
TG	r	0.147	0.312**	-0.044	0.022					
	P	0.135	0.001	0.664	0.829					
FBG	r	0.013	0.261**	-0.225	0.073	0.147				
	P	0.893	0.008	0.024*	0.473	0.133				
HbalC	r	0.145	0.069	-0.110	-0.107	0.157	0.494***			
	P	0.139	0.493	0.277	0.293	0.111	<0.001			
TyG index	r	0.095	0.369***	-0.181	0.065	0.730***	0.747***	0.422***		
	P	0.335	<0.001	0.071	0.523	<0.001	<0.001	<0.001		
VitD	r	0.109	-0.134	0.176	-0.017	-0.052	-0.327	-0.260**	-0.237*	
	P	0.267	0.180	0.080	0.865	0.595	0.001**	0.007	0.015	
BMI	r	-0.056	0.127	-0.143	0.280**	0.195*	0.166	0.019	0.255**	-0.104
	P	0.569	0.203	0.156	0.005	0.047	0.091	0.848	0.009	0.293

Note: The Spearman correlation test was used to assess the relationship between Vit D and HbA1c, glycemia, TG, LDL-C, HDL-C, and cholesterol. The Pearson correlation test was applied to examine the relationship between the TyG index and age and BMI. (* – P<0.05; ** – P<0.01; *** – P<0.001).

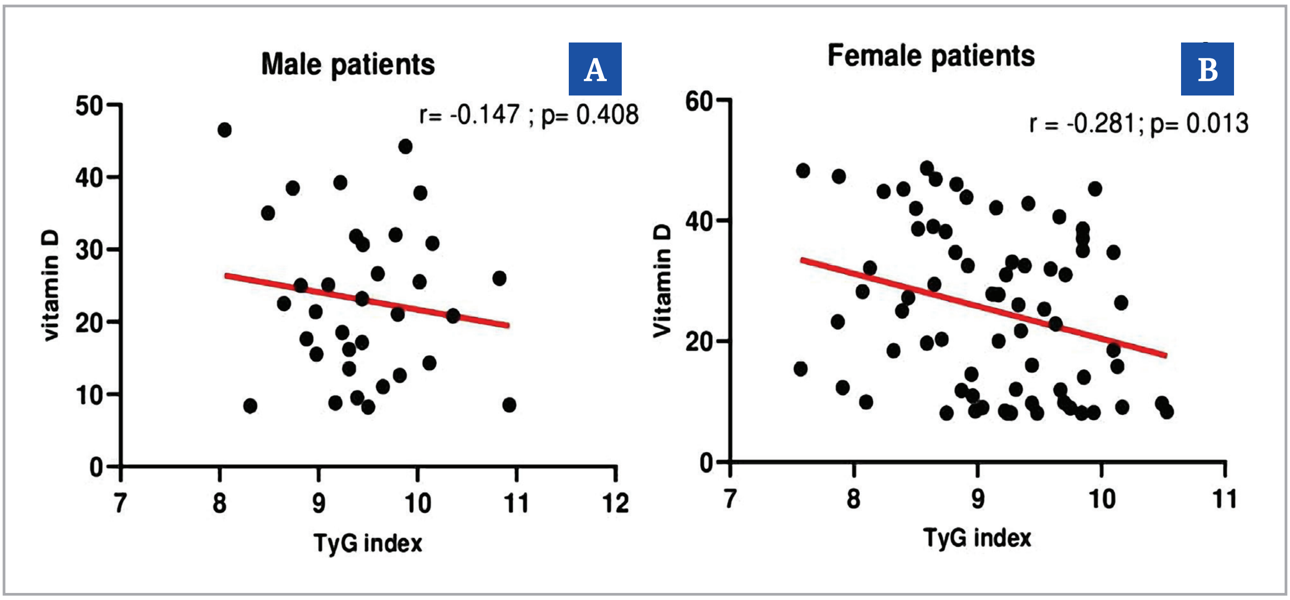

Figure 2: Correlation between vitamin D and TyG index in men (a) using Pearson correlation and in women (b) using Spearman correlation.

Table 5 supports the adequacy of the logistic regression model. The goodness-of-fit was confirmed by multiple tests, including Pearson's chi-square, the sum of squared residuals, the Hosmer-Lemeshow test, and both of Brown's methods (general and symmetric alternatives), all of which yielded non-significant results (P>0.05).

Discussion

The variability in reported vitamin D levels across studies may partly be attributed to differences in threshold definitions, as there is currently no universally accepted cut-off for vitamin D deficiency or insufficiency [16]. Most studies, however, adopt a threshold of <20 ng/mL to define vitamin D deficiency [17]. In our study, 41% of patients with T2DM had vitamin D levels below 20 ng/ml. This finding is particularly striking, given that Algeria is a sun-rich country, suggesting that other contributing factors, such as limited sun exposure, clothing style, dietary habits, age, and gender, may significantly influence vitamin D status [18]. A recent meta-analysis conducted in the MENA (Middle East and North Africa) region reported an alarming prevalence of hypovitaminosis D (<20–25 ng/mL) among T2DM patients, ranging from 37% to 96% across countries. For instance, in Bahrain, adults had the lowest mean vitamin D level of only 13 ng/mL, while in Morocco, 69% patients had vitamin D levels below 20 ng/mL. Similarly,

Table 4: Binary logistic regression models: factors associated with a low TyG Index (<Q1).

	Predictive Variable	Unadjusted OR (95% IC)	Unadjusted P-value	Adjusted model OR (95% IC)	Adjusted model P-value
Vitamin D	<20 ng/mL	3.159 (1.150–8.675)	0.026	4.065 (1.329–12.520)	0.014
	≥20 ng/mL	Reference		Reference	
Gender	Female	-	-	3.825 (1.048–13.958)	0.042
	Male	-	-	Reference	
	Cholesterol	-	-	3.023 (0.863–10.591)	0.084
	Creatinine	-	-	0.741 (0.574–0.958)	0.022
	BMI	-	-	1.158 (1.012–1.325)	0.033

Note: Adjusted model: adjustment for VitD (< and ≥20 ng/ml), gender, cholesterol, creatinine, and BMI.

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Table 5: Adjustment adequacy tests.

Methode	k-squire	DF	P-value
Pearson	116.340	99	0.112
Sum of the difference squares	98.059	99	0.508
Hosmer-Lemeshow	5.520	8	0.701
Brown:			
General alternative	3.240	2	0.198
Symmetrical alternative	2.618	1	0.106

Note: DF – degree of freedom.

a study in Egypt demonstrated that 76.2% of diabetic patients without metabolic syndrome were vitamin D deficient (<20 ng/mL) [17].

The association between VDD and T2DM has received growing attention in recent years, although the underlying mechanisms remain incompletely understood. A recent systematic review highlighted an inverse correlation between vitamin D levels and glycemic control, as well as a positive association between VDD and the pathogenesis of T2DM [19]. This may be explained by the vitamin D's effect on improving insulin sensitivity, which involves enhancing GLUT-4 expression and reducing the production of pro-inflammatory cytokines. Type 2 diabetes mellitus (T2DM) is characterized by a chronic inflammatory state, which plays a crucial role in the onset and progression of insulin resistance (IR). This low-grade inflammation is driven by the overactivation of the innate immune system, resulting in an increased production of cytokines, such as TNF-α and IL-6. These mediators disrupt insulin signaling by interfering with insulin receptor substrate-1 (IRS-1) pathways and inducing oxidative stress in key metabolic tissues, including the liver, skeletal muscle, and adipose tissue [20].

Several studies have demonstrated that elevated TyG index levels are positively associated with the risk of type 2 diabetes mellitus (T2DM), cardiovascular disease, and metabolic syndrome [21, 22]. Du *et al.* reported a strong correlation between the TyG index and HOMA-IR, suggesting that the TyG index may serve as a more relevant marker of IR than traditional lipid-based indices such as the visceral adiposity index [23]. Furthermore, due to its superior sensitivity compared to HOMA-IR, the TyG index offers a simple and accessible alternative in developing countries compared to the euglycemic-hyperinsulinemic clamp test, which remains the "gold standard" but is both complex and costly [8, 24]. In our study, vitamin D levels were negatively correlated with FBG, HbA1c, and the TyG index. These findings suggest a potential role for vitamin D in modulating metabolic imbalances, particularly those related to IR. Additionally, post-hoc Tukey analysis revealed that the first quartile of the TyG index was associated with the highest vitamin D concentrations. These results reinforce the association between VDD and the TyG index, consistent with previous studies [9].

Interestingly, we observed that the TyG index was significantly higher in women compared to men, suggesting a possible sex related difference in IR. This finding aligns with previous work by Zhao *et al.*, who demonstrated more pronounced insulin resistance in women [25]. However, another study found the opposite pattern, with the association observed only in men [9]. This discrepancy could be partially explained by hormonal differences, particularly the role of estrogens such as estradiol (E2), which enhances insulin sensitivity by increasing glucose uptake in muscle via GLUT-4 and suppressing hepatic gluconeogenesis [26–28].

Another important factor associated with the TyG index in our study was BMI. Patients with a BMI above normal levels had significantly higher TyG index values (P=0.020). This may reflect the effect of increased circulating free fatty acids in individuals with excess adiposity, which promote hepatic gluconeogenesis and interfere with insulin signaling, ultimately contributing to impaired glucose metabolism [29].

VDD is also known to impair pancreatic β-cell function, thereby enhancing the risk of IR and metabolic syndrome [1]. Our findings (Table 4) support this hypothesis, as vitamin D levels <20 ng/mL were associated with significantly higher TyG index levels (OR=3.159; 95% CI (1.150 – 8.675; P=0.026). This suggests that vitamin D sufficiency may play a protective role against IR, as reflected by index TyG values. At the same time, several large-scale observational studies in the U.S. have shown that even modest increases in vitamin D levels are correlated with improvements in IR and inflammatory markers [30]. Interventional studies have yielded mixed results. For example, high-dose vitamin D3 supplementation did not significantly improve insulin sensitivity or secretion in T2DM patients with baseline VDD [31, 32]. However, emerging evidence suggests that combining vitamin D supplementation with L-cysteine may offer better outcomes. This combination may enhance glutathione production and modulate genes involved in vitamin D metabolism, potentially improving IR more effectively than vitamin D alone [33].

One important limitation of our study is the absence of detailed data on antidiabetic therapies. Although most patients received oral agents such as metformin, sulfonylureas, or DPP-4 inhibitors, we did not assess dosage, duration, or adherence. These factors may influence glucose and lipid parameters, potentially confounding the observed associations between vitamin D and the TyG index. Additionally, a small proportion of patients were treated with insulin, either alone or in combination with oral agents. Future studies should consider stratified analyses or exclusion criteria to address this issue more robustly.

Conclusion

This cross-sectional study demonstrates a significant inverse association between vitamin D levels and insulin resistance, as measured by the TyG index, in Algerian adults with type 2 diabetes mellitus. These results reinforce the potential value of integrating vitamin D status assessment and the TyG index calculation into clinical practice for the metabolic management of type 2 diabetes mellitus (T2DM). Addressing hypovitaminosis D may represent a complementary, modifiable factor in the broader strategy to reduce the burden of insulin resistance and its associated complications.

Further research is needed to evaluate whether vitamin D supplementation, in combination with other agents, could offer clinical benefits in improving insulin sensitivity and overall metabolic control in this population.

Acknowledgments

The authors gratefully acknowledge the participation of all patient volunteers who contributed to this study. Special thanks are extended to the healthcare professionals at Dr. Tidjani Damerdji University Hospital in Tlemcen for their essential contributions.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the scientific council of the faculty as well as the Ethics and Deontology Committee of the University of Tlemcen (Approval ID: CESUT: 13/10/2022).

Consent to participate

Written informed consent was obtained from all the participants.

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