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Original Research Article

Triglyceride-Glucose (TyG) Index and Its Association with Vitamin D Status and Cardiovascular Risk Factors in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Insulin resistance, dyslipidemia, and increased risk of developing cardiovascular diseases have been identified in patients with type 2 diabetes mellitus (T2DM). Triglyceride – Glucose (TyG) index has been identified as the surrogate marker for insulin resistance and vitamin D deficiency is known to contribute to poor metabolic profile. This study aimed at exploring the relation between TyG index and vitamin D and their association with cardiovascular disease risk factors in patients with T2DM.
Materials and Methods: Hospital-based cross-sectional study was carried out on 156 patients with T2DM presenting in tertiary care hospital. Anthropometry, fasting blood glucose, HbA1c, lipid profile, and serum vitamin D were determined. TyG index, Cardiac Risk Ratio (CRR), Atherogenic Coefficient (AC) and Atherogenic Index of Plasma (AIP) were calculated. Group comparisons based on vitamin D deficiency and correlations were carried out using one-way ANOVA, Chi square and Spearman's rank correlation.
Results: The mean age of participants was 52.1 ± 10.4 years, mean BMI was 27.3 ± 3.2 kg/m², mean TyG index was 9.85 ± 0.24, and mean serum vitamin D concentration was 18.0 ± 7.3 ng/mL. Vitamin D deficiency was observed in 94 (60.3%) participants. Patients with vitamin D deficiency had higher BMI (28.6 ± 4.3 vs. 25.1 ± 3.2 kg/m²), TyG index (10.01 ± 0.25 vs. 9.63 ± 0.21), HbA1c (8.1 ± 1.6% vs. 7.5 ± 1.3%), Cardiac Risk Ratio (5.4 ± 1.7 vs. 4.5 ± 1.3), and Atherogenic Index of Plasma (0.32 ± 0.26 vs. 0.18 ± 0.20) than vitamin D-sufficient participants. One-way ANOVA demonstrated significant differences in BMI ($F(2,153) = 7.58$, $p < 0.001$), TyG index ($F(2,153) = 13.42$, $p < 0.001$), Cardiac Risk Ratio ($F(2,153) = 3.40$, $p = 0.036$), and Atherogenic Index of Plasma ($F(2,153) = 3.27$, $p = 0.040$), whereas differences in HbA1c were not statistically significant ($F(2,153) = 1.55$, $p = 0.216$). Vitamin D status showed significant associations with gender ($\chi^2 = 10.03$, df = 2, $p = 0.007$) and BMI category ($\chi^2 = 15.44$, df = 4, $p = 0.004$), whereas no significant association was observed with age group ($\chi^2 = 1.23$, df = 4, $p = 0.873$). Spearman correlation analysis demonstrated that the TyG index was positively correlated with HbA1c ($\rho = 0.46$), Cardiac Risk Ratio ($\rho = 0.52$), and Atherogenic Index of Plasma ($\rho = 0.61$), and negatively correlated with vitamin D ($\rho = -0.41$) (all $p < 0.001$).

Conclusions: The TyG index was significantly associated with adverse glycemic and atherogenic markers and inversely associated with vitamin D levels in patients with type 2 diabetes mellitus. These findings suggest that the TyG index and vitamin D status are associated with cardiometabolic risk factors; however, the cross-sectional design precludes causal inference, and prospective studies are needed to confirm these associations.
Keywords: TyG index, Vitamin D, Insulin resistance, Type 2 diabetes mellitus, Cardiovascular risk

INTRODUCTION

DM is an enduring condition caused by a dysfunction in insulin release or action leading to sustained hyperglycemia in an ever-increasing number of people worldwide. [1-3] Cardiovascular disorders are highly related to diabetes mellitus as risk factors for such morbidity include dyslipidemia and hypertension.[2] The prevalence of DM represents a considerable challenge for public health systems, with diabetic retinopathy complicating more than one third of the patient population. [4-5]

IR is an important pathological feature in the development of T2DM and is known to be involved in the development of both micro- and macroangiopathies. Insulin resistance contributes to glucose intolerance in peripheral tissues, as higher levels of triglycerides (TG) found in individuals suffering from IR interfere with normal glucose metabolism. [6] Even though HOMA-IR index is widely employed, its dependence on the level of insulin restricts its practical applications. [7]

The TyG index, computed from glucose and triglycerides concentrations, is now regarded as a simple and effective tool for measuring IR. In contrast with other markers, such as visceral adiposity index (VAI) and lipid accumulation product (LAP), the TyG index appears to be more accurate in predicting the early stage of IR, although anthropometrics such as BMI and WC is still commonly used due to their simplicity. [8-11]

Vitamin D is a fat-soluble micronutrient involved in maintaining bone strength. Vitamin D deficiency can lead to the development of IR, impairment of insulin secretion, and the prevalence of T2DM. Additionally, vitamin D can promote chronic inflammation, causing further damage. Recent research shows that vitamin D deficiency contributes to poor glycemic control, dyslipidemia, higher cardiovascular disease risk, and higher mortality rates among diabetics. [12]

The influence of vitamin D on lipids can indirectly affect the TyG index by regulating triglyceride production and removal. Several studies show an inverse association between the level of vitamin D in blood and the TyG index value. Therefore, enough vitamin D may improve insulin sensitivity and regulate glucolipid metabolism. [13]

Although vitamin D plays an important role in the development of the connection between TyG index and health problems, more studies are required in order to investigate its effects. [14] Furthermore, epidemiologic data show Serum levels of 25-hydroxyvitamin D are linked to metabolic syndrome, obesity, hypertension, and dyslipidemia; however, causality needs to be established by means of randomized controlled trials. [15-18]

MATERIALS AND METHODS

This cross-sectional study was conducted in the Departments of Biochemistry and Medicine at Muzaffarnagar Medical College & Hospital, Muzaffarnagar, over a period of 18 months. Patients attending the Medicine OPD were included in the study. A total sample size of 156 were selected using a systematic random sampling technique.

Inclusion Criteria & Exclusion Criteria

Subjects aged 40–75 years with BMI ≥25 kg/m², diagnosed with type 2 diabetes mellitus, and willing to provide informed consent were included. Patients with hepatic, renal, cardiovascular diseases, pulmonary tuberculosis, inflammatory conditions, gout, arthritis, prolonged illness, or those on medications affecting glucose and lipid metabolism were excluded.

Data Collection and Measurements

Fasting plasma glucose, total cholesterol, triglyceride, HDL-cholesterol, and glycated haemoglobin were assayed by standardized biochemical procedures in an automated clinical chemistry analyzer (Diatron Pictus-500). Vitamin D [25 hydroxyvitamin D] concentration in serum was determined by CLIA method in Beckmann Access -2 analyzer. The internal quality control was carried out by running commercial control samples each day at normal as well as abnormal concentrations; besides, the lab took part in external quality assurance programs. LDL-cholesterol and VLDL-cholesterol were calculated by using Friedewald's formula.

Calculated Indices

- Cardiac Risk Ratio (CRR) = TC/HDL
- Atherogenic Coefficient (AC) = (TC−HDL)/HDL
- Atherogenic Index of Plasma (AIP) = Log (TG/HDL)
- Triglyceride-Glucose (TyG) Index = Log [TG × FPG]/2

Statistical Analysis

The statistical analysis was done using IBM SPSS Statistics 20.0. The normally distributed continuous variables were identified using Shapiro-Wilk test and by looking at their histograms and Q-Q plots. The normally distributed continuous variables are presented as mean ± SD while categorical variables are reported as frequencies and percentages.

The comparisons among the groups of vitamin D deficiency levels (deficiency, insufficiency, and sufficiency) were made using one-way analysis of variance (ANOVA). Before performing ANOVA, normality of data, independence of samples, and equality of variances (using Levene's test) were checked. For those cases in which ANOVA was significant, post-hoc analysis for multiple comparisons was carried out.

The association between categorical variables (vitamin D deficiency status and age group, gender, and BMI group) was made using Chi-square (χ^2) test. Correlation between clinical, biochemical, and cardiovascular risk markers was made using Spearman's rank correlation coefficient (ρ). All analyses were two-tailed and p-value <0.05 was considered significant.

Ethical Approval

The study was approved by the Institutional Ethical Committee (Ref No. MMC/IEC/ 2024/405), and informed consent was obtained from all participants.

RESULTS

A total of 156 patients were included, comprising 85 males (54.5%) and 71 females (45.5%). The majority of participants belonged to the 61–70 years age group (38.5%), followed by 51–60 years (32.1%). Most subjects were overweight or obese, with 53.8% having BMI 26–30 kg/m² and 21.8% having BMI >30 kg/m². The mean age of participants was 52.1 ± 10.4 years, with an average BMI of 27.3 ± 3.2 kg/m². Mean systolic and diastolic blood pressures were 140.3 ± 14.1 mmHg and 81.5 ± 10.1 mmHg, respectively.

Mean diabetes duration was 10.1 ± 4.6 years (range 4.0–20.0 years). Mean fasting blood glucose (FBS) was 166.2 ± 28.9 mg/dL (range 127–218 mg/dL), while mean postprandial blood glucose (PPBS) was 255.4 ± 33.7 mg/dL (range 209–319 mg/dL). The overall mean HbA1c was 7.94 ± 1.50%, ranging from 6.4% to 11.6%. (Table 1)

Table: 1. Clinical and Glycaemic Characteristics of the Study Population

	N	Mean	SD	Minimum	Maximum
Duration of DM	156	10.1	4.6	4.0	20.0
FBS (mg/dl)	156	166.2	28.9	127	218
PPBS (mg/dl)	156	255.4	33.7	209	319
HbA1C (%)	156	7.94	1.5	6.4	11.6

Lipid profile analysis demonstrated an atherogenic pattern, characterized by elevated total cholesterol (233.6 ± 27.4 mg/dL), triglycerides (228.3 ± 41.6 mg/dL), LDL cholesterol (148.7 ± 29.6 mg/dL), and reduced HDL cholesterol (43.6 ± 8.1 mg/dL). The mean Cardiac Risk Ratio (TC/HDL) was 5.14 ± 1.59 (range 3.60–8.69), the mean Atherogenic Coefficient was 4.34 ± 1.22 (range 2.11–7.67), and the mean Atherogenic Index of Plasma (AIP) was 0.28 ± 0.13 (range 0.16–0.58). (Table 2)

Table: 2. Descriptive Statistics of TyG Index, Vitamin D and Cardiovascular Risk Indices

Parameter	Mean	Standard Deviation	Minimum	Maximum
TyG Index	9.85	0.24	9.34	10.33
Vitamin D (ng/ml)	18	7.3	8.0	34.0
Cardiac Risk Ratio (TC/HDL)	5.14	1.59	3.60	8.69
Atherogenic Coefficient	4.34	1.22	2.11	7.67
Atherogenic Index of Plasma (AIP)	0.28	0.13	0.16	0.58

Vitamin D status was significantly associated with gender ($\chi^2 = 10.03$, df = 2, p = 0.007), with a greater proportion of females classified as vitamin D deficient than males.
One-way ANOVA showed significant differences among vitamin D status groups for BMI (F (2,153) =7.58, p<0.001), TyG Index (F (2,153) =13.42, p<0.001), Cardiac Risk Ratio (F (2,153) =3.40, p=0.036), and Atherogenic Index of Plasma (F (2,153) =3.27, p=0.040). No significant differences were observed for age (F (2,153) =0.71, p=0.494) or HbA1c (F (2,153) =1.55, p=0.216). (Table 3)
Vitamin D deficiency was observed in 94 (60.3%) participants, insufficiency in 42 (26.9%), and sufficient vitamin D levels in 20 (12.8%).

Table: 3. Comparison of Clinical and Biochemical Parameters According to Vitamin D Status

Parameter	Deficient (n=94)	Insufficient (n=42)	Sufficient (n=20)	F (df = 2,153)	p-value
Age (years)	53.1 ± 11.8	51.2 ± 10.5	50.4 ± 10.9	0.71	0.494
BMI (kg/m²)	28.6 ± 4.3	26.8 ± 3.7	25.1 ± 3.2	7.58	<0.001
TyG Index	10.01 ± 0.25	9.82 ± 0.22	9.63 ± 0.21	13.42	<0.001
HbA1c (%)	8.1 ± 1.6	7.8 ± 1.4	7.5 ± 1.3	1.55	0.216
CRR	5.4 ± 1.7	4.9 ± 1.4	4.5 ± 1.3	3.40	0.036
AIP	0.32 ± 0.26	0.25 ± 0.22	0.18 ± 0.20	3.27	0.040

Spearman's rank correlation analysis demonstrated significant associations among metabolic and cardiovascular risk markers. The TyG Index correlated negatively with vitamin D levels (ρ = −0.41, p < 0.001) and positively with HbA1c (ρ = 0.46, p < 0.001), Cardiac Risk Ratio (ρ = 0.52, p < 0.001), and AIP (ρ = 0.61, p < 0.001). Vitamin D levels demonstrated inverse correlations with HbA1c (ρ = −0.29, p < 0.001), Cardiac Risk Ratio (ρ = −0.33, p < 0.001), and AIP (ρ = −0.38, p < 0.001). BMI showed weak-to-moderate positive correlations with TyG Index (ρ = 0.28, p < 0.001), Cardiac Risk Ratio (ρ = 0.31, p < 0.001), and AIP (ρ = 0.35, p < 0.001), while exhibiting a weak inverse correlation with vitamin D levels (ρ = −0.22, p < 0.001). (Table 4)

Table 4. Spearman Correlation Matrix of Clinical and Biochemical Variables

	Age	BMI	TyG	VitD	HbA1c	CRR	AIP
Age	1.00	0.12	-0.15	0.08	0.11	-0.09	-0.14
BMI	0.12	1.00	0.28	-0.22	0.19	0.31	0.35
TyG Index	-0.15	0.28	1.00	-0.41	0.46	0.52	0.61
Vitamin D	0.08	-0.22	-0.41	1.00	-0.29	-0.33	-0.38
HbA1c	0.11	0.19	0.46	-0.29	1.00	0.25	0.33
CRR	-0.09	0.31	0.52	-0.33	0.25	1.00	0.72
AIP	-0.14	0.35	0.61	-0.38	0.33	0.72	1.00

Values represent Spearman's rank correlation coefficients (ρ).

DISCUSSION

This current study was conducted with the aim of assessing the Triglyceride Glucose (TyG) index and their relationship with vitamin D deficiency and cardiovascular risk factors in diabetic patients. As the burden of diabetes increases across the globe and as the complications associated with diabetes continue to be a major health concern, it becomes necessary to have cheap and easy tools for identifying patients with metabolic and cardiovascular complications. This tool, known as the TyG index, is obtained using fasting triglyceride and glucose concentrations.

For this study, 156 subjects were selected. These subjects included 85 males and 71 females, accounting for about 54.5% and 45.5% respectively, based on the findings by Xiang Q et al. [19] The same gender distribution was also reported by Jia Y et al. [20]

In the current investigation, the overall mean TyG index was 9.85±0.24, indicating a relatively high degree of insulin resistance among the study participants. Indeed, insulin resistance represents one of the key pathophysiological mechanisms of the onset and progression of T2DM and has a close connection to cardiovascular disorders. The TyG index proved to be a reliable and practical substitute for the hyperinsulinemic-euglycemic clamp and HOMA-IR approaches that were tested in several scientific studies.

It should be stressed that the obtained results are in line with the outcomes of a study conducted by Guerrero-Romero et al. [21], wherein it was confirmed that the TyG index has a highly positive correlation with insulin resistance evaluated using gold standard methods. As for the findings of Simental-Mendía et al., also suggest the potential use of the TyG index in identifying patients with insulin resistance. [8]

In addition to these considerations, it needs to be emphasized that the TyG index is a marker reflecting the combined influence of hyperglycemia and hypertriglyceridemia, both representing key characteristics of diabetic dysmetabolism. High levels of triglycerides cause an increase in the rate of flux of free fatty acids, leading to a disturbance in insulin pathway signals and increasing insulin resistance.

In the current research, abnormal changes were also noted for lipid profile parameters like high total cholesterol, triglyceride, LDL, and low HDL concentrations. This pattern is typical of diabetic patients and leads to the rapid development of atherosclerosis. Besides traditional lipid profile parameters, the current research has also examined several derived indices, such as cardiac risk ratio (CRR), atherogenic coefficient (AC), and atherogenic index of plasma (AIP).

The mean values for CRR, AC, and AIP obtained during this research were relatively high, which means that patients had a high level of atherogenesis. AIP was calculated by taking the logarithm of the ratio between triglycerides and HDL concentration, and its value has proven to be a strong predictor of small dense LDL particles, which have an atherogenic effect. The concept of AIP was first proposed by Dobiasova, [22] who claimed that AIP can be used as a reliable marker of plasma atherogenicity.

It should be noted that the results of the current research align with the results obtained by Pokhrel et al. These researchers claim that AIP has proved to be significantly associated with cardiovascular risk factors and can be used as a predictor of coronary artery disease. [23] The most important point in this regard is that there is a trend of relationship seen between the TyG index and the studied atherogenic indices, thus supporting the role of insulin resistance, represented by TyG index, in contributing to the occurrence of dyslipidemia and atherogenesis. Studies published before on this topic have shown similar results.

Another crucial observation from this study was the high frequency of vitamin D deficiency among the subjects participating in this research. A relatively large percentage of patients showed a concentration of vitamin D less than 20 ng/mL, meaning that they had a deficient level, whereas only a very few had an adequate level, defined as being more than 30 ng/mL. These observations are consistent with previously published studies from India and around the world, wherein hypovitaminosis D was shown to be widely prevalent even where there is plenty of sunlight.

Hypovitaminosis D has been described as a major worldwide public health problem by Holick [24], both in developed and developing countries. In the Indian scenario, several publications by Harinarayan et al. [25] have highlighted the phenomenon of vitamin D deficiency despite having good sunlight exposure owing to lifestyle factors, cultural issues, and dietary insufficiency.

The current study also considered the prevalence of vitamin D levels among different age groups. Even though some age groups were found to be more deficient than others, there was no significant relationship between vitamin D and age, based on Chi-square test results. Thus, it can be concluded that vitamin D deficiency is a common phenomenon in any age group without being isolated to only one age range.

Recently, there has been an increasing amount of research regarding vitamin D and insulin resistance association. As it is known, vitamin D plays an essential part in glucose metabolism, affecting the functionality of the β-cell and sensitivity to insulin. Vitamin D helps insulin secretion via the regulation of calcium influx in β-cells and increases insulin sensitivity by suppressing inflammation.

In the present study, a statistically significant moderate inverse correlation was observed between the TyG index and vitamin D levels (Spearman's $\rho = -0.41$, $p < 0.001$), indicating that lower vitamin D concentrations were associated with higher TyG index values. This finding supports the hypothesis that vitamin D deficiency may be linked with greater insulin resistance in patients with type 2 diabetes mellitus. Although the cross-sectional design of the present study does not permit causal inference, the observed association is biologically plausible because vitamin D is involved in glucose homeostasis through its effects on pancreatic β-cell function, calcium-mediated insulin secretion, insulin receptor expression, and modulation of systemic inflammation. Previous studies by Chiu et al. [26] have similarly demonstrated an inverse association between vitamin D status and insulin resistance, while Pittas et al. [27] suggested that improving vitamin D status may contribute to better glucose metabolism. The present findings therefore add further evidence supporting an association between hypovitaminosis D and adverse metabolic status in individuals with type 2 diabetes, although prospective and interventional studies are required to establish causality.

The connection between the deficiency of vitamin D and insulin resistance is based on the following factors: the increase in the number of inflammatory cytokines, reduced expression of insulin receptors, and disrupted calcium balance. Vitamin D affects the expression of the genes responsible for glucose metabolism.

The most significant cause of morbidity and mortality among the population suffering from diabetes mellitus is cardiovascular disease. Hence, the search for biomarkers that could help detect cardiovascular diseases at an early stage is crucial. Among such indicators, one should pay attention to the TyG index because of its relationship to metabolic syndrome and insulin resistance.

For the current study, high TyG index, coupled with the presence of high atherogenic indexes, suggests the increased risk of cardiovascular diseases among the study population. These results are supported by the research carried out by Zhang et al., who noted that increased levels of TyG index were associated with a heightened risk of cardiovascular disease and subclinical atherosclerosis. [6,12]

The coexistence of a relatively elevated TyG index, dyslipidemia, and a high prevalence of vitamin D deficiency, together with the observed inverse association between TyG index and vitamin D levels, reflects a complex cardiometabolic risk profile in patients with type 2 diabetes mellitus. These findings support the potential utility of combining TyG index and vitamin D assessment for identifying individuals at increased metabolic and cardiovascular risk. However, because of the cross-sectional nature of the study, these associations should not be interpreted as evidence of a causal relationship.

Limitations of the Study

While the current study has many advantages, there are some aspects that can be seen as drawbacks of it. First, the cross-sectional study design does not provide an opportunity to investigate cause-and-effect relationships between the variables under consideration. Second, the number of subjects used is large enough but may not be completely representative of the whole population. Third, such variables as nutrition, exercise, and seasonality of the vitamin D status were not measured thoroughly.

CONCLUSION

The present study demonstrated a high prevalence of insulin resistance, atherogenic dyslipidemia, and vitamin D deficiency among patients with type 2 diabetes mellitus. The TyG index showed significant positive correlations with HbA1c, cardiac risk ratio (CRR), and atherogenic index of plasma (AIP), and a significant inverse correlation with vitamin D levels. Lower vitamin D levels were also associated with a less favorable metabolic and cardiovascular risk profile. These findings suggest that the TyG index and vitamin D status are associated with multiple metabolic and cardiovascular risk factors in patients with type 2 diabetes mellitus. However, because of the cross-sectional design, causal or temporal relationships cannot be established. Further well-designed prospective, longitudinal, and interventional studies are needed to confirm these associations and to determine the potential clinical utility of the TyG index and vitamin D assessment for cardiometabolic risk stratification and patient management.

Declaration

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