ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Correlation of triglyceride glucose-body mass index, triglyceride glucose/high-density lipoprotein cholesterol ratio, and triglyceride glucose index with blood sugar and hemoglobin A1C in patients with type 2 diabetes mellitus: A cross-sectional study

Srikanth Akula[1], Swetha Akkina[2], Rajeev Gandham[3], Preethi Batakala[4], Bhagyalakshmi Atla[5], Sunkara Uha Priya[6], Divija Reddy Bonthu[7]

[1,2]Associate Professor, [6,7]Postgraduate Resident, Department of General Medicine, [3]Assistant Professor, [4]Professor and Head, Department of Biochemistry, [5]Professor and Head, Department of Pathology, NRI Institute of Medical Sciences, Visakhapatnam, Andhra Pradesh, India

Submission: 01-02-2025 Revision: 30-03-2025 Publication: 01-05-2025

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is one of the most common endocrine diseases characterized by increased blood glucose. Uncontrolled diabetes is associated with the development of micro- and macrovascular complications. **Aims and Objectives:** This study aimed to assess and correlate triglyceride glucose-Body mass index (TyG-BMI) index, triglycerides (TG)/high-density lipoprotein cholesterol (HDL-C) ratio and TyG index with blood sugar and hemoglobin A1C (HbA1c) in patients with T2DM. **Materials and Methods:** This current study was a cross-sectional study where 252 subjects, were recruited and they were categorized into 126 diabetic and 126 nondiabetic subjects. All parameters and anthropometric measurements were done following standard guidelines. **Results:** In this study, a significant increase in mean age (56.3 ± 10.3 years), BMI (25.0 ± 2.4 kg/m^2), and, systolic blood pressure (120.0 ± 7.6 mmHg) were observed in T2DM subjects compared to nondiabetic subjects. Concerned with biochemical parameters, significant increase in fasting blood sugar (FBS), postprandial blood sugar, HbA1c, urea, creatinine, total cholesterol, triglycerides (TG), LDL-C, very low-density lipoprotein-cholesterol and non-HDL-C were observed in T2DM subjects compared to nondiabetic subjects. **Conclusion:** The present study may conclude that there is a significant increase in TyG-BMI index, TG/HDL-C, and TyG index in T2DM patients and their positive correlation with FBS and HbA1c. The measurement of these markers will provide better information on IR status.

Key words: Triglyceride glucose-body mass index; Triglyceride glucose high-density lipoprotein cholesterol ratio; Triglyceride glucose index; Insulin resistance

Access this article online

Website: https://ajmsjournal.info/index.php/AJMS/index

DOI: 10.71152/ajms.v16i5.4437

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Type 2 diabetes mellitus (T2DM), one of the most common endocrine diseases characterized by increased blood glucose. Uncontrolled diabetes is associated with micro- and macrovascular complications.[1] The prevalence of diabetes mellitus (DM) is increasing globally. According to the International Diabetes Federation, 463 million people suffered from diabetes in 2019 and is projected to reach 700 million by the year 2045.[2]

Address for Correspondence:
Dr. Rajeev Gandham, Assistant Professor, Department of Biochemistry, NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam - 531 162, Andhra Pradesh, India. **Mobile:** +91-8892551401. **E-mail:** gandhamrajeev33@gmail.com

Insulin resistance (IR) is associated with pathophysiology of DM.[3,4] However, the methods involved in the assessment of IR are depend on the hyperinsulinemic-euglycemic clamp technique, which is not done routinely.[5] Therefore, there is a need to establish simple, convenient, and cheaper biomarkers for the measurement of IR. In view of this, recently, in 2016, Er et al. proposed an alternative biomarker for the assessment of IR, i.e., triglyceride glucose-body mass index (TyG-BMI), calculated using the formula: Ln (triglycerides [TG] [mg/dL]×fasting blood glucose [mg/dL]/2)×BMI (kg/m^2). TyG-BMI has better diagnostic value in differentiating IR at an early stage.[6]

In 2019, a study conducted by Ramírez-Vélez et al. reported a positive correlation between diabetes and TyG-BMI.[7] Another study by Song et al., in 2022 reported a positive correlation between baseline TyG-BMI and risk of incident T2DM in Japanese subjects with normal glycemic levels, and this risk was significantly higher in the young people, women, the nonhypertensive population, and nondrinkers.[8] A recent study by Yang et al. reported that increased level of TyG-BMI is significantly associated with heart failure in patients with DM or prediabetes.[9]

Another risk factor for cardiovascular complications in diabetic patients is atherogenic dyslipidemia, characterized by elevated levels of TG, decreased high-density lipoprotein cholesterol (HDL-C), and postprandial lipemia. In addition, low-density lipoprotein cholesterol (LDL-C) is converted to small, dense LDL that is more atherogenic. The ratio of serum (TG/HDL-C), is known as the atherogenic index of plasma.[10] Elevated levels of triglycerides result in IR and subsequent consequence of a vicious circle, in which compensatory hyperinsulinemia and IR can further exacerbate hypertriglyceridemia.[11] Even, these increased triglycerides were associated with impaired glucose tolerance, fasting glucose, and subsequent development of T2DM.[12]

On the other hand, HDL-C levels were inversely associated with the risk of diabetes.[13] Further, TG/HDL-C has been reported as a biomarker of IR.[14] In 2019, a study by Babic et al. indicated TG/HDL-C ratio may be a useful predictor of glycemic control in T2DM patients with normal weight, overweight, and obese.[10] In 2023, a Panasonic Cohort Study 10 by Yuge et al. reported that TG/HDL-C was found to be a stronger predictor of T2DM development within 10 years than LDL-C, HDL-C, or TG, indicating that it may be useful in the future medical treatment support.[15]

Similarly, another marker for IR was TyG index, which was first proposed by Simental-Mendía et al., in 2008, and is calculated by formula: Ln (fasting triglyceride [mg/dL]×fasting glucose [mg/dL]/2).[16] In recent years, it was reported that TyG index can accurately identify IR.[17] In 2022, a study conducted by Lopez-Jaramillo et al. reported that TyG index is significantly associated with future cardiovascular mortality, myocardial infarction, stroke, and T2DM.[18] A limited studies were conducted in relation to TyG-BMI index, TG/HDL-C ratio, and TyG index in Andhra Pradesh diabetic subjects.

Aims and objectives

This study aimed to assess and correlate TyG-BMI index, TG/HDL-C ratio and TyG index with blood sugar and hemoglobin A1C (HbA1c) in patients with T2DM.

MATERIALS AND METHODS

Present cross-sectional study design was conducted in Department of Biochemistry in collaboration with Department of General Medicine, NRI Institute of Medical Sciences (NRIIMS), attached to Anil Neerukonda Hospital, Visakhapatnam, Andhra Pradesh, India. This study was initiated after obtaining the Institutional Ethics Committee (IEC/NRI/114/2024) and informed consent from all the study subjects. This study involved 252 subjects, categorized into 126 diabetic and 126 nondiabetic subjects. Calculation of sample size was done with a power of 80% and Type I error of 5% using the formula: $(Z1\text{-}\alpha/2)^2$ (b) (1-b)/d^2.[19] Simple random sampling method was followed for recruiting the study subjects.

Inclusion criteria

Diabetic and nondiabetic subjects willing to participate in the study, both genders with ages of 18–65 years, were included. Diagnosis of T2DM was made per the American Diabetes Association criteria.

Exclusion criteria

Subjects refused to participate in the study; patients with type 1 DM, diabetic patients with vascular complications, pregnancy, hyperthyroidism, hypothyroidism, malignancy, and autoimmune disorders were excluded from the study.

Anthropometric measurements

BMI was calculated (kg/m^2). Demographic details, blood pressure, clinical details, and family history of diabetes were recorded. TyG-BMI, TG/HDL-C ratio, and TyG index were calculated using the formula:

TyG-BMI=TyG index×BMI.

TG/HDL=TG (mg/dL)/HDL-C (mg/dL).

TyG index=ln (fasting TG [mg/dL]×fasting glucose [mg/dL]/2).

Estimation of biochemical parameters

Five ml fasting blood sample, transferred 3 mL into the plain tube and 2 mL into Ethylenediaminetetraacetic acid (EDTA) tube and also 2 mL postprandial blood sample was collected from all study subjects. Samples were centrifuged to obtain clear plasma/sera, which is used for analysis of biochemical parameters such as blood sugar (GOD-POD method), urea (urease), creatinine (Jaffe's), total cholesterol (cholesterol oxidase/peroxidase), triglycerides (glycerol phosphate oxidase/peroxidase), and HDL-C (HDL-C-Direct) were estimated by using Biosystems BA-200 Biochemistry fully auto analyzer. LDL-C and VLDL-C were calculated using Frieldwald's formula. EDTA samples were used for the measurement of HbA1c (HPLC method) using a BIORAD D-10 analyzer.

Statistical analysis

Results were presented as mean±SD. Categorical variables were expressed in numbers and percentages. Mann–Whitney *U* test was applied. Spearman's rho correlation was applied to correlate TyG-BMI, TG/HDL-C, and TyG index with blood sugar and HbA1c. P-value ($P<0.05$) was considered statistically significant. Data analysis was done using SPSS 22.0.

RESULTS

In this study, out of 126 T2DM subjects, 66 (52.4%) were male and 60 (47.6%) were female. In nondiabetic subjects, 58 (46.0%) were male and 68 (54.0%) were female. Significant increases in mean age (56.3±10.3 years), BMI (25.0±2.4kg/m^2), and SBP (120.0±7.6 mmHg) were observed in T2DM subjects compared to nondiabetic subjects.

Concerned with biochemical parameters, significant increase in fasting blood sugar (FBS) (171.0±34.5 mg/dL), postprandial blood sugar (230.6±47.8 mg/dL), HbA1c (8.3±2.1%), urea (29.1±7.6 mg/dL), creatinine (1.1±0.1 mg/dL), total cholesterol (190.6±34.8 mg/dL), triglycerides (177.6±42.7 mg/dL), LDL-C (119.0±29.1 mg/dL), VLDL-C (35.4±8.9 mg/dL), and non-HDL-C (154.0±32.9 mg/dL) and significant decrease in HDL-C (35.4±8.9 mg/dL) level was observed in T2DM subjects compared to nondiabetic subjects.

Concerned with IR markers, a significant increase in TyG-BMI (129.1±13.6), TG/HDL-C (5.2±1.7), and TyG index (5.1±0.1) was observed in T2DM subjects than nondiabetic subjects (Table 1).

In this study, Non-HDL-C (r=0.519), TyG-BMI (r=0.693), TG/HDL-C (r=0.451), and TyG index (r=0.844) were positively correlated with FBS. Similarly, HbA1c was positively correlated with non-HDL-C (r=0.257), TyG-BMI (r=0.509), TG/HDL-C (r=0.214), and TyG index (r=0.588) Table 2.

DISCUSSION

DM, the most common endocrine and metabolic disease associated with vascular complications. The present study results indicated significant elevation in TyG-BMI index, TG/HDL-C and TyG index in T2DM subjects and were positively correlated with FBS and HbA1c.

A few recent studies have indicated that TyG-BMI has been reported to be associated with prehypertension, nonalcoholic fatty liver disease and T2DM.[20-22] However, the association of the TyG-BMI index with diabetes was not well understood, but it was proposed that TyG-BMI index may be associated with IR. IR, key pathophysiological mechanism associated with diabetes. However, the performance of TyG-BMI might be explained by the effects of blood glucose, lipid metabolism, and obesity on insulin sensitivity. Chronic hyperglycemia has been demonstrated to increase oxidative stress in β cells of the pancreas, causing a continuous decline in β-cell function and resulting IR. On the other hand, hypertriglyceridemia can lead to fat deposition in muscle cells and pancreatic islet cells, thus impairing β-cell function.[23]

In support of our study findings, a very recent study conducted by Wang et al., in 2024, indicated that elevated TyG-BMI was associated with an increased risk of T2DM and demonstrated better predictability than TyG and HOMA-IR, and suggested that TyG-BMI may be a useful tool to evaluate the risk of T2DM.[22] Another study conducted by Yang et al., in 2022, reported that TyG-BMI and incident diabetes had a nonlinear positive association and serve as a useful tool for the identification of patients at risk of diabetes.[24] Another study conducted by Huang et al., in 2024, reported that TyG-BMI is increased in T2DM patients and associated with kidney impairment in these patients.[25]

Glucose metabolism is closely associated with lipid metabolism. The lipid ratios are well established and are better predictors of coronary artery disease, reflecting the interaction between atherogenic and anti-atherogenic fractions.[26] Among the lipid ratios, the TG/HDL-C ratio is closely associated with IR, atherogenesis, evidence of more dense and atherogenic LDL particles, arterial stiffness, and acute cardiovascular event in diabetic patients, serves as an important cardiovascular risk predictor.[27]

In addition, TG/HDL-C ratio reported to be an indicator of IR. Therefore, TG/HDL-C ratio may be used as a predictor

Table 1: Comparison of demographic details, biochemical, and hematological parameters in T2DM patients and nondiabetic subjects

Parameters	T2DM subjects (Mean±SD) (n=126)	Nondiabetic subjects (Mean±SD) (n=126)	P-value
Demographic details			
Age (years)	56.3±10.3	50.2±11.8	0.021
Males (n, %)	66 (52.4)	58 (46.0)	-
Females (n, %)	60 (47.6)	68 (54.0)	-
Body mass index (BMI) (kg/m^2)	25.0±2.4	22.9±1.2	0.000
Systolic blood pressure (SBP) (mmHg)	120.0±7.6	115.3±5.0	0.002
Diastolic blood pressure (DBP) (mmHg)	79.8±4.8	78.8±5.1	0.345
Biochemical parameters			
Fasting blood sugar (FBS) (mg/dL)	171.0±34.5	85.4±5.7	0.000
Postprandial blood sugar (PPBS) (mg/dL)	230.6±47.8	127.5±19.5	0.000
HbA1c (%)	8.3±2.1	5.3±0.2	0.000
Serum urea (mg/dL)	29.1±7.6	23.1±7.2	0.001
Serum creatinine (mg/dL)	1.1±0.1	0.8±0.2	0.001
Serum total cholesterol (mg/dL)	190.6±34.8	153.7±14.4	0.000
Serum triglycerides (mg/dL)	177.6±42.7	131.8±24.9	0.000
Serum HDL-C (mg/dL)	36.6±9.7	45.4±8.1	0.000
Serum LDL-C (mg/dL)	119.0±29.1	83.6±16.2	0.000
Serum VLDL-C (mg/dL)	35.4±8.9	26.3±4.9	0.000
Non-HDL-C (mg/dL)	154.0±32.9	107.3±15.8	0.000
Markers of insulin resistance			
TyG-BMI	129.1±13.6	106.6±5.6	0.000
TG/HDL-C	5.2±1.7	2.9±0.7	0.000
TyG index	5.1±0.1	4.6±0.1	0.000

P<0.05 statistically significant. HbA1c: Hemoglobin A1C, T2DM: Type 2 diabetes mellitus, HDL-C: High-density lipoprotein cholesterol, TyG-BMI: Triglyceride glucose-body mass index, VLDL-C: Very-low-density lipoprotein cholesterol

Table 2: Correlation of Non-HDL-C, TyG-BMI, TG/HDL-C, TyG index with FBS and HbA1c

Parameters	FBS		HbA1c	
	r-value	P-value	r-value	P-value
Non-HDL-C	0.519**	0.000	0.257**	0.007
TyG-BMI	0.693**	0.000	0.509**	0.000
TG/HDL-C	0.451**	0.000	0.214*	0.026
Tyg index	0.844**	0.000	0.588**	0.000

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). FBS: Fasting blood sugar, HbA1c: Hemoglobin A1C, HDL-C: High-density lipoprotein cholesterol, TyG-BMI: Triglyceride glucose-body mass index

of incident DM.[28] The proposed mechanism for association of TG/HDL-C with DM: Hypertriglyceridemia in T2DM may result in free fatty acids (FFA), decreased insulin sensitivity, and continued exposure to FFA may reduce the activity of AMP-activated kinase and increased accumulation of triglyceride, leading to changes in pancreatic α-cell insulin signaling and hypersecretion of glucagon, thereby creating a vicious cycle between triglycerides levels and IR.[29]

At the same time, HDL-C protects β cells from cytokine induced or glucose induced. Reduced HDL-C levels affect β-cell function or survival, which has a regulatory role in the pathogenesis of T2DM.[30] Therefore, the combination of increased triglycerides and reduced HDL-C, known as atherogenic dyslipidemia, is also a strong risk factor for vascular complications of diabetes. Hence, the TG/HDL-C ratio was considered a potential predictive marker of IR and β-cell dysfunction. It is closely associated with T2DM as well as CVD development.[31]

In support of our study findings, Yang et al., in 2022, reported that elevated TG/HDL-C ratio was correlated with the risk of pre-DM and T2DM.[32] Another study by Zheng et al., in 2020, reported that TG/HDL-C ratios were positively associated with the risk of T2DM. The elevated TG/HDL-C ratios increased the future risk of T2DM incidence. Lowering the TG/HDL-C ratio could assist in the prevention of diabetes for older adults.[28] Yet another study by Gedikli et al., in 2022, reported a significant positive correlation between HbA1c levels and TG/HDL-C ratio and TyG index.[33] Similarly, another recent study by Sultana et al., in 2024, reported a relationship between HbA1c and triglycerides, as well as HbA1c and TG/HDL-C, indicating that HbA1c is associated with dyslipidemia in patients with T2DM in addition to glycemic control.[34]

Another marker of IR is the TyG index. This study results showed a significant increase in the TyG index among T2DM subjects. In support of our findings, a study by Gounden et al., in 2024, reported the use of the TyG index as a valid biomarker to assess the risk of developing metabolic syndrome, T2DM, as well as atherosclerotic cardiovascular disease.[35] Yet, another study by Li and Wang in 2024, reported that the TyG index is positively

associated with albuminuria and chronic kidney disease in patients with T2DM and may be a marker for predicting the occurrence of early kidney injury in patients with T2DM.[36] Similarly, Abil et al., in 2024, reported that the TyG index has a significant correlation with HbA1c and can be used as a surrogate marker for assessing the glycemic status.[37]

Limitations of the study

The study has the following limitations, measurement of insulin and calculation of HOMA-IR, cross-sectional study design, and relatively small sample size.

CONCLUSION

The present study may conclude that significant increase in TyG-BMI index, TG/HDL-C, and TyG index in T2DM patients and their positive correlation with FBS and HbA1c. Measurement of these markers will provide better information on IR status and these markers are routinely done and are less expensive. Further studies with large sample size are recommended.

ACKNOWLEDGMENT

We would like to thank the authorities of NRIIMS, Visakhapatnam, Andhra Pradesh, India.

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Authors' Contribution:
SA- Definition of intellectual content, Literature survey, implementation of study protocol, data collection; **SwA-** Concept, design, implementation of study protocol, data collection clinical protocol; **RG-** Prepared first draft of manuscript, design of study, statistical analysis and interpretation, data analysis, manuscript preparation and submission of article, manuscript preparation, editing, and manuscript revision, coordination and manuscript revision; **PB-** Review manuscript; **BA-** Review manuscript; **SUP-** Literature survey and preparation of figures, literature survey, implementation of study protocol, data collection; **DRB-** Literature survey, implementation of study protocol, data collection

Work attributed to:
NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam - 531162, Andhra Pradesh, India.

Orcid ID:
Srikanth Akula- https://orcid.org/0009-0006-3386-6259
Swetha Akkina- https://orcid.org/0009-0006-8097-0331
Rajeev Gandham- https://orcid.org/0000-0002-5288-486X
Preethi Batakala- https://orcid.org/0009-0005-8690-8814
Bhagyalakshmi Atla- https://orcid.org/0009-0007-0606-7301
Sunkara Uha Priya- https://orcid.org/0009-0003-5286-9891
Divija Reddy Bonthu- https://orcid.org/0009-0000-9108-9829

Source of Support: Nil, **Conflicts of Interest:** None declared.