

Original Research Article

Decoding the Triglyceride/HDL-C Ratio: A Marker for Type-2 Diabetes Risk

Asha Gupta, Dinesh Kumar Sharma*

Department of Biochemistry, Shri Balaji Institute of Medical Science, Raipur, Chhattisgarh

*Correspondence: Dr Dinesh Kumar Sharma (dksharma0305@gmail.com)

ABSTRACT

Background: Diabetes mellitus (DM) is the most common endocrine disorder worldwide. Beyond the established markers of glycemic control and insulin resistance (IR), there remains a need for reliable, accessible, and reproducible indicators. To address this, our study evaluated the triglyceride to HDL cholesterol ratio (THR) as a potential marker for insulin resistance and glycemic regulation.

Materials and methods: We retrospectively analyzed TG, fasting serum glucose (FSG), and fasting insulin levels from 953 samples processed between March and August 2024. Based on homeostasis model assessment-estimated insulin resistance (HOMA-IR) values, patients were categorized into two groups: good versus poor glycemic control. The discriminatory power of the triglyceride-to-HDL cholesterol ratio (THR) for differentiating these groups was evaluated using Receiver operating characteristic (ROC) analysis, with statistical significance set at $p<0.05$. Furthermore, multivariate logistic regression analysis was performed.

Results: The mean age of participants was 40.83 ± 16.78 years. Significant differences ($p<0.001$) were observed between patients with good and poor glycemic control in gender, FSG, HOMA-IR, FI, TG, and THR, but not in age ($p=0.613$). Pairwise correlation showed THR had a moderate negative correlation with HDL ($r=-0.555$, $p<0.001$) and a strong positive correlation with TG ($r=0.959$, $p<0.001$). With a cutoff value of ≥ 2.64 , THR demonstrated high selectivity and positive predictive value (PPV) (AUC=0.72; Se=65%; Sp=70%; $p<0.001$; 95% CI: 0.66–0.78). Men were 2.247 times more likely than women to exhibit poor glycemic control ($p=0.022$). The risk of poor control increased by 1.045-fold with age and 1.056-fold with glucose ($p=0.007$).

Conclusion: Based on our findings, the THR appears to be a promising marker for assessing glycemic control and insulin resistance.

Keywords: Diabetes mellitus, Glycemic Control, HDL-C, Insulin resistance, Triglyceride

INTRODUCTION

Diabetes mellitus is one of the most pressing global health and socioeconomic challenges. The prevalence of type 2 diabetes mellitus (T2DM) continues to rise worldwide, with regional and national studies reporting rates between 12.7% and 14.7%.¹⁻⁴ Alarmingly, diabetes-related macrovascular and microvascular complications are contributing to an

increasing number of premature deaths.⁵ A key factor in the pathophysiology of both diabetes and metabolic syndrome is insulin resistance (IR)—the diminished sensitivity of peripheral tissues to insulin—which may appear one to two decades before the clinical diagnosis of T2DM.⁶ The role of IR as a predictor of future diabetes, along with evidence that insulin-sensitizing therapies can help prevent T2DM, further underscores its clinical significance.⁷ Diabetic dyslipidemia

represents an additional major cardiovascular disease (CVD) risk factor in individuals with T2DM. It is characterized by elevated triglycerides (TG), reduced high-density lipoprotein cholesterol (HDL-C), and postprandial lipemia. The atherogenic index of plasma, defined as the triglyceride-to-HDL cholesterol ratio (THR), is recognized as a significant predictor of both CVD and metabolic syndrome.^{8,9} A higher THR has been associated with endothelial dysfunction and is also proposed as a marker of insulin resistance (IR),¹⁰ given that the metabolic disturbances underlying IR disrupt lipid metabolism, reflected in serum TG and HDL-C levels.¹¹ Quispe et al¹² further demonstrated that THR can serve as an indicator of glycemic control, particularly in obese patients with T2DM. Another IR-related parameter is the triglyceride–glucose (TyG) index, which helps identify asymptomatic T2DM patients at elevated CVD risk.¹³ Most existing studies to date have focused on the interplay between THR and IR in diabetic populations.¹⁴ To evaluate insulin sensitivity, the medical field has long sought alternative indirect biomarkers. Among these, the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and Fasting Insulin (FI) are widely used due to their strong predictive power, specificity, and sensitivity. However, despite being more practical than the hyperinsulinaemic–euglycemic clamp—the gold standard—they remain challenging to apply in routine clinical settings.^{11,15} Practical barriers such as the lack of insulin testing in many hospitals, logistical issues in transporting blood samples from primary care centers, and the technical limitations of HOMA-IR have sustained the search for simpler biomarkers suitable for everyday use. Since triglyceride, HDL, and glucose measurements are inexpensive and routinely available, the triglyceride-to-HDL ratio (THR) can be readily calculated in clinical practice.¹⁶

Over the past two decades, considerable effort has gone into clarifying the predictive accuracy, limitations, and unique characteristics of THR, owing to its ease and accessibility. However, studies exploring the relationship between glycemic control and THR remain limited in our country. Therefore, the aim of this study was to investigate the association between THR and incident T2DM risk in our population.

MATERIALS AND METHODS

This cross-sectional retrospective study was conducted. A total of 953 participants aged 18–75 years, who underwent blood testing for fasting serum glucose (FSG), HOMA-IR, fasting insulin (FI), and triglyceride (TG) levels between March and August 2024, were included. The triglyceride-to-HDL cholesterol ratio (THR) was calculated as serum triglyceride (mg/dL) / serum HDL (mg/dL),¹⁷ and HOMA-IR was derived using the formula $FSG \text{ (mg/dL)} \times FI \text{ (\mu U/mL)} / 405$.¹⁸

Exclusion criteria included participants under 18 years, or those with chronic thyroid disease, liver disease, chronic kidney disease, haematological disorders, malignancy, systemic inflammatory or infectious diseases, prior metabolic or bariatric surgery, or current use of anti-inflammatory or steroid therapy. Laboratory analyses were performed using AU480 analyzer (Beckman Coulter Inc.) for FSG, TG and FI.

Statistical Analysis

Participants were stratified according to HOMA-IR values, using a cutoff of 2.5.¹⁹ Descriptive analyses were performed, with continuous variables presented as mean ± standard deviation and categorical variables as n (%). The independent samples t test was used for normally distributed variables (age, FSG, HDL), while the Mann–Whitney U test was applied for non-normally distributed variables (HOMA-IR, FI, TG, THR). The relationship between THR and significant variables within the HOMA-IR groups was assessed using Spearman correlation. Receiver Operating Characteristic (ROC) analysis was employed to determine cutoff values and diagnostic performance of THR. Logistic regression analysis was conducted to evaluate associations between selected variables and HOMA-IR. A p-value < 0.05 was considered statistically significant. All analyses were performed using SPSS software.

RESULTS

A total of 953 patients were included in the study, with a mean age of 40.83 ± 16.78 years. Based on the

HOMA-IR cutoff value of 2.5, significant differences ($p<0.001$) were observed between groups in FSG, HOMA-IR, FI, TG, and THR (Table-1). Pairwise correlation analysis revealed a moderate negative correlation between THR and HDL ($r = -0.555$, $p<0.001$) and a strong positive correlation between THR and TG ($r = 0.959$, $p<0.001$) (Table-2). In ROC analysis, THR demonstrated the highest selectivity and positive predictive value (PPV) for HOMA-IR at a cutoff ≥ 2.64 (AUC = 0.72, Se = 65%, Sp = 70%, $p<0.001$; 95% CI: 0.66–0.78) (Table-3, Figure-1). Multivariate logistic regression analysis showed that men were 2.247 times more likely than women to exhibit poor glycaemic control ($p=0.022$). The risk of poor control increased by 1.045-fold per year of age ($p=0.007$) and by 1.056-fold per unit rise in FSG ($p=0.001$) (Table-4).

Table-1: Distribution of quantitative variables

Variables		HOMA-IR group		p
	Total (n=953) Mean \pm SD	< 2.5 (n=379) Mean \pm SD	≥ 2.5 (n=574) Mean \pm SD	
Age (Years)	40.83 \pm 16.78	41.42 \pm 16.6	40.5 \pm 16.89	0.130
FSG (mg/dL)	115.28 \pm 59.91	99.88 \pm 34.48	123.77 \pm 68.67	< 0.001
HDL-C (mg/dL)	50.97 \pm 12.51	56.62 \pm 13.93	47.94 \pm 10.53	< 0.001
HOMA-IR	3.2 [2.08–5.22]	1.82 [1.34–2.24]	4.64 [3.47–7.13]	< 0.001*
FI (mIU/mL)	12.63 [8.14–19.36]	7.78 [5.32–9.36]	17.7 [13.79–25.12]	<0.001*
TG (mg/dL)	127 [93.3–179]	109 [77–141.95]	145.1 [107–204]	<0.001*
THR	2.65 [1.54–4.07]	1.74 [1.2–2.89]	3.26 [1.96–5.12]	<0.001*

Data are shown as mean \pm standard deviation or median [Quartile 1–Quartile 3]. Independent Samples t test was used. *: Mann Whitney U test was used. HOMA-IR: Homeostasis

Table-2: Pairwise correlation between variables

Variables	Total THR	HOMA-IR < 2.5 THR	HOMA-IR ≥ 2.5 THR
Age (year)			
r	0.069	0.268*	0.111
p	0.258	0.005	0.165
FSG (mg/dL)			
r	0.276*	0.399*	0.219*
p	< 0.001	< 0.001	0.006
HOMA-IR			
r	0.372*	0.239*	0.292*
p	< 0.001	0.012	< 0.001
HDL (mg/dL)			
r	-0.555*	-0.613*	-0.549*
p	< 0.001	< 0.001	< 0.001
FI (mIU/mL)			
r	0.254*	0.087	0.146
p	<0.001	0.364	0.066
TG (mg/dL)			
r	0.959*	0.924*	0.962*
p	< 0.001	< 0.001	< 0.001

Spearman correlation coefficient was used. *: Statistically significant positive correlations. HOMA-IR: Homeostasis model assessment-estimated insulin resistance; THR: Triglyceride/HDL-C ratio; FSG: Fasting serum glucose; HDL: High-density lipoprotein; FI: Fasting insulin; TG: Triglycerides.

Table-3: ROC analysis results for THR

Variable	Cut-off	AUC (95% CI)	Se	Sp	PPV	NPV	p
THR	≥ 2.64	0.72 (0.66–0.78)	0.65	0.70	0.76	0.58	< 0.001

ROC: Receiver operating characteristic; THR: Triglyceride/HDL-C ratio; AUC: Area under curve, CI: Confidence interval; Se: Sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value.

Table-4: Logistic regression analysis of selected variables

Model	Univariate			Multivariate				
	p	Odds ratio	95% CI for odds ratio	p	Odds ratio	95% CI for odds ratio		
			Lower	Upper			Lower	Upper
Gender (F/M)	0.026	1.382	1.040	1.835	0.022	2.247	1.051	4.504
Age (year)	0.130	1.007	0.986	1.002	0.001	1.056	1.033	1.081
FSG (mg/dL)	< 0.001	1.016	1.010	1.021	0.007	1.045	1.012	1.079
HDL_cholesterol	< 0.001	1.066	0.918	0.958	0.032	1.053	1.004	1.103
TG (mg/dL)	< 0.001	1.009	1.006	1.012	0.884	1.002	0.979	1.025
THR	< 0.001	1.534	1.295	1.818	0.991	0.996	0.487	2.034

Reference category: Women for Gender. CI: Confidence interval; FSG: Fasting serum glucose; HDL: High-density lipoprotein; TG: Triglycerides; THR: Triglyceride/HDL-C ratio.

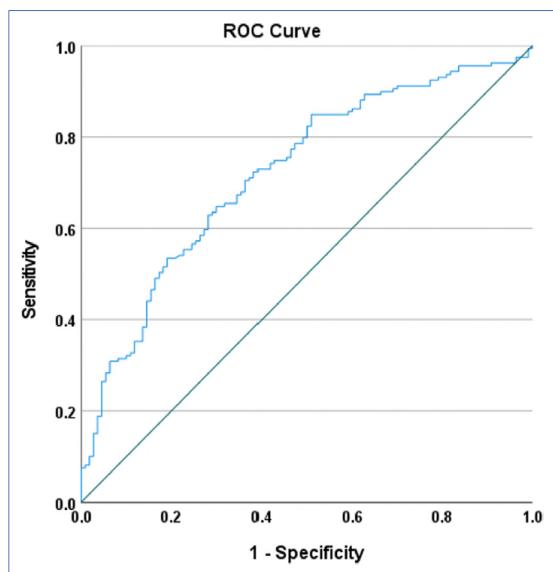


Figure-1: ROC curve of THR

ROC: Receiver operating characteristic; THR: Triglyceride/HDL-C ratio.

DISCUSSION

In our study, patients with uncontrolled T2DM exhibited elevated THR levels. THR showed a negative correlation with HDL, a strong positive correlation with TG, and weaker but significant positive correlations with FSG and HOMA-IR. These findings suggest that THR may serve as an independent predictor for increased risk of incident T2DM. Incident T2DM is characterized by both insulin resistance (IR) and impaired β -cell function.²⁰ IR contributes to hyperglycemia and hyperlipidemia across multiple tissues, including muscle, liver, adipose tissue, and pancreatic β -cells.²¹ Elevated triglycerides can impair glucokinase activity and glucose-stimulated insulin secretion in islets during hypertriglyceridaemia.²² Meanwhile, chronic hyperglycemia induces oxidative stress on β -cells, which possess limited antioxidant capacity, ultimately accelerating β -cell dysfunction.²³ Together, lipotoxicity and glucotoxicity drive β -cell failure, underscoring the critical importance of IR assessment in T2DM and metabolic syndrome. HOMA-IR, derived from FSG and insulin levels, remains one of the most widely validated methods for estimating IR in both epidemiological studies and clinical practice.²⁴ A review of 28 studies confirmed HOMA-IR as the most commonly used technique.¹⁸ In our study, HOMA-IR was significantly elevated in the poor glycemic control group and positively correlated with THR, consistent with previous findings. Baneru et al²⁵ reported that ROC analysis for IR demonstrated an AUC > 0.7 in 17 studies, reflecting reasonable predictive power. Similarly, our analysis yielded an AUC of 0.72, supporting the moderate predictive utility of THR. Fasting insulin (FI), though simple to measure, provides only a limited assessment of insulin sensitivity.^{26,27} In our study, FI was significantly higher in the poor glycemic control group and demonstrated a positive correlation with THR, further reinforcing its association with IR. The hyperinsulinaemic-euglycemic clamp remains the gold standard for assessing insulin sensitivity and resistance; however, its labor-intensive nature, high cost, and technical demands limit its feasibility in routine practice.^{28,29} For this reason, we were unable to apply this method in our cross-sectional study. Clinical guidelines highlight that asymptomatic adults

with elevated triglycerides and reduced HDL cholesterol are at increased risk of prediabetes and diabetes.³⁰ Identifying reliable biomarkers such as THR may therefore support early detection, patient monitoring, and the development of new therapeutic strategies aimed at improving survival.³¹ Our findings are consistent with previous research. Jabeen et al¹⁷ reported elevated THR levels in uncontrolled T2DM patients, while Gedikli et al³² demonstrated a positive association between FSG and THR in Chinese T2DM patients. Similarly, in our study, THR levels were significantly higher in patients with poor glycaemic control. The determination of cutoff values for THR remains clinically important. While around half of published studies propose specific thresholds, others treat THR as a continuous variable. Reported cutoffs vary widely—some general, others stratified by race or gender. Between 2005 and 2008, studies suggested maximum thresholds of 3.5 for both sexes, with median cutoffs of 2.53 for women and 2.8 for men.³³⁻³⁵ Li et al³⁶ further explored ethnicity-related differences, reporting no significant variation in odds ratios across non-Hispanic whites, non-Hispanic blacks, and Mexican Americans, though ethnicity-specific cutoffs were identified. In our study, the THR cutoff value was determined as 2.64, indicating moderate predictive power. Moreover, men were 2.2 times more likely than women to have poor glycaemic control. The risk of poor control also increased incrementally—by 1.045-fold with age and by 1.1-fold with rising FSG levels.

CONCLUSIONS

Our findings highlight the potential of THR as a practical tool for diabetes risk assessment, both in routine clinical practice and in large-scale epidemiological studies, given its simplicity and derivation from standard laboratory tests.

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