Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(2), 1415-1421 | ISSN:2251-6727

Triglycerides\HDL Ratio as a Screening Tool for Metabolic Dysfunction in Newly Diagnosed DM Type 2

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(Received: 16 January 2026 Revised: 25 February 2026 Accepted: 17 March 2026)

KEYWORDS

Type 2 diabetes mellitus; TG/HDL-C ratio; TyG index; Dyslipidemia; Insulin resistance; Glycemic control; Metabolic dysfunction.

ABSTRACT

Background: Diabetes mellitus is a growing global health issue associated with high morbidity, mortality, and health care costs. Diabetic dyslipidemia involving increased triglycerides (TG) and lower high-density lipoprotein cholesterol (HDL-C) are key predictors of insulin resistance and cardiovascular disease. Triglyceride-to-HDL cholesterol (TG/HDL-C) ratio is a crude surrogate index for metabolic derangement and insulin resistance.

Objective: To assess the TG/HDL-C ratio as a screening method to identify metabolic dysfunction in patients and evaluate its utility for predicting the glycemic control of newly diagnosed type 2 diabetes mellitus (DM2) patients.

Methods: A cross-sectional study with 80 recently diagnosed DM2 patients in both groups based on HbA1c is recommended to assess good glycemic control (HbA1c <7%, n=40) and poor glycemic control (HbA1c ≥7%, n=40). Measurement of anthropometric parameters was performed including blood pressure, fasting glucose, lipid profile, TG/HDL-C ratio, and TyG index. Traditionally, Spearman correlation analysis was applied to assess association of TG/HDL-C ratio and clinical variables. We ran multiple linear regressions on all HbA1c predictors within normal weight sub-groups and overweight/obese subgroups.

Results: DBP, fasting glucose, triglycerides and TG/HDL-C ratio were statistically significantly higher in patients with HbA1c ≥7% than in patients with HbA1c <7% ($p<0.05$). TG/HDL-C ratio positively and negatively significantly influenced the BMI ($r=0.21$), DBP ($r=0.27$), and TG ($r=0.94$) and HDL-C ($r=-0.59$) ($p<0.05$). In normal weight patients (BMI < 25 kg/m²), logTG/HDL-C predicted HbA1c independently (OR=0.21; $p=0.017$; $R^2=0.47$). For overweight/obese patients (BMI > 25 kg/m²) TyG index was the only significant independent predictor of HbA1c (OR=0.063; $p=0.027$; $R^2=0.25$).

Conclusion: The TG/HDL-C ratio is a remarkable predictor of glycemic control in newly diagnosed DM2 patients and can be considered a potential practical screening tool for metabolic dysfunction, especially in the normal weight population. In overweight/obese patients, the TyG index seems the more robust predictor of glycemic control. These low-cost and readily available markers may offer an adjunct to HbA1c in everyday clinical practice.

1. Introduction

The report predicted that 10.5% of the 20-to-79-year age cohort (536.6 million) would be diagnosed with diabetes by 2021. The percentage is predicted to increase to 12.2% (783.2 million) worldwide by 2045. Diabetes increases the risk of atherosclerosis and is associated with an increased risk of mortality from malignancy, infectious diseases, and cardiovascular diseases. Global healthcare expenditure for diabetes will be over US$ 966

Journal of Chemical Health Risks
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JCHR (2026) 16(2), 1415-1421 | ISSN:2251-6727

billion in 2021 and over US$ 1,054 billion by 2045. Diabetes and complications, and the accompanying increase in healthcare costs, are serious global issues. Regulating the onset of diabetes is essential to prevent the aggravation of complications. [1-3] Increased cardiovascular disease risk has been linked to lipid metabolic abnormalities. Diabetes dyslipidemia reflects increased triglyceride (TG) and decreased high density lipoprotein cholesterol (HDL-C), with a consequent elevation in low density lipoprotein cholesterol (LDL-C) especially small dense LDL-C. Moreover, lipid metabolic abnormalities play a role in the development of diabetes [4,5,6], but exact data is lacking regarding the correlation of dyslipidemia with type 2 diabetes (T2D), including certain threshold values. Previous studies have shown that the TG/HDL-C ratio is a reliable predictor of insulin resistance [7,8]. The TG/HDL-C ratio has been studied for several phenomena above; it increases the risk of fatty liver development independent of other factors and is positively associated with arterial stiffness [9,10]. Previous research evaluated the relationship between the TG/HDL-C ratio and the prevalence of diabetes in adults and found an increased TG/HDL-C ratio to be associated with an increased risk of developing diabetes.10 We examined the TG/HDL ratio to test its value as a predictive factor in glycemic control in newly diagnosed individuals with type 2 diabetes mellitus.

2. Objectives

To assess the TG/HDL-C ratio as a screening method to identify metabolic dysfunction in patients and evaluate its utility for predicting the glycemic control of newly diagnosed type 2 diabetes mellitus (DM2) patients.

3. Methods and material

This cross-sectional study comprised 80 patients with type 2 diabetes mellitus (DM2), evenly divided into 2 groups according to HbA1c values: DM2 subjects with good glycemic control (HbA1c <7%, n=40) and DM2 subjects with poor glycemic control (HbA1c ≥7%, n=40).

The study objectives were explained to all participants and the process required to provide written informed consent was undertaken. Demographic information, medical history, and lifestyle characteristics (smoking habits, alcohol use, and physical activity) were obtained with a structured questionnaire. Patients with conditions known to affect lipid metabolism (chronic heart, kidney, thyroid or liver disease, severe infection, malignancy) or those taking medications that influence lipid metabolism were excluded.

The protocol of the study was developed following the Declaration of Helsinki (2000 revision). Subjects were instructed to adhere to a low-fat diet and avoid intensive physical activity and alcohol intake for 3 days before obtaining samples. Venous blood samples were taken following overnight fasting. Fasting glucose (FG) was determined through glucose oxidase method, HbA1c by high-performance liquid chromatography, total cholesterol (TC) by cholesterol oxidase method, HDL-C by direct homogeneous enzymatic method, and triglycerides (TG) by enzymatic hydrolysis with glycerol determination. LDL-C was determined according to Friedewald's formula. TG: HDL-C ratio (TG divided by HDL-C: mg/dL) was calculated. TyG value was determined by the following equation: Ln [TG (mg/dL) × FG (mg/dL)/2]. Weight and height were recorded using standardized measures; BMI was measured as weight (kg)/height (m^2).

Statistical analysis was conducted with SPSS version 16.0. Group differences were assessed from independent t-test or Mann–Whitney test as indicated. Associations between variables were evaluated using Spearman correlation analysis. All HbA1c independent predictors (age, gender, smoking, BMI, duration of DM, TG/HDL-C ratio, TyG index) were performed using multiple linear regression analysis. Non-normally distributed variables (TG/HDL-C and HbA1c) were log-transformed before the regression was conducted on them. The results were presented as regression coefficients (β), odds ratios (OR), 95% confidence intervals (CI). Statistical significance was defined as a p-value <0.05.

4. Results

Baseline characteristics

Regarding baseline characteristics of 80 DM2 patients stratified by HbA1c (<7% vs ≥7%, n=40 each), there were no significant differences in age, gender, smoking status, duration of diabetes, BMI, SBP, TC, HDL-C, or LDL-C between groups. Patients with HbA1c ≥7% had significantly higher DBP (p=0.005), fasting glucose (p<0.001), triglycerides (p=0.010), and TG/HDL-C ratio

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JCHR (2026) 16(2), 1415-1421 | ISSN:2251-6727

(p=0.002). As expected, HbA1c levels were markedly higher in the poorly controlled group (p<0.001).

Table 1. Baseline characteristics of patients with DM2 according to HbA1c value (n=40 per group)

Data are presented as mean ± SEM, median (IQR), or number (%).

Variables	DM2 HbA1c <7% (n=40)	DM2 HbA1c ≥7% (n=40)	p-value
Age (years)	63.9 ± 1.9	60.4 ± 1.7	NS
Gender (Male; n, %)	15 (37.5%)	22 (55.0%)	NS
Smoking (Yes; n, %)	14 (35.0%)	17 (42.5%)	NS
Duration of DM (years)	4 (2–10)	6 (2–11)	0.41
BMI (kg/m²)	29.6 ± 0.7	29.9 ± 0.6	NS
SBP (mmHg)	130 (120–148)	138 (128–150)	NS
DBP (mmHg)	80 (80–90)	90 (80–100)	0.005
FG (mmol/L)	6.9 (6.1–8.2)	8.3 (7.1–10.5)	<0.001
HbA1c (%)	6.5 (6.1–6.8)	9.1 (7.9–10.3)	<0.001
TC (mmol/L)	5.6 (5.0–6.1)	5.5 (4.8–6.3)	NS
TG (mmol/L)	1.75 (1.32–2.40)	2.35 (1.55–3.50)	0.010
HDL-C (mmol/L)	1.12 (0.90–1.42)	1.01 (0.85–1.16)	NS
LDL-C (mmol/L)	3.58 ± 0.18	3.35 ± 0.17	NS
TG/HDL-C ratio	3.38 (2.10–6.20)	5.76 (3.50–8.90)	0.002

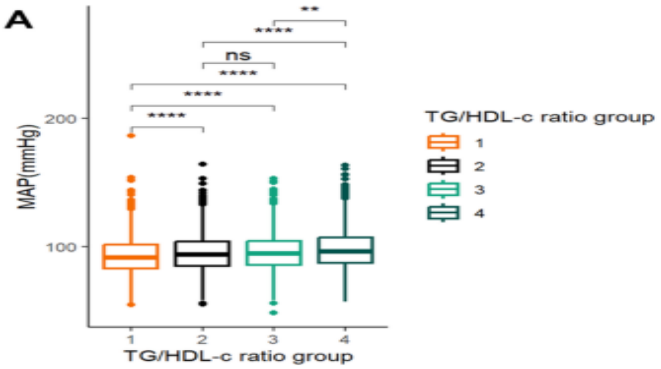

Figure 1. Box-and-whisker plot comparing TG/HDL-C ratio between DM2 patients with good glycemic control (HbA1c <7%) and poor glycemic control (HbA1c ≥7%).

Spearman correlation coefficients between TG/HDL-C ratio and clinical/laboratory parameters

Regarding Spearman correlations between TG/HDL-C ratio and clinical/laboratory parameters in 80 DM2 patients, the TG/HDL-C ratio was positively correlated with BMI (r=0.21, p<0.05), DBP (r=0.27, p<0.05), and strongly with TG (r=0.94, p<0.01), while it showed a significant negative correlation with HDL-C (r=–0.59, p<0.01). Weak negative correlations were observed with age (r=–0.22, p<0.05) and DM duration (r=–0.24, p<0.05). No significant associations were found with SBP, FG, TC, or LDL-C.

Table 2. Spearman correlation coefficients between TG/HDL-C ratio and clinical/laboratory parameters (n = 80)

Variables	TG/HDL-C ratio (r)
Age	–0.22*
DM2 duration	–0.24*
BMI	0.21*
SBP	0.11
DBP	0.27*
FG	0.17
TG	0.94**
TC	0.13
HDL-C	–0.59**
LDL-C	0.07

* p < 0.05
** p < 0.01

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JCHR (2026) 16(2), 1415-1421 | ISSN:2251-6727

Figure 2. Spearman correlation coefficients between TG/HDL-C ratio and clinical/laboratory parameters

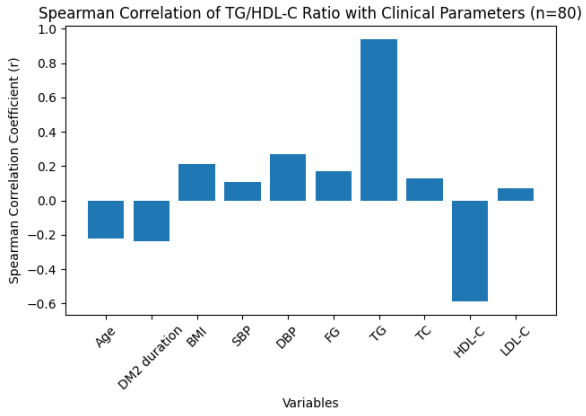
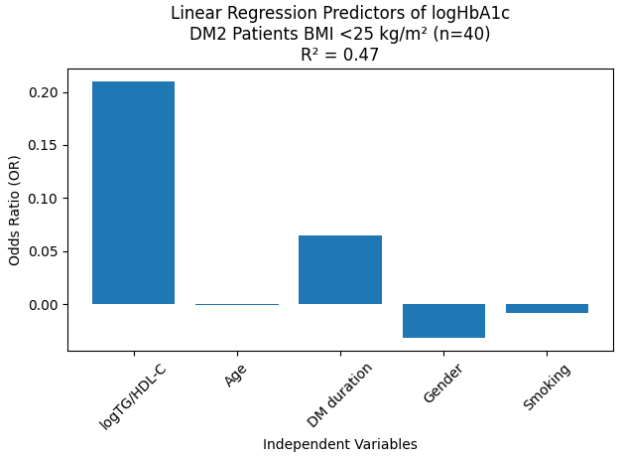


Figure 3. Linear Regression Analysis with Independent Predictors of HbA1c in Normal Weight



Linear Regression Analysis with Independent Predictors of HbA1c in Normal Weight

Regarding linear regression analysis of predictors of logHbA1c in normal-weight DM2 patients (BMI <25 kg/m², n=40; R^2=0.47), among the variables analyzed, only logTG/HDL-C was a significant independent predictor of HbA1c (OR=0.21, 95% CI: 0.05–0.37, p=0.017). Age, duration of diabetes, gender, and smoking status were not significantly associated with HbA1c (all p>0.05). This indicates that in normal-weight patients, the TG/HDL-C-related metabolic parameter was independently associated with glycemic control.

Table 3. Linear Regression Analysis with Independent Predictors of HbA1c in Normal Weight

DM2 Patients with BMI < 25 kg/m² (n = 40)

Dependent variable: logHbA1c | R^2 = 0.47

Variables	OR	95% CI	p
logTG/HDL-C	0.21	0.05 – 0.37	0.017*
Age	-0.001	-0.01 – 0.05	0.66
DM duration	0.065	-0.11 – 0.24	0.43
Gender	-0.032	-0.14 – 0.08	0.54
Smoking	-0.008	-0.13 – 0.12	0.89

Linear Regression Analysis with Independent Predictors of HbA1c in Overweight/Obese DM2 Patients

Regarding linear regression analysis of predictors of logHbA1c in overweight/obese DM2 patients (BMI >25 kg/m², n=40; R^2=0.25), the TyG index was the only significant independent predictor of HbA1c (OR=0.063, 95% CI: 0.01–0.12, p=0.027). Age, duration of diabetes, gender, and smoking status were not significantly associated with HbA1c (all p>0.05). This suggests that in overweight/obese patients, insulin resistance–related metabolic status (TyG index) is independently associated with glycemic control.

Table 4. Linear Regression Analysis with Independent Predictors of HbA1c in Overweight/Obese DM2 Patients

DM2 Patients with BMI > 25 kg/m² (n = 40)

Dependent variable: logHbA1c | R^2 = 0.25

Variables	OR	95% CI	p
TyG index	0.063	0.01 – 0.12	0.027*
Age	0.00	-0.00 – 0.001	0.62
DM duration	0.025	-0.02 – 0.07	0.43
Gender	-0.02	-0.06 – 0.02	0.31
Smoking	-0.05	-0.03 – 0.04	0.24

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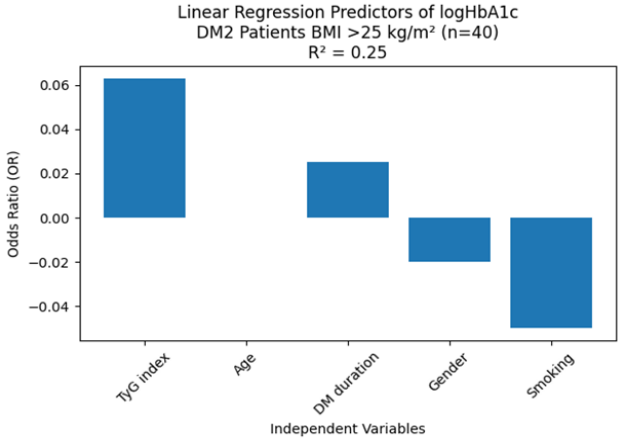
JCHR (2026) 16(2), 1415-1421 | ISSN:2251-6727

* $p < 0.05$

Figure 4. Linear Regression Analysis with Independent Predictors of HbA1c in Overweight/Obese DM2 Patients



5. Discussion

In the current study with 80 type 2 diabetes mellitus (DM2) patients, separated by glycemic control (HbA1c <7% vs ≥7%), diabetic control subgroups evidenced a significantly more elevated DBP, fasting glucose, triglycerides, and TG/HDL-C ratio, while other baseline characteristics were comparable. This is consistent with past evidence indicating higher TG/HDL-C ratio and TyG index in patients with HbA1c ≥7%, indicating a robust association between dyslipidemia and poor glycemic control [11]. The sharply greater TG/HDL-C ratio of the poorly controlled group validates the underlying hypothesis about the ratio as a manifestation of insulin resistance. TG/HDL-C has been reported as one of the most simple and inexpensive surrogate markers of insulin resistance, appropriate in both clinical and epidemiological scenarios [12]. Given that insulin resistance contributes to the hyperglycemia in DM2, a greater TG/HDL-C ratio within the HbA1c ≥7% group would probably be due to worsening metabolic derangements.

Our correlation analysis showed that TG/HDL-C ratio was positively associated with BMI and DBP and strongly associated with triglycerides, while negatively associated with HDL-C. Previous work has demonstrated similar associations between TG/HDL-C and cardiometabolic risk clustering, such as vascular stiffness [13]. Weak negative correlations with age and diabetes duration suggest that lipid-mediated metabolic derangements are more pronounced in earlier or metabolically active stages of DM2. Large prospective cohort studies back up the efficacy of TG/HDL-C in predicting dysglycemia. Increased TG/HDL-C tertiles were significantly associated with incident diabetes in males and females in the same direction [14]. Other studies [15] showed that higher TG/HDL-C quartiles were also related with incidence of prediabetes and type 2 diabetes independently of standard risk factors. While our study is cross-sectional, the significant association between TG/HDL-C and HbA1c reflects these longitudinal findings.

A key finding from this BMI-stratified regression analysis was that logTG/HDL-C was the only independent predictor for HbA1c in patients with normal weight (BMI <25 kg/m²). Indeed, earlier cohort literature has shown that TG/HDL-C is an independent predictor of incident diabetes and possibly signaling a metabolic threat independently of conventional lipid parameters [16]. This implies that in lean participants with DM2, lipid-mediated insulin resistance is a disproportionately important risk factor of glycemic management. In comparison, in overweight/obese patients (BMI > 25 kg/m²), the TyG index served as the only significant independent predictor of HbA1c. TyG is well known to have superior discriminant value for diagnosis of diabetes and prediabetes than several conventional lipid markers [17]. The superior predictive power of TyG in overweight and obese individuals might be attributed to the dominating role of adiposity-induced insulin resistance in the current group.

In terms of mechanism, abnormalities in triglyceride-rich lipoproteins have been demonstrated to precede insulin resistance and β-cell dysfunction and to be independently associated with incident type 2 diabetes. These results also lend biological plausibility to the observed associations between lipid-derived markers and poor glycemic control in our cohort. Clinically, our findings imply that TG/HDL-C ratio might be especially useful in identifying poor glycemic control in normal-weight DM2 patients, whereas TyG index may be more valuable

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for overweight/obese individuals. Due to their simplicity, low cost, and availability in routine laboratory testing, these markers might serve as practical adjuncts to HbA1c assessment and are particularly applicable to resource-limited settings.

Nonetheless, the cross-sectional design limits causal inference, and the relatively small sample size may affect generalizability. Future investigations are needed to establish whether interventions addressing these lipid-derived markers improve glycemic outcomes. In conclusion, TG/HDL-C ratio and TyG index are closely associated with glycemic control. TG/HDL-C independently predicts HbA1c in normal-weight subjects, whereas TyG index is a stronger predictor in overweight/obese individuals, highlighting the heterogeneity of metabolic drivers of hyperglycemia in DM2.

6.Conclusion

TG/HDL-C ratio shows high correlation with glycemic control in newly diagnosed patients with type 2 diabetes mellitus. Patients with uncontrolled glucose (HbA1c ≥7%) showed higher triglyceride levels with TG/HDL-C ratios, emphasizing the significant association of dyslipidemia with metabolic dysfunction. Thus, as it is simple and inexpensive and is available at routine laboratory tests, it may serve as an alternative, practical screening technique for the early detection of metabolic dysfunction as well as poor glycemic control in resource-constrained societies. Nevertheless, larger prospective studies will be needed to confirm its predictive utility and to provide clinically relevant cut-off values for risk stratification.

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