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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

The Role Of The Triglyceride–Glucose (TyG) Index And The Triglyceride/HDL-Cholesterol (TG/HDL-C) Ratio In Predicting Gestational Diabetes Mellitus

Gestasyonel Diyabeti Tahmin Etmede Trigliserit-Glikoz (TyG) indexi ve Trigliserit /HDL -Kolesterol (TG/HDL-C) Oranının Rolü

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ABSTRACT

Aim: To evaluate the predictive performance of the triglyceride–glucose (TyG) index and the triglyceride/HDL-cholesterol ratio (TG/HDL-c) for gestational diabetes mellitus (GDM).

Material and Method: A retrospective case–control study was conducted at Tepecik Training and Research Hospital between 2023 and 2025. Singleton pregnancies in women aged 18–45 years were included; those with pregestational diabetes or major systemic/metabolic disease were excluded. GDM was diagnosed using a 75-g oral glucose tolerance test at 24–28 gestational weeks according to International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria. The TyG index ln(TG(mg/dL)×fastingglucose(mg/dL)/2)ln(TG (mg/dL) × fasting glucose (mg/dL)/2)ln(TG(mg/dL)×fastingglucose(mg/dL)/2) and TG/HDL-c were calculated from fasting blood samples. Receiver operating characteristic (ROC) analysis was used to estimate areas under the curve (AUCs) with 95% confidence intervals (CIs) and to determine optimal cut-offs using the Youden index. Multivariable logistic regression analyses were performed with adjustment for age, parity, and gestational week at the time of sampling.

Results: A total of 199 women were analyzed (100 with GDM and 99 controls). Both TyG (4.02±0.21 vs 3.84±0.18) and TG/HDL-c (3.92±2.12 vs 2.80±1.29) were significantly higher in the GDM group (both p<0.001). TyG demonstrated the highest discriminative ability (AUC 0.73; 95% CI 0.66–0.80), with an optimal cut-off of 3.937 (sensitivity/specificity: 0.67/0.67). TG/HDL-c and triglycerides also showed moderate performance (AUC 0.71 and 0.70, respectively). After adjustment, both TyG (OR 2.05 per 0.1-unit increase; 95% CI 1.45–2.90) and TG/HDL-c (OR 1.52 per 1-unit increase; 95% CI 1.24–1.87) remained independently associated with GDM.

Conclusion: The TyG index and TG/HDL-c ratio, derived from routine fasting laboratory tests, provide moderate discrimination for GDM and may support risk stratification as adjuncts to OGTT. Prospective external validation is warranted.

Keywords: Gestational diabetes mellitus, triglyceride–glucose index (TyG), TG/HDL-cholesterol ratio, insulin resistance

ÖZ

Amaç: Trigliserit–glukoz (TyG) indeksi ile trigliserit/HDL-kolesterol oranının (TG/HDL-c) gestasyonel diyabet mellitus (GDM) öngörüsündeki performansını değerlendirmek.

Gereç ve Yöntem: Tepecik Eğitim ve Araştırma Hastanesi'nde 2023–2025 yılları arasında retrospektif vaka-kontrol çalışması yürütüldü. 18–45 yaş arası tekil gebelikler çalışmaya dahil edildi; gebelik öncesi diyabeti veya majör sistemik/metabolik hastalığı olanlar dışlandı. GDM tanısı, Uluslararası Diyabet ve Gebelik Çalışma Grupları Derneği (IADPSG) kriterlerine göre 24–28. gebelik haftalarında uygulanan 75 g oral glukoz tolerans testi (OGTT) ile konuldu. TyG indeksi ln(TG(mg/dL)×ac\clıkglukozu(mg/dL)/2) ln(TG (mg/dL) × açlık glukozu (mg/dL) / 2)ln(TG(mg/dL)×ac\clıkglukozu(mg/dL)/2) ve TG/HDL-c, açlık kan örneklerinden hesaplandı. Alıcı işletim karakteristiği (ROC) analizi ile %95 güven aralıkları (GA) ile eğri altında kalan alan (AUC) değerleri hesaplandı ve Youden indeksi kullanılarak en uygun eşik değerler belirlendi. Çok değişkenli lojistik regresyon analizleri yaş, parite ve örnekleme anındaki gebelik haftasına göre düzeltildi.

Bulgular: Toplam 199 kadın analiz edildi (100 GDM, 99 kontrol). TyG (4,02±0,21 vs 3,84±0,18) ve TG/HDL-c (3,92±2,12 vs 2,80±1,29) GDM grubunda anlamlı olarak daha yüksekti (her ikisi için p<0,001). TyG en yüksek ayırt ediciliği gösterdi (AUC 0,73; %95 GA 0,66–0,80) ve en uygun eşik değer 3,937 idi (duyarlılık/özgüllük: 0,67/0,67). TG/HDL-c ve trigliserit de orta düzey performans gösterdi (AUC sırasıyla 0,71 ve 0,70). Düzeltme sonrası hem TyG (0,1 birim artış başına OR 2,05; %95 GA 1,45–2,90) hem de TG/HDL-c (1 birim artış başına OR 1,52; %95 GA 1,24–1,87) GDM ile bağımsız olarak ilişkili kalmıştır.

Sonuç: Rutin açlık laboratuvar testlerinden elde edilen TyG indeksi ve TG/HDL-c oranı, GDM için orta düzey ayırt edicilik sağlar ve OGTT'ye yardımcı olarak risk sınıflamasını destekleyebilir. Prospektif dış doğrulama çalışmaları gereklidir.

Anahtar Kelimeler: Gestasyonel diyabet mellitus, trigliserit–glukoz indeksi (TyG), TG/HDL-kolesterol oranı, insülin direnci

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first recognized during pregnancy and is associated with adverse short- and long-term outcomes for both the mother and the fetus. Large-scale data demonstrating that hyperglycemia influences pregnancy outcomes across a continuous risk spectrum have shown that increasing maternal glycemia is linked to adverse outcomes such as macrosomia, neonatal hypoglycemia, and operative delivery (1). Current diagnostic and classification approaches rely largely on the 75-g oral glucose tolerance test (OGTT); the recommendations of the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) and the World Health Organization (WHO) classification are widely used within this framework, and screening in clinical practice is most commonly performed at 24–28 gestational weeks (2, 3). Similarly, the American Diabetes Association (ADA) guidelines emphasize an OGTT-based approach for the diagnosis and follow-up of GDM, as well as glycemic targets during pregnancy (4). However, the relatively late timing of standard screening constitutes a limitation in terms of identifying high-risk pregnant women earlier and optimizing the timing of preventive strategies such as lifestyle interventions.

In the pathogenesis of GDM, pregnancy-specific physiological insulin resistance, inadequate beta-cell compensation, and an accompanying metabolic/atherogenic profile play major roles. Accordingly, there has been increasing interest in practical biomarkers that are easy to implement and indirectly reflect insulin resistance. The triglyceride–glucose (TyG) index, calculated using fasting triglyceride and fasting glucose levels, has been proposed as a simple surrogate marker of insulin resistance (5). Likewise, the TG/HDL-cholesterol ratio (TG/HDL-c) is a readily accessible measure that reflects an atherogenic dyslipidemia pattern and may predict insulin resistance (6). Because both indices can be obtained from standard biochemical panels without additional cost, they have emerged as attractive candidates for early risk stratification during pregnancy.

In recent years, an increasing number of studies have reported that TyG and TG/HDL-c values measured in the first trimester or early pregnancy may predict the risk of developing GDM later in gestation. For instance, several studies have indicated that first-trimester TyG and TG/HDL-c are associated with subsequent GDM development, and some analyses have suggested that TyG may exhibit stronger discriminative ability (7). Similarly, prospective cohort data have shown a positive association between the TG/HDL-c ratio in early pregnancy and the incidence of GDM (8). Nevertheless, due to heterogeneity across populations in metabolic characteristics, diagnostic criteria, and measurement timing, the clinical thresholds and incremental predictive value of these indices remain unclear. Therefore, evaluating the performance of TyG and TG/HDL-c for predicting GDM in local populations and clarifying their added contribution beyond classical clinical risk factors are of clinical importance.

MATERIAL AND METHOD

Ethical Approval and Declarations

This study was approved by the Tepecik Training and Research Hospital Non-interventional Research Ethics Committee (Date: 04/06/2024, Decision No: 2024/05-14). Because retrospective data were used, individual informed consent was not required. The study underwent external independent peer review. The authors declare no conflicts of interest and report no financial support for this study. All authors contributed to the study design, conduct, analysis, and approval of the final manuscript.

Study Design and Setting

This retrospective case–control study was conducted at Tepecik Training and Research Hospital between 2023 and 2025. The case group comprised pregnant women diagnosed with gestational diabetes mellitus (GDM), whereas the control group consisted of healthy pregnant women followed at the same center.

Participants and Eligibility Criteria

Singleton pregnancies in women aged 18–45 years without systemic, metabolic, or inflammatory disease were eligible. Exclusion criteria were multiple gestation; a history of pregestational diabetes or thyroid dysfunction; previously diagnosed hyperlipidemia; other systemic disease; and incomplete data.

Diagnosis of Gestational Diabetes Mellitus

GDM was diagnosed using a 75-g oral glucose tolerance test (OGTT) performed at 24–28 gestational weeks in accordance with the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria. Participants maintained a diet containing at least 150 g/day of carbohydrates for at least 3 days prior to testing and fasted for 8 hours. Women were classified as having GDM if any of the following plasma glucose values were met or exceeded: fasting ≥5.1 mmol/L (91.90 mg/dL), 1-hour ≥10.0 mmol/L (180.20 mg/dL), or 2-hour ≥8.5 mmol/L (153.17 mg/dL).

Variables and Laboratory Measurements

The primary exposure was the presence of GDM. Outcomes/biomarkers assessed included fasting plasma glucose, triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol, blood urea, uric acid, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), and the triglyceride–glucose (TyG) index.

LDL-cholesterol was calculated using the Friedewald formula: total cholesterol − HDL-cholesterol − (triglycerides/5). HOMA-IR was computed as fastingglucose(mmol/L)×fastinginsulin(mU/L) fasting glucose (mmol/L) × fasting insulin (mU/L) fastingglucose(mmol/L)×fastinginsulin(mU/L) / 22.5. The TyG index was calculated as Ln fastingglucose(mg/dL)×fastingtriglycerides(mg/dL)/2fasting glucose (mg/dL) × fasting triglycerides (mg/dL) / 2fastingglucose(mg/dL)×fastingtriglycerides(mg/dL)/2. All biochemical analyses were performed using an Olympus AU 2700 analyzer.

Potential confounders evaluated included maternal age, pre-pregnancy and post-pregnancy body mass index (BMI), gravidity, parity, history of miscarriage/curettage, gestational weight gain, and gestational week at the time of assessment.

Statistical Methods

Data were analyzed using a statistical software package. The distribution of continuous variables was assessed using visual methods (histograms and Q–Q plots) and the Shapiro–Wilk test. Normally distributed continuous variables are presented as mean ± standard deviation, and non-normally distributed variables as median (interquartile range, IQR). Categorical variables are presented as number (n) and percentage (%).

Between-group comparisons (GDM vs controls) were performed using Student's t-test or the Mann–Whitney U test for continuous variables, as appropriate, and the chi-square test or Fisher's exact test for categorical variables when expected cell counts were low. All tests were two-sided, and p<0.05 was considered statistically significant.

To evaluate the ability of TyG, TG/HDL-c, and triglycerides to predict GDM, receiver operating characteristic (ROC) analyses were conducted and areas under the curve (AUCs) with 95% confidence intervals (CIs) were reported. The optimal cut-off value was determined by maximizing the Youden index (J = sensitivity + specificity − 1). Based on the selected cut-offs, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated (PPV/NPV calculations were based on the GDM prevalence in the study sample). When comparison of AUCs across ROC curves was required, the DeLong method was used.

To identify independent factors associated with GDM, multivariable logistic regression models were fitted with GDM status (yes/no) as the dependent variable. Because TyG and TG/HDL-c share biomarker components, two separate models were constructed to reduce potential collinearity: Model A included TyG, and Model B included TG/HDL-c (both adjusted for age, parity, and gestational week at sampling). Results are reported as odds ratios (ORs) with 95% CIs. Model calibration was assessed using the Hosmer–Lemeshow test, explanatory power using Nagelkerke's R^2, and discrimination using model-based AUC. The assumptions of linearity in the logit for continuous variables and multicollinearity (when needed, via variance inflation factor [VIF]) were evaluated. Analyses were performed using a complete-case approach for variables with missing data.

RESULTS

A total of 199 pregnant women were evaluated: 99 (49.7%) were healthy controls and 100 (50.3%) were in the GDM group. Maternal age was higher in the GDM group than in controls (31.67±4.78 vs 29.27±5.83 years; p=0.001). Similarly, gravidity (3.33±1.24 vs 2.86±1.02; p=0.010) and parity (1.73±0.85 vs 1.46±0.83; p=0.027) were significantly higher among women with GDM. Gestational week at the time of sampling was lower in the GDM group (23.92±2.05 vs 24.21±0.44 weeks; p=0.038). No significant between-group differences were observed for height, blood pressure, waist circumference, or weight-related variables (all p>0.05). Maternal demographic and clinical characteristics are presented in **Table 1**.

Table 1. Maternal demographic and clinical characteristics

Variable	Healthy (n=99) Mean±SD	GDM (n=100) Mean±SD	p
Age (years)	29.27±5.83	31.67±4.78	0.001
Height (cm)	162.86±5.33	162.60±5.98	0.835
Gravidity	2.86±1.02	3.33±1.24	0.010
Parity	1.46±0.83	1.73±0.85	0.027
Number of abortions	0.35±0.52	0.46±0.63	0.296
Number of curettages	0.08±0.27	0.16±0.40	0.124
Pre-pregnancy weight (kg)	66.04±7.92	68.67±7.95	0.051
Current weight (kg)	73.81±8.54	75.47±7.21	0.111
BMI (kg/m^2)	27.90±3.01	28.61±2.68	0.072
Waist circumference (cm)	79.92±7.42	80.60±5.69	0.261
Systolic BP (mmHg)	107.98±12.29	108.10±10.32	0.945
Diastolic BP (mmHg)	66.67±9.26	67.00±8.82	0.800
Gestational week at sampling	24.21±0.44	23.92±2.05	0.038

BMI, body mass index; BP, blood pressure. Data are presented as mean±SD. Between-group comparisons were performed using Student's t-test or the Mann–Whitney U test, as appropriate. p<0.05 was considered statistically significant.

The cesarean delivery rate was higher in the GDM group (41.0% vs 26.3%; p=0.02). Neonatal intensive care unit (NICU) admission was more frequent among neonates born to mothers with GDM (12.0% vs 4.0%; p=0.034). Difficult delivery was also significantly more common in the GDM group (14.0% vs 2.0%; p=0.02). There were no significant differences between groups with respect to intrauterine growth restriction (IUGR), neonatal sex, gestational age at delivery (by last menstrual period or ultrasound), or 1- and 5-minute APGAR scores (all p>0.05). In contrast, birth weight was markedly higher in the GDM group (3674±379.69 g vs 3223.64±323.95 g; p<0.001). Obstetric and neonatal outcomes are summarized in **Table 2**.

Table 2. Obstetric and neonatal outcomes by group

Variable	Healthy (n=99)	GDM (n=100)	p
Mode of delivery			0.02
Vaginal delivery	73 (73.7%)	59 (59.0%)	
Cesarean delivery	26 (26.3%)	41 (41.0%)	
IUGR			0.507
No	94 (94.9%)	94 (94.0%)	
Yes	5 (5.1%)	6 (6.0%)	
NICU admission			0.034
No	95 (96.0%)	88 (88.0%)	
Yes	4 (4.0%)	12 (12.0%)	
Difficult delivery			0.02
No	97 (98.0%)	86 (86.0%)	
Yes	2 (2.0%)	14 (14.0%)	
Neonatal sex			0.472
Male	50 (50.5%)	52 (52.0%)	
Female	49 (49.5%)	48 (48.0%)	
GA at delivery by LMP (weeks)	38.43±1.27	38.64±1.18	0.212
GA at delivery by ultrasound (weeks)	37.58±1.64	37.89±1.58	0.089
APGAR at 1 min	6.70±0.76	6.75±0.67	0.651
APGAR at 5 min	7.91±0.83	7.78±0.91	0.371
Birth weight (g)	3223.64±323.95	3674±379.69	<0.001

Vaginal delivery, normal spontaneous delivery; IUGR, intrauterine growth restriction; NICU, neonatal intensive care unit; LMP, last menstrual period; GA, gestational age. Data are presented as n (%) or mean±SD. Categorical variables were compared using the chi-square test or Fisher's exact test, and continuous variables using Student's t-test or the Mann–Whitney U test, as appropriate. p<0.05 was considered statistically significant.

In laboratory assessments, OGTT glucose values at 0, 1, and 2 hours and fasting glucose were significantly higher in the GDM group than in controls (all p<0.001). HbA1c levels were also higher in the GDM group (5.43±0.61 vs 5.11±0.38; p<0.001). Regarding lipid parameters, triglyceride levels were higher (232.29±102.62 vs 185.78±72.40 mg/dL; p<0.001) and HDL-cholesterol levels were lower (62.20±12.04 vs 69.47±13.93 mg/dL; p<0.001) in women with GDM. Creatinine was higher in the GDM group (0.56±0.11 vs 0.51±0.12 mg/dL; p<0.001), whereas most other biochemical parameters did not differ significantly between groups. Laboratory findings are shown in **Table 3**.

Table 3. Laboratory findings by group

Variable	Healthy (n=99) Mean±SD	GDM (n=100) Mean±SD	p
OGTT 0 h (mg/dL)	86.16±5.65	185.84±49.51	<0.001
OGTT 1 h (mg/dL)	104.24±25.11	177.40±30.84	<0.001
OGTT 2 h (mg/dL)	90.27±13.15	133.88±32.60	<0.001
Fasting glucose (mg/dL)	80.93±9.78	100.55±27.27	<0.001
Urea (mg/dL)	15.21±4.62	15.59±8.20	0.516
Creatinine (mg/dL)	0.51±0.12	0.56±0.11	<0.001
Triglycerides (mg/dL)	185.78±72.40	232.29±102.62	<0.001
Total cholesterol (mg/dL)	223.25±51.86	226.79±51.42	0.429
HDL (mg/dL)	69.47±13.93	62.20±12.04	<0.001
LDL (mg/dL)	119.11±42.77	133.94±61.23	0.076
HbA1c (%)	5.11±0.38	5.43±0.61	<0.001
Insulin (μU/mL)	14.62±14.09	17.13±17.37	0.111
CRP (mg/L)	1.53±9.11	1.07±1.51	<0.001
GGT (U/L)	14.78±8.70	13.28±4.40	0.026
ALT (U/L)	16.08±9.70	15.95±10.27	0.566
AST (U/L)	17.85±9.27	17.99±8.93	0.385

OGTT, oral glucose tolerance test; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, glycated hemoglobin; CRP, C-reactive protein; GGT, gamma-glutamyl transferase; ALT, alanine aminotransferase; AST, aspartate aminotransferase. Data are presented as mean±SD. Between-group comparisons were performed using Student's t-test or the Mann–Whitney U test, as appropriate. p<0.05 was considered statistically significant.

Receiver operating characteristic (ROC) analyses indicated AUC values ranging from 0.70 to 0.73, with the highest AUC observed for the TyG index (AUC=0.73). In multivariable logistic regression analyses, maternal age was positively associated with GDM in both models, and TyG (Model A) and TG/HDL-c (Model B) were independently associated with increased odds of GDM. The ROC performance of TG/HDL-c, TyG, and triglycerides for predicting GDM is provided in **Table 4**, and multivariable logistic regression results are presented in **Table 5**. ROC curves are illustrated in **Figure 1**.

Table 4. Diagnostic performance of TG/HDL-c, TyG, and triglycerides for predicting GDM

Variable	Healthy (n=99) Mean±SD	GDM (n=100) Mean±SD	AUC (95% CI)	p (AUC≠0.5)	Cut-off	Sensitivity	Specificity	Youden J	PPV	NPV
TG/HDL-c	2.80±1.29	3.92±2.12	0.71 (0.64–0.78)	<0.001	3.044	0.64	0.64	0.28	64.2%	63.8%
TyG	3.84±0.18	4.02±0.21	0.73 (0.66–0.80)	<0.001	3.937	0.67	0.67	0.34	67.2%	66.8%
Triglycerides (mg/dL)	185.78±72.40	232.29±102.62	0.70 (0.63–0.77)	<0.001	198.5	0.64	0.64	0.28	64.2%	63.8%

ROC analysis was used to report AUC (area under the curve) with 95% confidence intervals (CIs). The optimal cut-off value was selected by maximizing the Youden index (J = sensitivity + specificity – 1). PPV/NPV were calculated based on the study-sample prevalence of GDM (100/199=50.3%). Index definitions: TG/HDL-c = triglycerides/HDL; TyG = ln TG(mg/dL)×fastingglucose(mg/dL)/2TG (mg/dL) × fasting glucose (mg/dL) / 2TG(mg/dL)×fastingglucose(mg/dL)/2.

Table 5. Factors associated with GDM in multivariable logistic regression analysis				
Variable	Model A (TyG) OR (95% CI)	p	Model B (TG/HDL-c) OR (95% CI)	p
Age (per 1-year increase)	1.08 (1.02–1.14)	0.006	1.07 (1.01–1.13)	0.012
Parity (per 1-unit increase)	1.26 (1.01–1.58)	0.041	1.22 (0.98–1.52)	0.072
Gestational week at sampling (per 1-week increase)	0.90 (0.82–0.99)	0.030	0.91 (0.83–1.00)	0.048
TyG (per 0.1-unit increase)	2.05 (1.45–2.90)	<0.001	—	—
TG/HDL-c (per 1-unit increase)	—	—	1.52 (1.24–1.87)	<0.001

Model A: Nagelkerke R^2=0.28; Hosmer–Lemeshow p=0.44; model AUC=0.79. Model B: Nagelkerke R^2=0.24; Hosmer–Lemeshow p=0.51; model AUC=0.77. The dependent variable was GDM (yes/no). Results are presented as odds ratios (ORs) with 95% CIs.

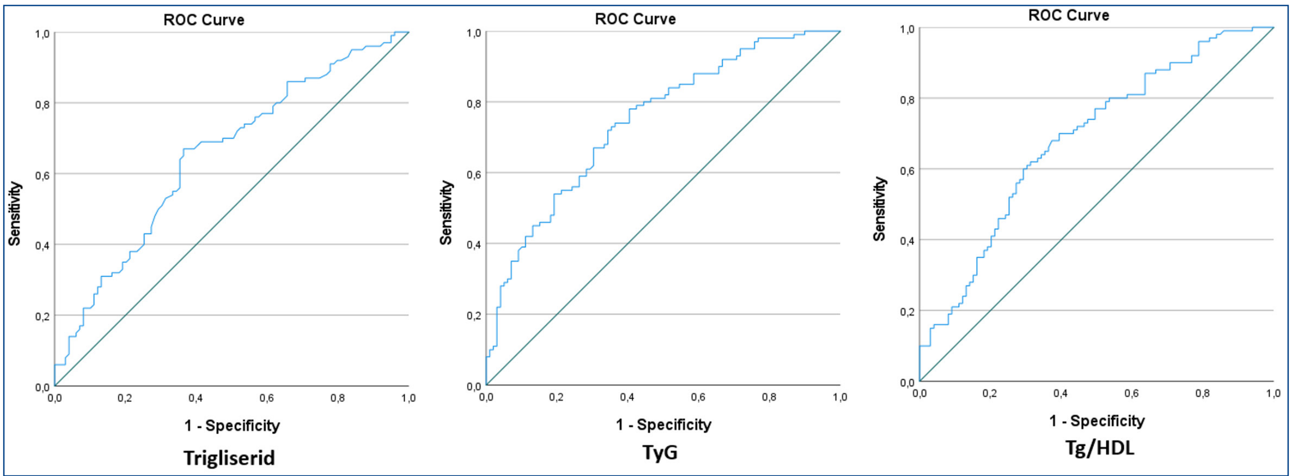

Figure 1. Receiver operating characteristic (ROC) curves for the TyG index, TG/HDL-c ratio, and triglycerides in predicting gestational diabetes mellitus.

DISCUSSION

In this sample, both the TyG index and the TG/HDL-c ratio were significantly higher in the GDM group, and each remained an independent predictor in multivariable models. The AUC range of 0.70–0.73 in ROC analyses (with the highest AUC for TyG at 0.73) indicates moderate discriminative ability. These findings suggest that, rather than being stand-alone diagnostic tests, these markers may serve as complementary tools for risk stratification and early screening. This interpretation is consistent with the current clinical paradigm in which GDM screening remains OGTT-based and clinical decisions are guided by established diagnostic thresholds.

The TyG index is a practical surrogate that aims to capture insulin resistance (IR) without direct insulin measurement by integrating fasting triglycerides and fasting glucose. Its conceptual basis derives from early studies demonstrating that the product/transformation of triglyceride and glucose values correlates reasonably well with reference methods such as the euglycemic–hyperinsulinemic clamp (5, 9). In addition, accurate reporting of the TyG formula is essential, and the literature includes publications emphasizing correction and standardization of TyG calculation and reporting (10).

The relevance of TyG to GDM has been supported by meta-analyses synthesizing large samples. For example, a meta-analysis by Song et al. reported that TyG (measured pre-pregnancy or in the first trimester) was independently associated with increased GDM risk, while also noting heterogeneity attributable to differences in measurement timing and population characteristics (11). Similarly, a meta-analysis published in Endocrine Connections by Liu et al. highlighted the association between TyG and GDM development, particularly in Asian populations, and underscored its predictive potential (12). The TyG AUC of 0.73 observed in this study is broadly aligned with the moderate performance summarized in these meta-analyses. However, variability in AUC estimates across studies may reflect differences in sampling (e.g., referral-based or higher-risk populations), gestational timing of measurements, and diagnostic criteria.

Evidence from prospective cohorts further suggests that TyG may be useful for early risk identification. In a prospective cohort published in Lipids in Health and Disease (<14 weeks), higher TyG was associated with an increased risk of subsequent GDM, with an AUC of approximately 0.64; notably, combining TyG with age and pre-pregnancy BMI improved discrimination (13). Likewise, a large nationwide cohort from Korea reported a positive association between pre-pregnancy TyG and subsequent GDM risk (14). Additional cohort studies have also linked first-trimester TyG with GDM and, in some reports, with outcomes such as large-for-gestational-age infants (15). Conversely, some studies in certain populations (e.g., Latin American cohorts) have suggested that the incremental predictive contribution of TyG may be limited, potentially reflecting ethnic differences in metabolic distributions and baseline risk profiles (16).

In this cohort, the optimal TyG cut-off was 3.937, which differs from higher thresholds frequently reported elsewhere (e.g., in the ~7–9 range). This discrepancy may relate to differences in calculation and reporting conventions (e.g., logarithmic base, constants, and unit transformations) as well as population-specific metabolic characteristics. Accordingly, population-specific calibration and external validation are required before clinically actionable thresholds can be recommended (10,13).

The TG/HDL-c ratio integrates elevated triglycerides and reduced HDL-cholesterol into a single metric that reflects IR and an atherogenic dyslipidemia pattern. Prior clinical and epidemiological studies have demonstrated associations between TG/HDL-c and IR (13). Moreover, the logarithmic form of this ratio, the atherogenic index of plasma (AIP = log[TG/HDL-c]), has been widely referenced in the literature, particularly in the work of Dobiásová (17,18).

In pregnancy, prospective cohort analyses indicate that TG/HDL-c in the first trimester can predict subsequent GDM. For instance, You et al., in a secondary analysis of prospective cohort data, reported that higher TG/HDL-c was significantly associated with increased GDM risk in multivariable models (8). Similarly, Ma et al., in an analysis comparing four IR surrogates, found that both TyG and TG/HDL-c showed meaningful AUC values for GDM prediction, with TyG performing slightly better (TyG AUC≈0.69 vs TG/HDL-c AUC≈0.66) (7). In the present study, TG/HDL-c demonstrated an AUC of 0.71 and remained independently associated with GDM (OR=1.52), consistent with the direction of these findings and supporting TG/HDL-c as a readily available risk indicator.

Physiologically, pregnancy is characterized by dynamic changes in lipid metabolism; with rising estrogen levels and progressive IR, hypertriglyceridemia becomes more pronounced in the second half of pregnancy and is often interpreted as an adaptive response to fetoplacental energy demands (19). In GDM, these physiological changes are frequently described as exaggerated, with a more pronounced atherogenic lipid pattern. The higher triglycerides and lower HDL observed in the GDM group are consistent with large meta-analytic evidence. In a comprehensive meta-analysis including 292 studies, Hu et al. reported that adverse lipid profiles in early-to-mid pregnancy were associated with GDM (20). A meta-analysis by Ryckman et al. likewise identified significant associations between pregnancy lipid levels and GDM (21). More recent cohort studies evaluating the dynamic evolution of lipid levels and lipid ratios across early-to-mid pregnancy have also described patterns linked to GDM risk (22). Mechanistically, these findings support the plausibility of TyG and TG/HDL-c: TyG may capture the glucose–triglyceride axis related to hepatic VLDL production and fatty acid flux in the context of IR, whereas TG/HDL-c summarizes an atherogenic dyslipidemia–IR phenotype (10,17,23).

The higher rates of cesarean delivery, NICU admission, difficult delivery, and increased birth weight in the GDM group are consistent with the impact of maternal hyperglycemia and fetal hyperinsulinemia on fetal growth and delivery complications. The HAPO study provided foundational evidence that maternal glycemia—even below conventional diagnostic thresholds—is gradedly associated with outcomes such as large-for-gestational-age/macrosomia, primary cesarean delivery, and neonatal complications (1). A more recent systematic review and meta-analysis likewise summarized the association of GDM with cesarean delivery, LGA/macrosomia, neonatal hypoglycemia, and NICU admission (24). Thus, beyond diagnostic considerations, readily measurable indices such as TyG and TG/HDL-c may also facilitate early identification of women at increased risk for adverse obstetric and neonatal outcomes, potentially enabling earlier lifestyle counseling and more intensive surveillance.

The positive association between maternal age and GDM observed in both models aligns with meta-analytic evidence identifying advanced maternal age as a strong risk factor for GDM. A systematic review and meta-analysis by Li et al. reported a significant increase in GDM risk with increasing maternal age (25). The borderline/significant association observed for parity in some analyses may be compatible with clinically observed risk accumulation; however, parity-related associations may be strongly modified by BMI, prior GDM, and family history, and should be interpreted accordingly.

The inverse association between gestational week at sampling and the odds of GDM is more likely to reflect timing and selection phenomena than a true biological protective effect. High-risk women may have been evaluated earlier, and earlier testing or referral patterns could have introduced referral bias. Prospective designs with standardized sampling windows and time-dependent modeling would be better suited to disentangle such timing effects (26).

Current guidelines continue to endorse OGTT as the cornerstone for GDM diagnosis (2,24). The moderate AUC values observed for TyG and TG/HDL-c support their potential role not as replacements for OGTT, but as low-cost, routine biochemistry–based tools that may help answer a practical clinical question at early visits:

"Who should be monitored more closely and considered for earlier OGTT?" Moreover, prospective cohorts have shown that combining indices with clinical variables (e.g., age, BMI) can improve AUC, reinforcing the rationale for developing multivariable prediction models (13). If such a model is pursued, reporting in accordance with TRIPOD guidelines and ensuring comprehensive evaluation of calibration, discrimination (AUC), clinical utility (e.g., decision-curve analysis), and—critically—external validation would be essential (27).

With respect to threshold selection, the Youden index is a commonly used approach; however, PPV and NPV are prevalence-dependent, and optimal cut-offs should be tailored to the intended clinical purpose (sensitivity-oriented early screening vs specificity-oriented selective OGTT) (28). For AUC comparisons across ROC curves, standard methods such as DeLong's test are appropriate, but cross-study comparisons should be interpreted in light of differences in population characteristics and sampling timing (29). Finally, while HOMA-IR (mmol/L × mU/L / 22.5) and the Friedewald formula are widely used in clinical research, the limitations of Friedewald estimation at higher triglyceride concentrations and the importance of unit consistency should be acknowledged in reporting (30). Overall, given the observational design, reporting should adhere to STROBE principles with clear discussion of selection bias, measurement timing, confounding, and generalizability (30).

CONCLUSION

The TyG index and TG/HDL-c ratio, derived from routine fasting laboratory tests, provide moderate discrimination for GDM and may support risk stratification as adjuncts to OGTT. Prospective external validation is warranted.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Tepecik Training and Research Hospital Non-interventional Research Ethics Committee (Date: 04/06/2024, Decision No: 2024/05-14)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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