

Section: Gynaecology

Original Research Article

FIRST-TRIMESTER TRIGLYCERIDE-GLUCOSE INDEX AS AN EARLY PREDICTOR OF GESTATIONAL DIABETES MELLITUS AND PREECLAMPSIA: A PROSPECTIVE COHORT STUDY

Prachi Singh¹, Abhinaya Gattamaneni²

¹Associate Professor, Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India.

²Junior Resident 3rs year, Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India.

ABSTRACT

Background: Gestational diabetes mellitus (GDM) and preeclampsia are major contributors to maternal and perinatal morbidity worldwide. The triglyceride–glucose (TyG) index has emerged as a simple surrogate marker of insulin resistance and may serve as an early predictor of adverse pregnancy outcomes. The objective of the study is to evaluate the association between first-trimester TyG index and the subsequent development of gestational diabetes mellitus and preeclampsia.

Materials and Methods: This prospective cohort study included 580 singleton pregnancies recruited between 11 and 13+6 weeks of gestation. Fasting plasma glucose and triglyceride levels were measured during the first trimester, and the TyG index was calculated as $\ln$ [fasting triglycerides (mg/dL) $\times$ fasting glucose (mg/dL)/2]. Participants were followed until delivery. GDM was diagnosed according to the International Association of Diabetes and Pregnancy Study Groups criteria, while preeclampsia was defined using American College of Obstetricians and Gynecologists guidelines. Multivariable logistic regression and receiver operating characteristic (ROC) curve analyses were performed.

Result: Among 580 participants, 84 (14.5%) developed GDM and 41 (7.1%) developed preeclampsia. Women who developed GDM and preeclampsia had significantly higher first-trimester TyG index values than unaffected women (both $p < 0.001$). After adjustment for confounding factors, the TyG index remained independently associated with GDM (adjusted OR: 3.84, 95% CI: 2.41–6.11, $p < 0.001$) and preeclampsia (adjusted OR: 3.27, 95% CI: 1.92–5.57, $p < 0.001$). ROC analysis demonstrated good predictive performance for GDM (AUC=0.823) and preeclampsia (AUC=0.801).

Conclusion: An elevated first-trimester TyG index is independently associated with an increased risk of gestational diabetes mellitus and preeclampsia. The TyG index may

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Corresponding Author:

Dr. Prachi Singh,

Email: singh.prachi.dr@gmail.com

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represent a simple, inexpensive, and readily available biomarker for early pregnancy risk stratification and targeted preventive interventions.

Keywords: Triglyceride–glucose index, TyG index, gestational diabetes mellitus, preeclampsia, insulin resistance, pregnancy complications, first trimester, prospective cohort study.

INTRODUCTION

Gestational diabetes mellitus (GDM) and preeclampsia (PE) are among the most common pregnancy complications and remain major contributors to maternal and perinatal morbidity worldwide. GDM affects approximately 5–20% of pregnancies depending on the population studied and is associated with adverse outcomes including macrosomia, cesarean delivery, neonatal hypoglycemia, and future cardiometabolic disease in both mother and offspring.^[1-3] Similarly, preeclampsia complicates 2–8% of pregnancies and is a leading cause of maternal mortality, fetal growth restriction, and preterm birth.^[4,5]

Accumulating evidence suggests that insulin resistance plays a pivotal role in the pathogenesis of both GDM and preeclampsia. Physiological insulin resistance increases during pregnancy; however, excessive insulin resistance in early gestation may predispose women to abnormal glucose metabolism, endothelial dysfunction, placental malperfusion, and hypertensive disorders of pregnancy.^[6,7]

Therefore, identifying simple and reliable biomarkers of insulin resistance during early pregnancy may facilitate timely risk stratification and preventive interventions.

The triglyceride–glucose (TyG) index, calculated from fasting triglyceride and fasting plasma glucose concentrations, has emerged as a practical surrogate marker of insulin resistance.^[8] Previous studies have demonstrated that the TyG index correlates closely with the hyperinsulinemic–euglycemic clamp technique and the homeostasis model assessment of insulin resistance (HOMA-IR), while requiring only routinely available laboratory parameters.^[9,10] Owing to its simplicity and cost-effectiveness, the TyG index has gained increasing attention as a potential predictor of metabolic and cardiovascular disorders.

Recent investigations have explored the association between first-trimester TyG index and adverse pregnancy outcomes. A large prospective birth cohort study reported that elevated first-trimester TyG levels were significantly associated with an increased risk of GDM and other pregnancy-related complications.^[6]

Similarly, Guo et al. demonstrated that the TyG index measured before 14 weeks of gestation independently predicted the subsequent development of GDM in a prospective cohort of pregnant women.^[7] Emerging evidence also indicates a positive association between elevated TyG index and the risk of preeclampsia, suggesting a common metabolic pathway linking insulin resistance and hypertensive disorders of pregnancy.^[8,11-13]

Despite these findings, data evaluating the predictive utility of the first-trimester TyG index for both GDM and preeclampsia simultaneously remain limited, particularly in diverse obstetric populations. Furthermore, the applicability of this inexpensive biomarker in routine antenatal screening requires further validation.

Therefore, the present prospective cohort study aimed to investigate the association between the first-trimester TyG index and the subsequent development of gestational diabetes mellitus and preeclampsia. We hypothesized that an elevated TyG index in early pregnancy would be associated with an increased risk of both complications and could serve as an accessible tool for early risk assessment.

MATERIALS AND METHODS

Study Design and Participants: This prospective cohort study was conducted at the Department of Obstetrics and Gynecology, from January 2025 to December 2025. Pregnant women with singleton pregnancies attending their first antenatal visit between 11 and 13+6 weeks

of gestation were consecutively recruited. Women with pre-existing diabetes mellitus, chronic hypertension, renal disease, autoimmune disorders, multiple pregnancies, or incomplete follow-up data were excluded. Written informed consent was obtained from all participants. The study protocol was approved by the Institutional Ethics Committee.

Data Collection and TyG Index Assessment: Maternal age, parity, body mass index (BMI), family history of diabetes mellitus, blood pressure, and relevant obstetric characteristics were recorded at enrollment. Following an overnight fast of 8–12 hours, venous blood samples were collected for estimation of fasting plasma glucose and triglyceride levels using standardized laboratory methods. The triglyceride–glucose (TyG) index was calculated using the following formula;^[14]

$$\text{TyG Index} = \ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$$

Participants were followed prospectively through pregnancy until delivery.

Outcome Measures: The primary outcomes were gestational diabetes mellitus (GDM) and preeclampsia. GDM was diagnosed between 24 and 28 weeks of gestation using a 75-g oral glucose tolerance test according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Preeclampsia was diagnosed according to the American College of Obstetricians and Gynecologists (ACOG) criteria as new-onset hypertension ($\geq 140/90$ mmHg) after 20 weeks of gestation with proteinuria and/or evidence of maternal organ dysfunction.

Statistical Analysis: Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), whereas categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. Multivariable logistic regression analysis

was used to determine the independent association between first-trimester TyG index and the development of GDM and preeclampsia after adjustment for potential confounders. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive accuracy of the TyG index and determine optimal cutoff values. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

A total of 612 pregnant women were screened during the study period. Thirty-two women were excluded owing to pre-existing diabetes mellitus ($n=9$), chronic hypertension ($n=7$), multiple gestation ($n=5$), and incomplete follow-up data ($n=11$). Consequently, 580 participants completed follow-up and were included in the final analysis.

[Table 1] compares baseline maternal characteristics between women who developed GDM and those who remained normoglycemic. Maternal age, BMI, family history of diabetes, blood pressure, and first-trimester TyG index were significantly higher among women who subsequently developed GDM (all $p<0.05$). These findings suggest that adverse metabolic profiles are already evident during early pregnancy in women at increased risk of developing gestational diabetes mellitus. [Table 2] presents baseline characteristics according to the development of preeclampsia. Women who developed preeclampsia had significantly higher maternal age, BMI, mean arterial pressure, previous history of preeclampsia, and TyG index compared with normotensive women. The results indicate a strong association between early-pregnancy metabolic dysfunction and the subsequent occurrence of hypertensive disorders of pregnancy.

[Table 3] summarizes the multivariable logistic regression analysis evaluating independent predictors of GDM and preeclampsia. After adjustment for potential confounders, the first-trimester TyG index remained a significant independent predictor of both outcomes. The magnitude of the adjusted odds ratios highlights the

substantial contribution of early insulin resistance to the development of adverse pregnancy complications. [Table 4] demonstrates the predictive performance of the first-trimester TyG index for GDM and preeclampsia using ROC curve analysis. The TyG index exhibited good discriminatory ability with clinically relevant sensitivity and specificity values for both outcomes. These findings support the potential utility of the TyG index as a simple and cost-effective screening biomarker during routine antenatal care.

[Table 5] illustrates the relationship between increasing TyG quartiles and the risk of adverse pregnancy outcomes. A progressive increase in the prevalence and adjusted risk of both GDM and preeclampsia was observed across quartiles. The presence of a clear dose-response pattern strengthens the evidence for an independent association between elevated TyG index and pregnancy-related metabolic and vascular complications.

[Figure 1] depicts the trend in mean fasting plasma glucose across increasing TyG

quintiles. A gradual and consistent rise in fasting glucose levels was observed with increasing TyG values. This positive trend demonstrates the close relationship between the TyG index and underlying disturbances in glucose metabolism during early pregnancy.

[Figure 2] presents the distribution of composite adverse pregnancy outcomes within the study population. Most women experienced uncomplicated pregnancies, whereas GDM represented the most frequent adverse outcome. The figure highlights the substantial contribution of metabolic complications to the overall burden of adverse pregnancy outcomes. [Figure 3] illustrates the variation in neonatal birth weight across maternal TyG quartiles. Mean birth weight increased progressively from the lowest to the highest TyG quartile. These findings suggest that maternal insulin resistance in early pregnancy may influence fetal growth and contribute to higher neonatal birth weight.

Table 1: Baseline Characteristics According to Development of Gestational Diabetes Mellitus

Variable	GDM (n=84)	No GDM (n=496)	p-value
Maternal age (years)	29.6 ± 4.1	27.5 ± 4.2	<0.001
BMI (kg/m ²)	27.4 ± 3.8	24.8 ± 3.5	<0.001
Nulliparity, n (%)	31 (36.9)	224 (45.2)	0.168
Family history of diabetes, n (%)	32 (38.1)	92 (18.5)	<0.001
Systolic BP (mmHg)	116.8 ± 8.5	113.9 ± 8.2	0.004
Diastolic BP (mmHg)	74.1 ± 6.3	71.8 ± 5.9	0.002
TyG index	8.71 ± 0.41	8.29 ± 0.37	<0.001

Table 2: Baseline Characteristics According to Development of Preeclampsia

Variable	PE (n=41)	No PE (n=539)	p-value
Maternal age (years)	30.2 ± 4.5	27.6 ± 4.2	<0.001
BMI (kg/m ²)	28.1 ± 3.9	25.0 ± 3.6	<0.001
Previous PE, n (%)	8 (19.5)	21 (3.9)	<0.001
Family history of hypertension, n (%)	14 (34.1)	91 (16.9)	0.005
Mean arterial pressure (mmHg)	87.9 ± 6.8	83.4 ± 6.1	<0.001
TyG index	8.79 ± 0.43	8.33 ± 0.38	<0.001

Table 3: Multivariable Logistic Regression Analysis

Variable	Adjusted OR	95% CI	p-value
Outcome: GDM			
TyG index	3.84	2.41–6.11	<0.001
Maternal age	1.08	1.03–1.14	0.002
BMI	1.12	1.06–1.19	<0.001
Family history of diabetes	2.01	1.18–3.42	0.010
Outcome: Preeclampsia			
TyG index	3.27	1.92–5.57	<0.001
Maternal age	1.07	1.01–1.14	0.028
BMI	1.10	1.03–1.18	0.005
Previous PE	4.92	2.01–12.03	<0.001

Table 4: Predictive Performance of First-Trimester TyG Index

Outcome	AUC	95% CI	Optimal Cut-off	Sensitivity (%)	Specificity (%)
GDM	0.823	0.779–0.867	8.48	80.9	72.8
Preeclampsia	0.801	0.736–0.866	8.55	78.0	71.6

Table 5: Risk of Adverse Outcomes Across TyG Quartiles

TyG Quartile	GDM n (%)	Adjusted OR (95% CI)	PE n (%)	Adjusted OR (95% CI)
Q1 (<8.05)	7 (4.8)	Reference	2 (1.4)	Reference
Q2 (8.05–8.29)	13 (9.0)	1.94 (0.76–4.91)	5 (3.4)	2.49 (0.48–12.84)
Q3 (8.30–8.54)	24 (16.6)	3.92 (1.68–9.15)	11 (7.6)	5.88 (1.29–26.78)
Q4 (>8.54)	40 (27.6)	7.54 (3.34–17.03)	23 (15.9)	12.14 (2.85–51.68)

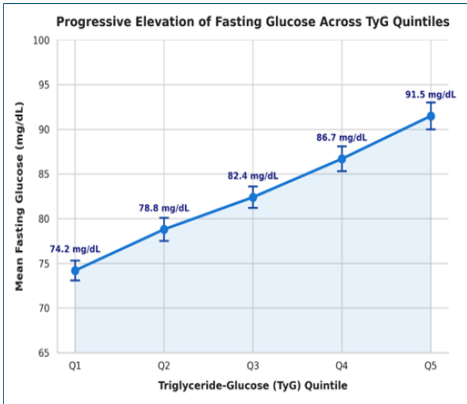


Figure 1: Mean Fasting Glucose Across TyG Quintiles

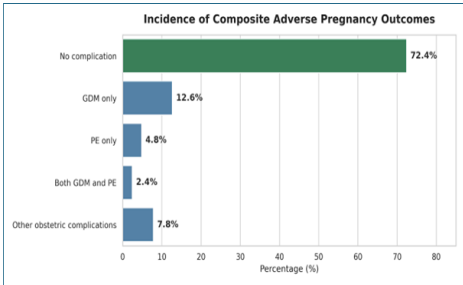


Figure 2: Incidence of Composite Adverse Pregnancy Outcome

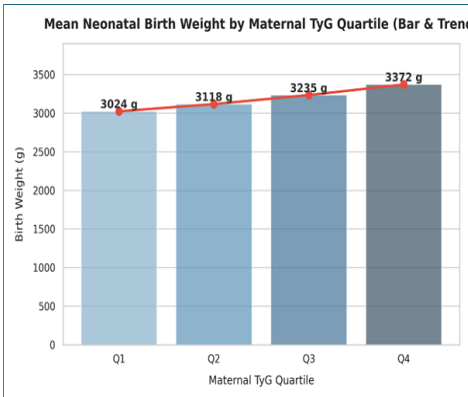


Figure 3: Mean Neonatal Birth Weight by Maternal TyG Quartile

DISCUSSION

The present prospective cohort study demonstrated that an elevated first-trimester triglyceride–glucose (TyG) index was significantly associated with the subsequent development of both gestational diabetes mellitus (GDM) and preeclampsia. Women who developed either complication exhibited significantly higher early-pregnancy TyG values, and the association remained significant after adjustment for maternal age, body mass index, parity, and family history. Furthermore, the TyG index showed good discriminatory performance for predicting GDM and preeclampsia, suggesting its potential utility as an inexpensive and readily available biomarker for early risk stratification.

Our findings regarding GDM are consistent with accumulating evidence supporting the TyG index as a surrogate marker of insulin resistance during pregnancy. Guo et al,^[1] reported that an elevated TyG index in early pregnancy independently predicted the subsequent development of GDM in a prospective cohort study. Similarly, Mo et al,^[2] observed a significant positive association between increasing TyG levels and incident GDM among Korean pregnant women. In a cross-sectional analysis of U.S. pregnant women, Zeng et al,^[3] also demonstrated that higher TyG index values were associated with a greater prevalence of GDM. The consistency between our findings and these studies across different populations suggests that the predictive value of the TyG index may be broadly applicable across ethnic and geographic settings.

The biological plausibility of these findings is supported by the established relationship between insulin resistance and glucose

dysregulation during pregnancy.^[15] The TyG index reflects both fasting glycemia and triglyceride metabolism, two key metabolic pathways involved in insulin resistance. Hufnagel et al,^[16] highlighted the central role of maternal hyperinsulinemia and metabolic dysfunction in adverse cardiometabolic programming during pregnancy. Consequently, elevated TyG values in early gestation may represent an early manifestation of metabolic impairment preceding the clinical diagnosis of GDM.

A notable finding of the present study was the significant association between the TyG index and preeclampsia. Women who subsequently developed preeclampsia demonstrated significantly higher first-trimester TyG values, and increasing TyG quartiles were associated with progressively greater risks of disease occurrence. These observations are in agreement with the study by Bulbul and Yakistir,^[5] who reported that first-trimester TyG index and lipid parameters were significant predictors of late-onset preeclampsia. Likewise, Song et al,^[4] found that elevated first-trimester TyG levels were associated with a spectrum of adverse pregnancy outcomes, including hypertensive disorders of pregnancy.

The mechanisms linking TyG index and preeclampsia are likely multifactorial. Insulin resistance promotes endothelial dysfunction, oxidative stress, chronic low-grade inflammation, and impaired placental vascular remodeling, all of which are recognized contributors to preeclampsia pathogenesis. Our findings therefore support the concept that metabolic dysfunction may precede and contribute to the development of placental and vascular abnormalities later in pregnancy.

Several studies have investigated alternative first-trimester predictors of preeclampsia, including inflammatory biomarkers, angiogenic factors, mean arterial pressure, pregnancy-associated plasma protein-A (PAPP-A), and uterine artery Doppler parameters. İpek et al,^[7] reported promising predictive utility of inflammatory indices, whereas Beyazit et al,^[8] demonstrated the usefulness of PAPP-A and mean arterial pressure for predicting early-onset disease. Similarly, Bonacina et al,^[9] emphasized the

role of uterine artery Doppler assessment following first-trimester screening. More recently, Liang et al,^[6] developed a machine-learning model incorporating multiple predictors to improve risk estimation. Compared with these approaches, the TyG index offers the advantage of requiring only routine fasting glucose and triglyceride measurements, making it particularly attractive for implementation in low-resource settings.

The ROC analysis in our study demonstrated good predictive performance of the TyG index for both GDM and preeclampsia. These findings align with the systematic review and meta-analysis by Liu et al,^[15] which concluded that the TyG index possesses significant diagnostic and predictive potential for GDM. Although the predictive accuracy observed in our study was not intended to replace established screening algorithms, it suggests that incorporation of the TyG index into existing first-trimester prediction models may improve risk stratification and facilitate targeted preventive interventions.

Current recommendations from the American Diabetes Association,^[10] the International Association of Diabetes and Pregnancy Study Groups,^[11] and FIGO,^[12] emphasize the importance of early identification of women at increased risk for pregnancy-related complications. Our findings support the integration of simple metabolic indicators into early antenatal assessment. Furthermore, the growing emphasis on maternal metabolic health throughout pregnancy, as highlighted by Price et al,^[13] reinforces the need for accessible biomarkers capable of identifying high-risk women before clinical manifestations become evident.

The present study contributes to the existing literature by simultaneously evaluating the predictive role of the first-trimester TyG index for both GDM and preeclampsia within the same prospective cohort. While previous investigations have largely focused on either GDM,^[1–3,14,15] or preeclampsia,^[5] separately, our findings suggest that the TyG index may represent a common metabolic marker underlying multiple adverse pregnancy outcomes. This observation supports the concept of shared

pathophysiological pathways linking insulin resistance, endothelial dysfunction, and placental maladaptation.

Limitations: Several limitations should be acknowledged. First, this was a single-center study, which may limit the generalizability of the findings to other populations. Second, insulin resistance was not directly measured using gold-standard methods such as the hyperinsulinemic-euglycemic clamp or HOMA-IR. Third, residual confounding related to dietary factors, physical activity, and socioeconomic variables cannot be completely excluded. Finally, external validation in larger multicenter cohorts is required before the TyG index can be routinely incorporated into clinical prediction algorithms.

CONCLUSION

An elevated first-trimester triglyceride-glucose index was independently associated with an increased risk of both gestational diabetes mellitus and preeclampsia. The TyG index demonstrated good predictive performance and may serve as a simple, inexpensive, and widely accessible biomarker for early pregnancy risk assessment. Incorporation of the TyG index into first-trimester screening strategies may facilitate earlier identification of high-risk women and enable timely preventive interventions aimed at improving maternal and perinatal outcomes.

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