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Association between triglyceride-glucose index in early pregnancy and risk of preeclampsia: a multicenter retrospective cohort study

Qiong Li[1†], Chenyang Zhao[1†], Miao Liu[1], Meng Li[2], Ying Zhang[2*] and Chaoyan Yue[2*]

Abstract

Background Previous evidence has indicated that insulin resistance may be an early pathological state of preeclampsia (PE). As a novel biomarker, the triglyceride glucose (TyG) index can reflect the level of insulin resistance in the body. The present study aimed to investigate the association between the TyG index and risk of PE.

Methods This study included 41,694 singleton pregnant women, comprising 2,308 PE patients and 39,386 healthy controls from three tertiary hospitals from January 2019 to June 2024. Datas were retrospectively collected via medical record review. The TyG index was measured before 20 weeks of gestation, and participants were grouped via the TyG index quartiles. The primary outcome was PE, and the secondary outcomes were preterm birth and low birth weight (LBW). Multivariable logistic regression was used to calculate the odds ratios (ORs) for the TyG index quartiles compared to the lowest quartile for the primary and secondary outcomes. Subgroup analyses were conducted to evaluate the effect of age, body mass index (BMI), parity and TyG test week on these associations. The predictive efficacy of the TyG index for PE was assessed using receiver operating characteristic (ROC) curve analysis.

Results After adjusting for confounders, compared to TyG index Q1, a higher TyG index was positively associated with PE (TyG index Q3 OR = 1.23, 95% confidence interval (CI): 1.06–1.43, $P = 0.0067$; TyG index Q4 OR = 1.31, 95% CI: 1.11–1.53, $P = 0.0011$) and preterm birth (TyG index Q4 OR = 1.18, 95% CI: 1.01–1.37, $P = 0.0376$), negatively associated with LBW (TyG index Q3 OR = 0.84, 95% CI: 0.74–0.97, $P = 0.0147$). In Model I, a significant association was observed between higher TyG quartiles and preterm birth ($P = 0.0472$ for Q3 and $P = 0.0000$ for Q4), but this association was not significant in Model II after adjusting for confounders. Subgroup analyses revealed that age, pre-pregnancy BMI, parity and test week did not influence these associations (interaction $P > 0.05$). The area under the ROC curve (AUC) for the predictive model was 0.596 (95% CI: 0.584–0.608), with a sensitivity of 65.4% and a specificity of 49.6%.

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Conclusion The present findings suggested that the TyG index associated with a high risk of PE. Clinical evaluation incorporating the TyG index during early pregnancy may help in screening for patients at high risk of PE.

Keywords Triglyceride glucose index, Preeclampsia, Early pregnancy, Insulin resistance

Background

Preeclampsia (PE) is a severe complication of pregnancy with an incidence of 5 ~ 8% [1]. PE is clinically characterized by the emergence of hypertension and proteinuria following the 20th week of gestation [2]. This condition poses significant risks to both maternal and neonatal health, potentially resulting in adverse outcomes such as preterm delivery, restricted fetal growth, neonatal asphyxia, placental abruption, and maternal death [3]. Timely detection and appropriate management of PE are critical to ensuring the health and safety of both pregnant individuals and their offspring. The exact etiology of PE remains unclear, and researchers have been working to identify maternal blood biomarkers that can predict the onset of PE, such as soluble fms-like tyrosine kinase 1 (sFlt-1) [4] and placental growth factor (PlGF) [5]. However, the effectiveness of these biomarkers still needs validation. Despite advances in obstetric care, there remains a significant clinical gap in the early prediction and prevention of PE.

Insulin resistance (IR), as part of metabolic syndrome, is reported to be one of the early pathological states in hypertensive disorders of pregnancy [6]. This pathological state may exist even before the clinical symptoms of PE appear after 20 weeks of gestation [7]. While physiological IR in normal pregnancy is beneficial for fetal nutrition supply and growth [8], excessive IR can have harmful effects on both maternal and fetal health, including an elevated risk of PE [7]. In recent years, the triglyceride-glucose (TyG) index, derived from fasting plasma levels of triglycerides and glucose, has gained recognition as a robust marker for detecting IR and related metabolic abnormalities. Due to its ease of measurement, the TyG index has become a popular topic and is widely applicable in clinical practice. Researches have demonstrated that the TyG index is linked to an increased risk of gestational diabetes mellitus [9, 10], cardiovascular disease [11, 12], and metabolic syndrome [13]. Nevertheless, there is limited literature exploring the association between the TyG index and PE. A recent retrospective analysis has shown that among pregnant women with normal glucose tolerance, a higher TyG index correlates with an elevated risk of PE. Furthermore, the integration of the TyG index with glycated hemoglobin levels demonstrates potential predictive significance for identifying PE [14]. Another retrospective study has also reported similar results [15]. However, a recent prospective cohort study revealed that no significant association was found between the TyG index and the risk of PE [10]. Previous studies on the TyG index and PE have some limitations, such as small sample size [10, 15], insufficient control of confounding factors [15], and the acquisition of the TyG index in the mid-to-late stages of pregnancy after the diagnosis of PE [14]. These limitations reduce the generalizability of the findings and may fail to capture early pathological changes that occur before clinical symptoms manifest. By focusing on early pregnancy TyG measurements and the stratification of TyG index based on quartiles, the present study aimed to overcome these limitations and provide a more comprehensive understanding of the role of IR in the development of PE.

This study leverages large-scale, multicenter clinical data to examine the relationship between the TyG index during early pregnancy and the risk of PE. Multivariable logistic regression analysis was performed to evaluate the utility of the TyG index in predicting PE risk while accounting for various potential confounding factors. Subgroup analyses were conducted, stratified by maternal age, body mass index (BMI), parity and TyG index test week, to assess whether these variables modify the association between the TyG index and PE. The predictive efficacy of the TyG index for PE was assessed using receiver operating characteristic (ROC) curve analysis. Unlike prior studies, this investigation utilized the TyG index measured before 20 weeks of gestation and analyzed its association with PE after stratifying the TyG index, offering novel perspectives on PE prediction. The present findings may assist clinical practitioners in offering early monitoring, preventive measures, and treatment strategies for pregnant individuals with elevated TyG index values in early pregnancy, potentially improving overall pregnancy outcomes.

Methods

Design and participants

This retrospective cohort analysis encompassed women with singleton pregnancies who visited Obstetrics and Gynecology Hospital of Fudan University, Huangpu Branch (Center 1) and Yangpu Branch (Center 2) and the First People's Hospital of Chenzhou (Center 3) from January 2019 to June 2024. Clinical data and assessments were collected and evaluated during the participants' first visit which was defined as the initial prenatal visit, typically occurring between 12 and 20 weeks of gestation. Variability in gestational weeks at TyG testing was due to differences in when women initiated prenatal care. To address this variability, a sensitivity analysis restricting the sample to those tested within a narrower gestational

window (< 14 weeks and 14 ~ 20 weeks) was conducted to ensure consistency in the timing of measurements.

All participants delivered at the hospital where they received care, with all clinical and laboratory data being retrieved from the Hospital Information System (HIS) and Laboratory Information System (LIS). The inclusion criteria for this study were as follows: (1) age ≥ 20 years; (2) singleton pregnancy; and (3) visits and deliveries at one of the participating centers. The following criteria were applied for exclusion: (1) first triglyceride and fasting glucose measurements taken after 20 weeks of gestation; (2) twin or multiple pregnancies; (3) pre-existing hypertension; (4) comorbidities such as type 1 diabetes mellitus or type 2 diabetes mellitus, hyperlipidemia or metabolic syndrome diagnosed before pregnancy; kidney disease, heart diseases, or other internal or surgical diseases; and (5) incomplete clinical or laboratory data. Ultimately, 41,694 pregnant women were included in the present study, including 2,308 women with PE and 39,386 women without PE. The study process diagram is depicted in Fig. 1.

The study received ethical approval from the Medical Ethics Committees of the Obstetrics and Gynecology Hospital of Fudan University and the First People's

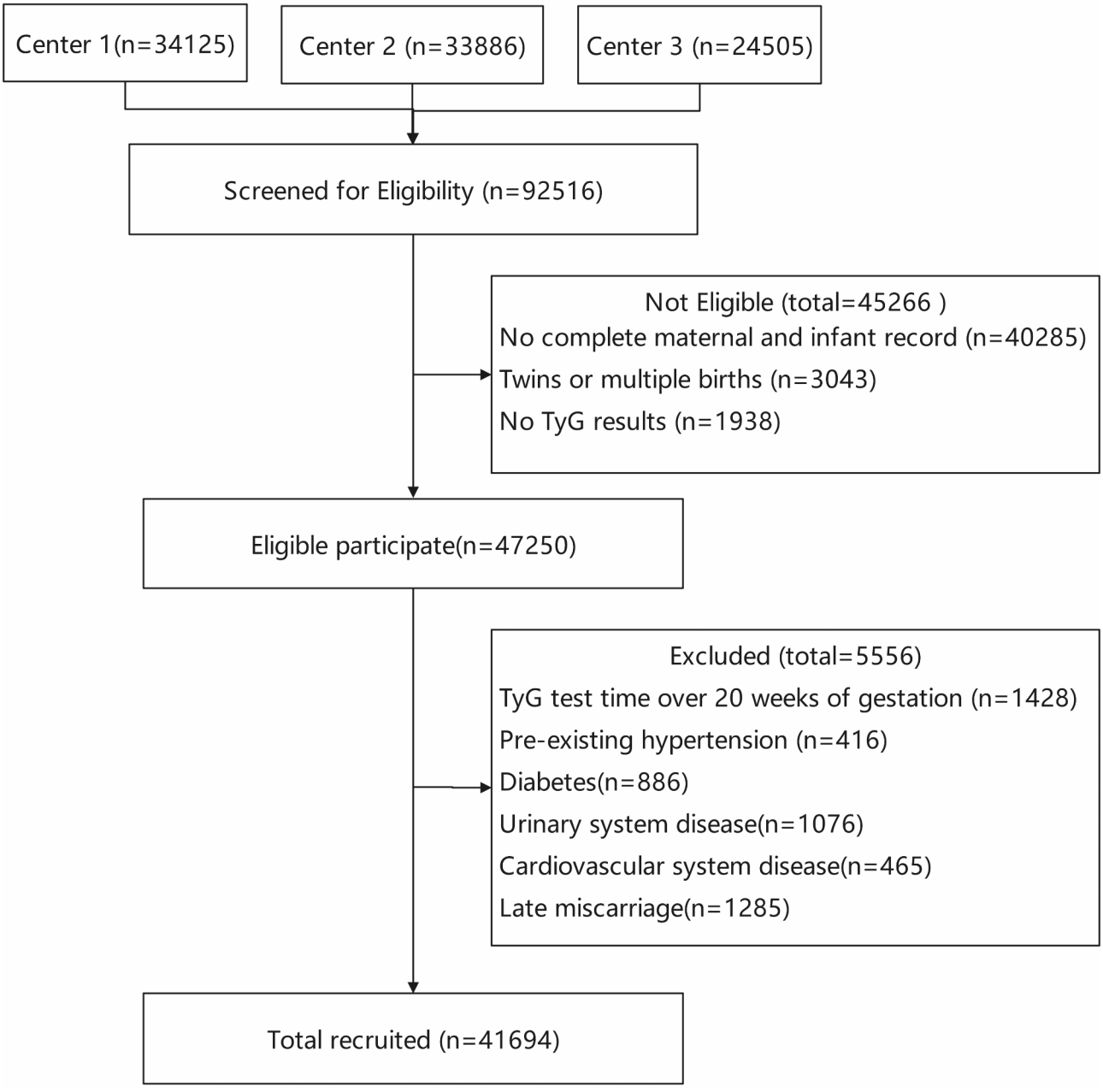

Fig. 1 Flowchart illustrating the participant selection process

Hospital of Chenzhou. It was conducted in accordance with the principles set forth in the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013). All participants provided broad informed consent upon their first visit.

Variables and measurements

The TyG index served as the exposure variable of interest. Clinical and laboratory data was gathered from pregnant women prior to 20 weeks of gestation. Venous blood samples were obtained after a minimum fasting period of 8 h, and the subsequent laboratory parameters were analyzed using an automated hematology analyzer: triglycerides (mg/dL), total cholesterol (TC, mg/dL), fasting plasma glucose (FPG, mg/dL), alanine transaminase (ALT, U/L), uric acid (UA, μmol/L), and creatinine (μmol/L). The TyG index was computed using the formula: TyG = ln[triglycerides (mg/dL) × fasting glucose (mg/dL) / 2]. Participants were categorized into quartiles based on their TyG index values.

The selection of confounders was guided by a combination of literature review and univariate analysis. Variables that showed significant associations ($P < 0.001$) in univariate analyses were adjusted in Model II. All included confounders had variance inflation factors (VIF) less than 5, indicating no significant multicollinearity issues. Confounding variables included age, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), aspirin use, antihypertensive medication use, history of hypertension, tobacco use, alcohol consumption, in vitro fertilization (IVF), ALT, UA, creatinine, TC, FPG, test week, adverse pregnancy history, and educational level. BMI was computed by dividing pre-pregnancy weight (kg) by the square of height (m^2) and was classified into two categories: underweight or normal (< 24 kg/m^2) and overweight (≥ 24 kg/m^2). Age was categorized as normal (< 35 years) and advanced (≥ 35 years). BMI and age cutoffs were determined based on clinical relevance and World Health Organization (WHO) classifications [16]. Adverse pregnancy history was defined as prior PE, miscarriage, or other significant obstetric complications. Education levels were categorized into postgraduate, bachelor's degree or above, college diploma, high school, and less than junior high school.

Outcomes and measurements

The main outcome assessed in this study was PE. The diagnostic criteria for PE were based on the 2020 guidelines established by the American College of Obstetricians and Gynecologists (ACOG) [17]. PE was diagnosed when a patient with normal blood pressure prior to pregnancy developed systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg after 20 weeks of gestation, along with proteinuria (+ or higher) or a 24-hour urine protein level exceeding 300 mg. PE was also diagnosed if any of the following characteristics were present without proteinuria: platelet count < 100×10^9/L, liver function impairment (serum transaminases > 2 times the upper limit of normal), renal function impairment (serum creatinine > 1.1 mg/dL or > 2 times the upper limit of normal), pulmonary edema, new-onset headache unexplained by other causes, or visual disturbances.

The secondary outcomes included low birth weight (LBW) and preterm birth. LBW was defined by the WHO as a birth weight of less than 2500 g [16], while preterm birth was characterized as delivery occurring before 37 weeks of gestation, in accordance with WHO guidelines [18]. For women with regular menstrual cycles, fetal gestational age was determined based on the first day of the last menstrual period. In cases of irregular menstrual cycles, early pregnancy ultrasound was utilized to estimate gestational age.

Statistical analysis

Baseline characteristics of the study population were described according to the TyG index quartiles (Q1-Q4). Continuous variables were expressed as means ± standard deviations, while categorical variables were reported as percentages. To assess differences in covariates among participants, continuous variables were compared using weighted t-tests, and categorical variables were evaluated using weighted chi-square tests.

Multivariable logistic regression analyses was applied to investigate the association between the TyG index and the primary and secondary pregnancy outcomes. The findings were reported as odds ratios (ORs) accompanied by 95% confidence intervals (CIs). The lowest TyG index quartile (TyG Q1) served as the reference group. Model I did not adjust for any covariates, while Model II adjusted for age, BMI, SBP, DBP, aspirin use, antihypertensive medication use, history of hypertension, tobacco use, alcohol consumption, parity, IVF, ALT, UA, creatinine, TC, test week, adverse pregnancy history, and education levels.

To further understand the relationship between the TyG index and the risk of PE, subgroup analyses were conducted by stratifying participants according to age (< 35 years or ≥ 35 years), BMI (< 24 kg/m^2 or ≥ 24 kg/m^2), parity (primiparous or multiparous), and test week (< 14 weeks or 14 ~ 20 weeks) to determine the impact of these variables on the outcomes. Likelihood ratio tests were used to assess interactions between subgroups.

Additionally, to evaluate the predictive performance of the TyG index for PE, ROC curves were plotted. Predictive models were established with PE as the dependent variable and the TyG index, maternal SBP and DBP as independent variables. The area under the curve (AUC)

was calculated. We not only assessed the predictive ability of the TyG index alone for PE but also compared the predictive performance of the "SBP and DBP alone" versus the "combination of the TyG index with SBP and DBP" for PE.

The statistical analyses were conducted using IBM SPSS (version 21.0, IBM, Armonk, NY) and R statistical packages (R Foundation, version 4.4.1). A significance level of $P<0.05$ was employed for determining statistical significance. The retrospective cohort study followed the guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and the Reporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) checklists [19, 20].

Results

Baseline characteristics

Table 1 summarizes the baseline characteristics of the study participants grouped by the TyG index quartiles. According to strict inclusion and exclusion criteria, 41,694 singleton pregnant participants were enrolled in the present study, including 2,308 PE patients and 39,386 healthy pregnant women. The mean TyG level and its standard deviation (SD) were measured as 7.86 ± 0.18, 8.24 ± 0.08, 8.51 ± 0.08, and 8.96 ± 0.24 for quartile 1, quartile 2, quartile 3 and quartile 4 respectively. As shown in Table 1, cases with any missing clinical data were excluded, accounting for the difference in the sample sizes for other variables from the total number of cases in the primary outcome analysis. Overall, the number of participants in each group was balanced. Differences between groups were statistically significant, except for LBW, hypertension history, and tobacco use. The incidence of PE across different TyG index groups ranged from 3.81 to 8.14%. The risk of PE increased with higher TyG index values. Similarly, maternal age, BMI, SBP, DBP, IVF, preterm birth, tobacco, alcohol consumption, adverse pregnancy history, triglycerides, TC, UA, ALT, and FPG all increased with higher TyG index values ($P<0.001$).

Association between the TyG index and PE

As shown in Table 2, the TyG index was stratified into quartiles, with the lowest quartile (TyG index Q1) serving as the reference. Multivariate regression analysis results revealed that, in Model I, compared to TyG index Q1, participants of TyG index Q3 and TyG index Q4 had a higher risk of PE and preterm birth (OR > 1) and a lower risk of LBW (OR < 1). However, in Model II, compared to TyG index Q1, only participants in TyG index Q3 and TyG index Q4 showed a significant increased risk of PE by 23% (95% CI: 1.06–1.43, $P=0.0067$) and 31% (95% CI: 1.11–1.53, $P=0.0011$) respectively. In Model II, compared to TyG index Q1, participants in TyG index Q4 showed a significant increased risk of preterm birth by 18% (95% CI: 1.01–1.37, $P=0.0376$). Conversely, participants in TyG index Q3 had a 16% reduced risk of LBW (95% CI: 0.74–0.97, $P=0.0147$). Figure 2 illustrates the relationship between TyG index quartiles and PE after adjusting for confounding factors.

Subgroup analyses

To better explore the association between the TyG index and PE risk, subgroup analyses were conducted. As detailed in Table 3, subgroup analyses based on maternal age, BMI, parity, and test week demonstrated consistent association between TyG index quartiles and PE across all strata. After multivariable adjustment for potential confounders, interaction tests indicated no significant effect modification by these variables on the TyG index-PE association (all interaction $P>0.05$). Figure 3 visually depicts the stratified dose-response relationships across the analyzed subgroups.

ROC curve analyses of TyG index in predicting PE

As shown in Fig. 4, the results of the ROC curve analysis indicated that when the TyG index was used alone as a diagnostic marker for PE, the AUC was 0.596 (95% CI: 0.584–0.608), with a sensitivity of 65.4% and a specificity of 49.6%. When the TyG index was combined with SBP and DBP, the AUC increased to 0.736 (95% CI: 0.725–0.747), surpassing the AUC of 0.729 (95% CI: 0.718–0.740) obtained from using SBP and DBP. The sensitivity decreased from 69.3 to 63.3%, while the specificity increased from 64.6 to 72.4%.

Discussion

PE represents a serious pregnancy-related complication that carries considerable risks for both maternal and neonatal health, potentially leading to severe adverse outcomes. Previous studies have shown that physiological IR in normal pregnancy is beneficial for fetal nutrition supply and growth [8] but that excessive IR can lead to adverse maternal and fetal outcomes, such as PE [7]. As a part of metabolic syndrome, IR may be an early pathological state in hypertensive disorders of pregnancy [6]. This pathological state exists before clinical symptoms of PE appear. Nevertheless, while some patients with IR progress to develop PE, others do not, indicating that the exact relationship and mechanism by which IR impacts PE remain unclear. There is a lack of large-scale clinical studies to further validate these associations. The present study analyzed clinical and laboratory data from three large tertiary hospitals to explore the relationship between the TyG index and PE, uncovering a significant positive correlation between the TyG index and PE risk. Even after accounting for all potential confounding

Table 1 Baseline characteristics of participants

Characteristic	TyG Q1 *n* = 10,399	TyG Q2 *n* = 10,440	TyG Q3 *n* = 10,427	TyG Q4 *n* = 10,428	*P*-value
Age (years)	30.68 ± 3.68	30.99 ± 3.92	31.48 ± 4.12	32.22 ± 4.44	< 0.001
BMI (kg/m^2)	20.62 ± 2.55	21.05 ± 2.77	21.56 ± 3.09	22.63 ± 3.45	< 0.001
SBP (mmHg)	113.14 ± 11.69	114.19 ± 11.90	115.35 ± 12.41	117.96 ± 13.34	< 0.001
DBP (mmHg)	67.75 ± 8.94	69.12 ± 9.30	70.30 ± 9.62	71.83 ± 10.11	< 0.001
TyG Test week	9.82 ± 1.90	10.62 ± 2.21	11.40 ± 2.83	13.43 ± 5.51	< 0.001
TyG	7.86 ± 0.18	8.24 ± 0.08	8.51 ± 0.08	8.96 ± 0.24	< 0.001
Alanine transaminase (U/L)	15.88 ± 11.37	17.47 ± 14.22	19.05 ± 17.22	20.11 ± 19.23	< 0.001
Uric acid (μmol/L)	203.87 ± 41.93	210.25 ± 43.52	216.82 ± 46.22	230.92 ± 51.74	< 0.001
Creatinine (U/L)	43.44 ± 5.91	43.69 ± 5.98	43.51 ± 6.00	43.04 ± 6.21	< 0.001
Total cholesterol (mg/dL)	4.16 ± 0.65	4.44 ± 0.68	4.68 ± 0.75	5.05 ± 0.94	< 0.001
Triglycerides (mg/dL)	0.76 ± 0.14	1.07 ± 0.12	1.40 ± 0.16	2.18 ± 0.59	< 0.001
Fast blood glucose (mg/dL)	4.38 ± 0.35	4.46 ± 0.36	4.52 ± 0.39	4.65 ± 0.62	< 0.001
Preeclampsia (%)					< 0.001
No	10,003 (96.19%)	10,004 (95.82%)	9800 (93.99%)	9579 (91.86%)	
Yes	396 (3.81%)	436 (4.18%)	627 (6.01%)	849 (8.14%)	
Preterm birth (%)					< 0.001
No	9834 (95.55%)	9856 (95.16%)	9768 (94.26%)	9613 (92.74%)	
Yes	458 (4.45%)	501 (4.84%)	595 (5.74%)	752 (7.26%)	
Low birth weight (%)					0.078
No	9799 (94.27%)	9877 (94.63%)	9900 (94.97%)	9899 (94.95%)	
Yes	596 (5.73%)	561 (5.37%)	524 (5.03%)	527 (5.05%)	
Aspirin (%)					< 0.001
No	9999 (98.88%)	9788 (98.54%)	9482 (98.24%)	8856 (96.89%)	
Yes	113 (1.12%)	145 (1.46%)	170 (1.76%)	284 (3.11%)	
Depressor (%)					< 0.001
No	10,096 (99.96%)	9908 (99.92%)	9611 (99.75%)	9046 (99.44%)	
Yes	4 (0.04%)	8 (0.08%)	24 (0.25%)	51 (0.56%)	
Hypertension history (%)					0.053
No	8882 (85.41%)	8963 (85.86%)	8999 (86.34%)	8868 (85.07%)	
Yes	1517 (14.59%)	1476 (14.14%)	1424 (13.66%)	1556 (14.93%)	
Tobacco (%)					0.614
0	9914 (98.18%)	9746 (98.32%)	9454 (98.21%)	8887 (98.06%)	
Yes	184 (1.82%)	167 (1.68%)	172 (1.79%)	176 (1.94%)	
Alcohol (%)					< 0.001
No	9617 (95.24%)	9496 (95.79%)	9269 (96.29%)	8788 (96.97%)	
Yes	481 (4.76%)	417 (4.21%)	357 (3.71%)	275 (3.03%)	
Parity (%)					< 0.001
Primipara	8482 (83.71%)	8073 (78.77%)	7395 (72.19%)	6243 (60.95%)	
Multipara	1651 (16.29%)	2176 (21.23%)	2849 (27.81%)	3999 (39.05%)	
IVF (%)					< 0.001
No	9797 (97.02%)	9456 (95.39%)	8995 (93.44%)	8205 (90.53%)	
Yes	301 (2.98%)	457 (4.61%)	631 (6.56%)	858 (9.47%)	
Adverse pregnancy history (%)					< 0.001
No	10,060 (96.74%)	10,048 (96.25%)	9947 (95.40%)	9653 (92.57%)	
Yes	339 (3.26%)	392 (3.75%)	480 (4.60%)	775 (7.43%)	
Education (%)					< 0.001
Postgraduate	2765 (27.67%)	2359 (23.95%)	1921 (20.00%)	1495 (16.27%)	
Bachelor's degree or above	4797 (48.01%)	4699 (47.70%)	4529 (47.16%)	3897 (42.40%)	
College diploma	1630 (16.31%)	1933 (19.62%)	2078 (21.64%)	2326 (25.31%)	

Table 1 (continued)

Characteristic	TyG Q1 *n* = 10,399	TyG Q2 *n* = 10,440	TyG Q3 *n* = 10,427	TyG Q4 *n* = 10,428	*P*-value
High school	204 (2.04%)	263 (2.67%)	316 (3.29%)	461 (5.02%)	
Less than junior high school	595 (5.96%)	597 (6.06%)	760 (7.91%)	1011 (11.00%)	

Q1 < 8.09, Q2 = 8.09 ~ 8.67, Q3 = 8.67 ~ 9.75, Q4 > 9.75

Mean ± SD for continuous variables: *P* value was calculated by weighted linear regression model

% for categorical variables: *P* value was calculated by weighted chi-square test

TyG, triglyceride-glucose; Q, quartile; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; IVF, in vitro fertilization

Table 2 Risk of primary and secondary outcomes

Outcome	No. of PE (%)	Model I		Model II	
		OR (95% CI)	*P*-value	Adjust OR (95% CI)	*P*-value
Primary Outcome					
Preeclampsia					
TyG Q1	396 (3.81%)	Reference		Reference	
TyG Q2	436 (4.18%)	1.10 (0.96, 1.26)	0.1748	0.96 (0.83, 1.13)	0.6525
TyG Q3	627 (6.01%)	1.62 (1.42, 1.84)	< 0.0001	1.23 (1.06, 1.43)	0.0067
TyG Q4	849 (8.14%)	2.24 (1.98, 2.53)	< 0.0001	1.31 (1.11, 1.53)	0.0011
Secondary Outcomes					
Preterm birth					
TyG Q1	458 (4.45%)	Reference		Reference	
TyG Q2	501 (4.84%)	1.09 (0.96. 1.24)	0.1862	1.02 (0.89. 1.18)	0.7328
TyG Q3	595 (5.74%)	1.31 (1.15, 1.48)	< 0.0001	1.08 (0.94.1.24)	0.3003
TyG Q4	752 (7.26%)	1.68 (1.49. 1.89)	< 0.0001	1.18 (1.01, 1.37)	0.0376
Low birth weight					
TyG Q1	596 (5.73%)	Reference		Reference	
TyG Q2	561 (5.37%)	0.93 (0.83, 1.05)	0.2581	0.94 (0.83, 1.07)	0.3722
TyG Q3	524 (5.03%)	0.87 (0.77, 0.98)	0.0239	0.84 (0.74, 0.97)	0.0147
TyG Q4	527 (5.05%)	0.88 (0.78, 0.99)	0.0302	0.87 (0.75, 1.02)	0.0774

Model I: No covariates were adjusted

Model II: Adjusted for age, pre-pregnancy BMI, systolic blood pressure; diastolic blood pressure, aspirin, depressor, hypertension history, tobacco, alcohol, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education levels

PE, preeclampsia; TyG, triglyceride-glucose index; Q, quartile; BMI, body mass index; IVF, in vitro fertilization; OR, odds ratio; CI, confidence interval

variables, a higher TyG index was consistently and significantly linked to an increased risk of PE. Specifically, women in the highest TyG index quartile demonstrated a 31% greater risk of developing PE compared to those in the lowest quartile. A similar positive association was observed between the highest TyG index quartile and preterm birth. Conversely, an inverse relationship was noted between the TyG index and LBW. Subgroup analyses further revealed that maternal age, BMI, and parity did not significantly modify these associations, underscoring the robustness and reliability of the findings. The AUC for the predictive model was 0.596, with a sensitivity of 65.4% and a specificity of 49.6%.

The TyG index, a biochemical marker that integrates the effects of blood triglycerides and glucose, has been shown to exhibit high sensitivity in detecting IR in individuals [21]. While prior researches have predominantly concentrated on its association with cardiovascular diseases [22, 23], fewer studies have investigated its relationship with hypertensive disorders during pregnancy. Notably, Pan et al. demonstrated that the TyG index is strongly associated with the development of gestational hypertension [24]. A recent retrospective study has discovered that in women with normal glucose tolerance during pregnancy, an elevated TyG index is associated with an increased risk of PE, and the combination of the TyG index and glycated hemoglobin levels has predictive value for PE [14]. Another study highlighted the TyG index's potential predictive value for PE, preterm birth, and macrosomia, indicating its possible utility as a surrogate marker for these adverse pregnancy outcomes [15]. However, a recent prospective cohort study revealed that no significant association was found between the TyG index and the risk of PE [10]. The recent study had a relatively small sample size, with only 41 cases of PE. In contrast, this study included a large sample size of 41,694 participants comprising 2,308 PE patients and 39,386 healthy controls from multiple centers. This substantial increase in sample size allowed us to overcome potential biases and provided more robust and reliable

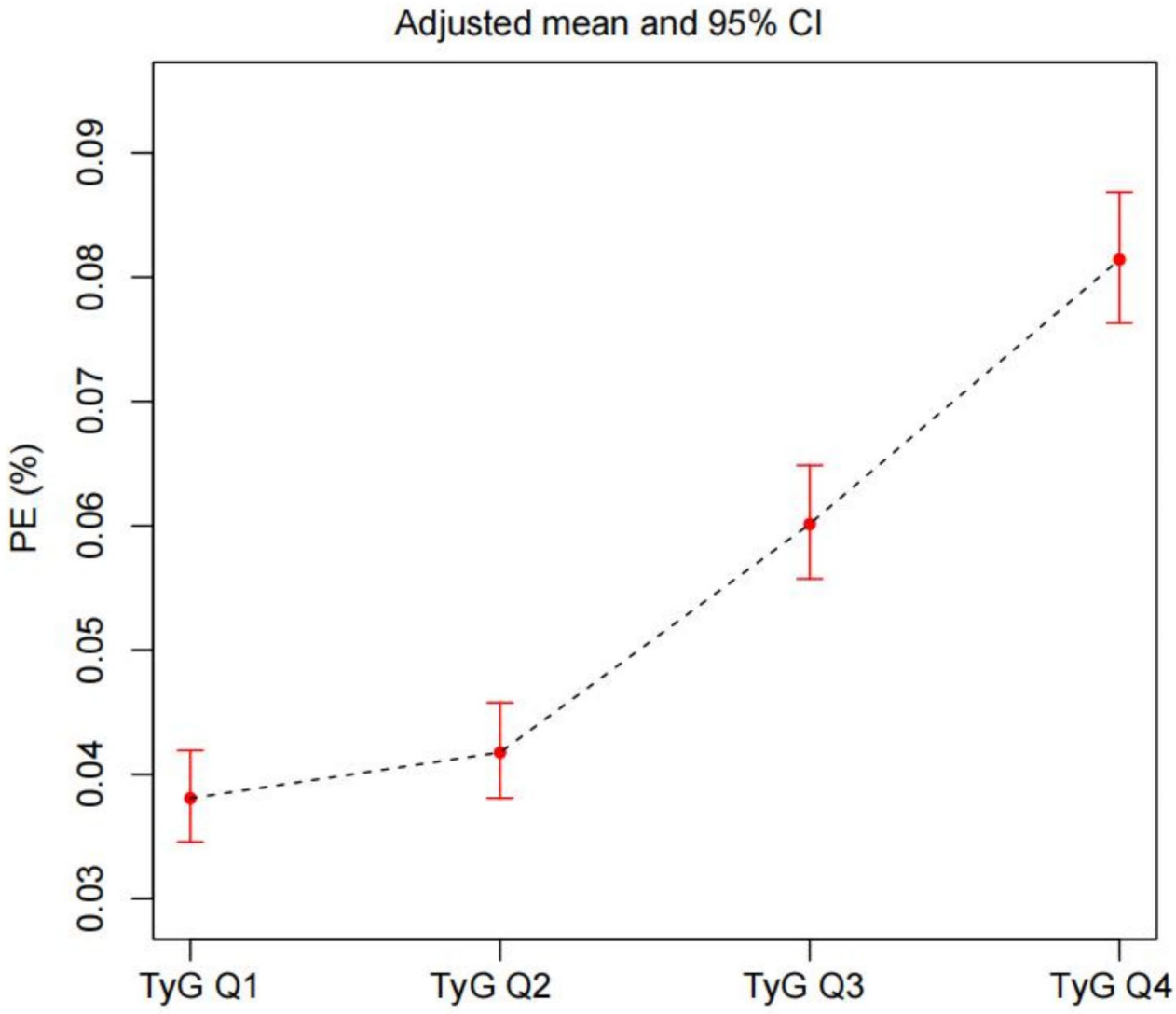

Fig. 2 The overall relationship between the TyG index and the risk of PE based on TyG index quartiles. Age, pre-pregnancy BMI, parity, SBP, DBP, aspirin, depressor, hypertension history, tobacco, alcohol, IVF, ALT, UA, creatinine, TC, FPG, test week, adverse pregnancy history and education levels were adjusted

results. Secondly, in this study, PE is the primary outcome of interest. Detailed analysis was conducted based on the TyG index quartiles to assess its association with PE. After adjusting for over ten confounding factors, this study showed that higher TyG indices were significantly associated with an increased risk of PE compared to lower TyG indices. Furthermore, this study employed sophisticated statistical methods, including multivariable logistic regression and subgroup analyses, to control for various confounders. By using these rigorous analytical techniques, we aimed to provide a clearer picture of the relationship between the TyG index and PE risk.

After accounting for confounding factors, the present study identified that only the third quartile (Q3) of the TyG index was associated with a reduced risk of LBW (OR = 0.84, 95% CI: 0.74–0.97, $P = 0.0147$). In contrast, no significant association was observed for the second (Q2) and fourth (Q4) quartiles. The relationship between the TyG index and neonatal birth weight has been inconsistent across previous studies [15]. While one study reported a positive correlation between the TyG index and macrosomia [25], another investigation found that the TyG index served as an independent risk factor for LBW [24]. Moreover, a protective effect against LBW was observed in Q3 compared to Q1, suggesting that moderate IR, as represented by mid-range TyG values, may be beneficial for fetal growth, potentially through mechanisms such as optimized glucose and lipid metabolism [8, 26]. In contrast, excessive IR, which was observed in higher TyG quartiles, could impair placental function

Table 3 Subgroup analysis of the TyG index and preeclampsia

Subgroup	OR (95% CI)	*P*-value	*P*-value for interaction	Adjusted OR (95% CI)	*P*-value	*P*-value for interaction
Age (years)			0.7802			0.9164
< 35						
TyG Q1	Reference			Reference		
TyG Q2	1.06 (0.91, 1.23)	0.4641		0.94 (0.80, 1.12)	0.4882	
TyG Q3	1.55 (1.35, 1.79)	< 0.0001		1.20 (1.02, 1.42)	0.0275	
TyG Q4	2.13 (1.86, 2.44)	< 0.0001		1.29 (1.08, 1.55)	0.0044	
≥ 35						
TyG Q1	Reference			Reference		
TyG Q2	1.29 (0.91, 1.84)	0.1580		1.10 (0.73, 1.65)	0.6538	
TyG Q3	1.79 (1.29, 2.47)	0.0004		1.35 (0.92, 1.97)	0.1277	
TyG Q4	2.38 (1.76, 3.24)	< 0.0001		1.38 (0.94, 2.03)	0.1013	
BMI (kg/m^2)			0.6142			0.5301
< 24						
TyG Q1	Reference			Reference		
TyG Q2	1.03 (0.88, 1.21)	0.7054		0.91 (0.76, 1.08)	0.2689	
TyG Q3	1.51 (1.29, 1.75)	< 0.0001		1.21 (1.02, 1.43)	0.0307	
TyG Q4	1.77 (1.52, 2.06)	< 0.0001		1.18 (0.98, 1.43)	0.0887	
≥ 24						
TyG Q1	Reference			Reference		
TyG Q2	1.14 (0.85, 1.52)	0.3929		1.15 (0.82, 1.62)	0.4252	
TyG Q3	1.38 (1.05, 1.81)	0.0209		1.28 (0.92, 1.77)	0.1395	
TyG Q4	1.79 (1.39, 2.31)	< 0.0001		1.53 (1.11, 2.11)	0.0092	
Parity			0.8933			0.9932
Primipara						
TyG Q1	Reference			Reference		
TyG Q2	1.14 (0.98, 1.32)	0.0876		0.96 (0.81, 1.13)	0.5964	
TyG Q3	1.74 (1.52, 2.01)	< 0.0001		1.21 (1.03, 1.43)	0.0179	
TyG Q4	2.63 (2.29, 3.01)	< 0.0001		1.29 (1.08, 1.53)	0.0041	
Multipara						
TyG Q1	Reference			Reference		
TyG Q2	1.21 (0.79, 1.84)	0.3830		0.98 (0.61, 1.57)	0.9208	
TyG Q3	1.82 (1.24, 2.66)	0.0021		1.29 (0.83, 2.00)	0.2595	
TyG Q4	2.51 (1.76, 3.59)	< 0.0001		1.35 (0.87, 2.09)	0.1823	
Test week			0.9676			0.8142
<14						
TyG Q1	Reference			Reference		
TyG Q2	1.10 (0.96, 1.27)	0.1738		0.95 (0.81, 1.11)	0.5151	
TyG Q3	1.64 (1.44, 1.87)	< 0.0001		1.21 (1.04, 1.41)	0.0159	
TyG Q4	2.31 (2.04, 2.63)	< 0.0001		1.24 (1.06, 1.47)	0.0087	
14 ~ 20						
TyG Q1	Reference			Reference		
TyG Q2	1.37 (0.50, 3.76)	0.5352		1.51 (0.48, 4.74)	0.4807	
TyG Q3	1.80 (0.70, 4.61)	0.2218		1.36 (0.46, 4.06)	0.5817	
TyG Q4	3.00 (1.21, 7.45)	0.0180		1.85 (0.63, 5.42)	0.2607	

Non-adjusted model had no adjustments;

Model of age was adjusted for BMI, systolic blood pressure, diastolic blood pressure, aspirin, depressor, hypertension history, tobacco, alcohol, parity, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education levels

Model of BMI was adjusted for: age, systolic blood pressure, diastolic blood pressure, aspirin, depressor, hypertension history, tobacco, alcohol, parity, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education levels

Models of parity and test week were adjusted for age, BMI, systolic blood pressure, diastolic blood pressure, aspirin, depressor, hypertension history, tobacco, alcohol, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education levels

PE, preeclampsia; TyG, triglyceride-glucose index; Q, quartile; BMI, body mass index; IVF, in vitro fertilization; OR, odds ratio; CI, confidence interval

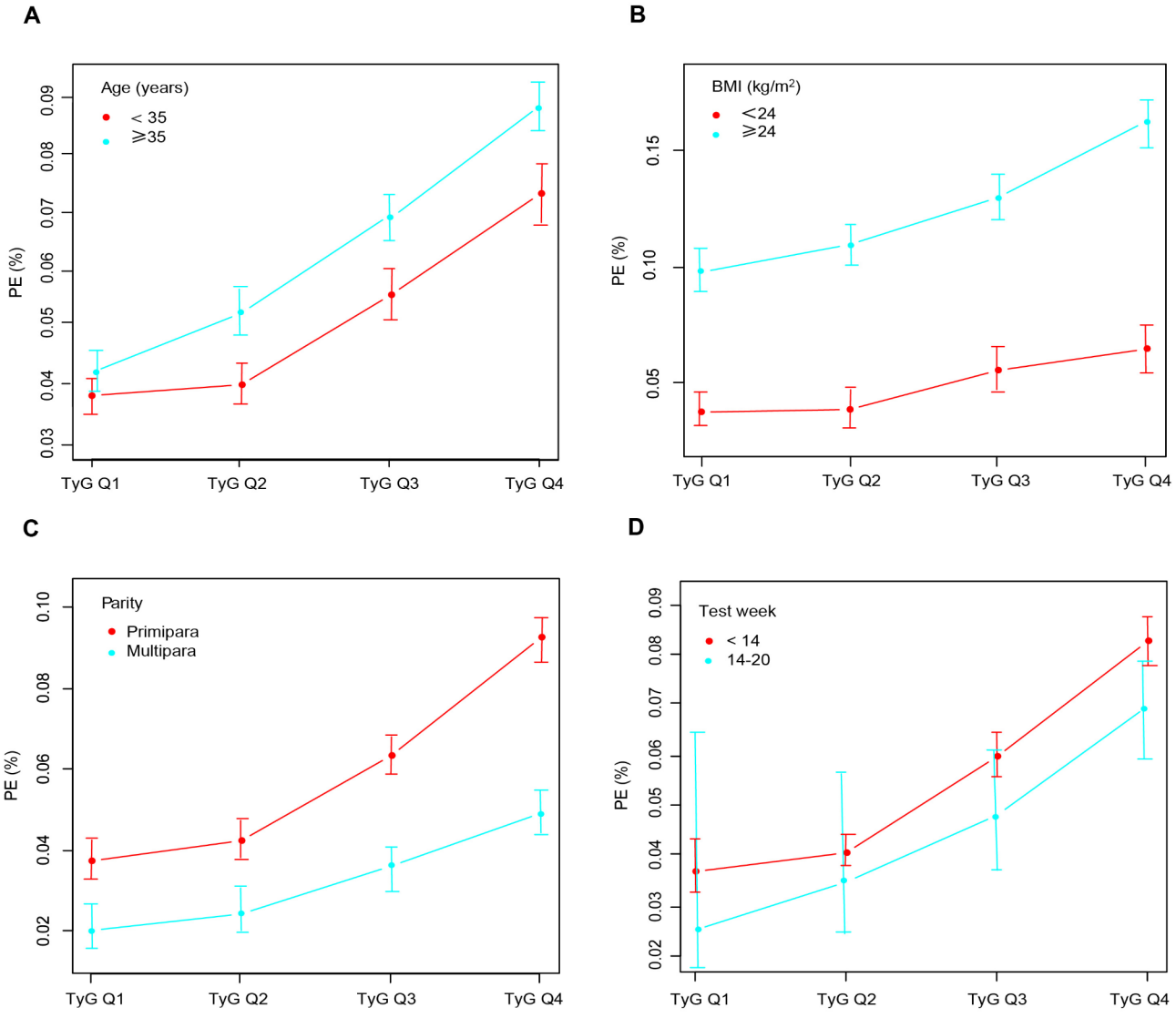

Fig. 3 Stratified fitting curves among different subgroups. The results of the subgroup analyses were adjusted for age (**A**), pre-pregnancy BMI (**B**), parity (**C**), and test week (**D**). PE, preeclampsia; TyG, triglyceride-glucose index; Q, quartile; CI, confidence interval

and fetal nutrition, leading to adverse outcomes, such as LBW or preterm birth [27, 28]. This study suggested that different levels of the TyG index may result in contrasting outcomes and should be interpreted objectively in clinical settings when estimating neonatal birth weight.

The results of the ROC curve analysis showed that when the TyG index was used alone as a diagnostic marker for PE, the AUC was 0.596, indicating that it may not be sufficient as an independent diagnostic criterion for PE. This result may be attributed to the highly heterogeneous nature of PE, where IR is just one of many contributing factors, alongside other factors such as endothelial dysfunction and inflammatory responses. Although the AUC of the TyG index did not reach the conventional diagnostic threshold of 0.7, we believe it still holds potential clinical significance. The further analysis revealed that when the TyG index was combined with SBP and DBP alone, the AUC increased to 0.736, surpassing the AUC of 0.729 obtained from using SBP and DBP alone. Therefore, we suggest that the TyG index can serve as an auxiliary screening tool, and when used in conjunction with traditional indicators such as blood pressure, it can enhance the accuracy of risk stratification for PE.

The underlying mechanisms through which the TyG index impacts the development and progression of PE may be linked to the IR it reflects. IR is a marker of hyperglycemia, dyslipidemia, and obesity. In pregnant women, hyperglycemia, dyslipidemia, and obesity are risk factors for PE [29, 30]. IR may contribute to vascular endothelial cell injury by stimulating the release of nitric oxide (NO), which in turn can worsen endothelial dysfunction [31, 32]. Inflammatory mediators, such as tumor

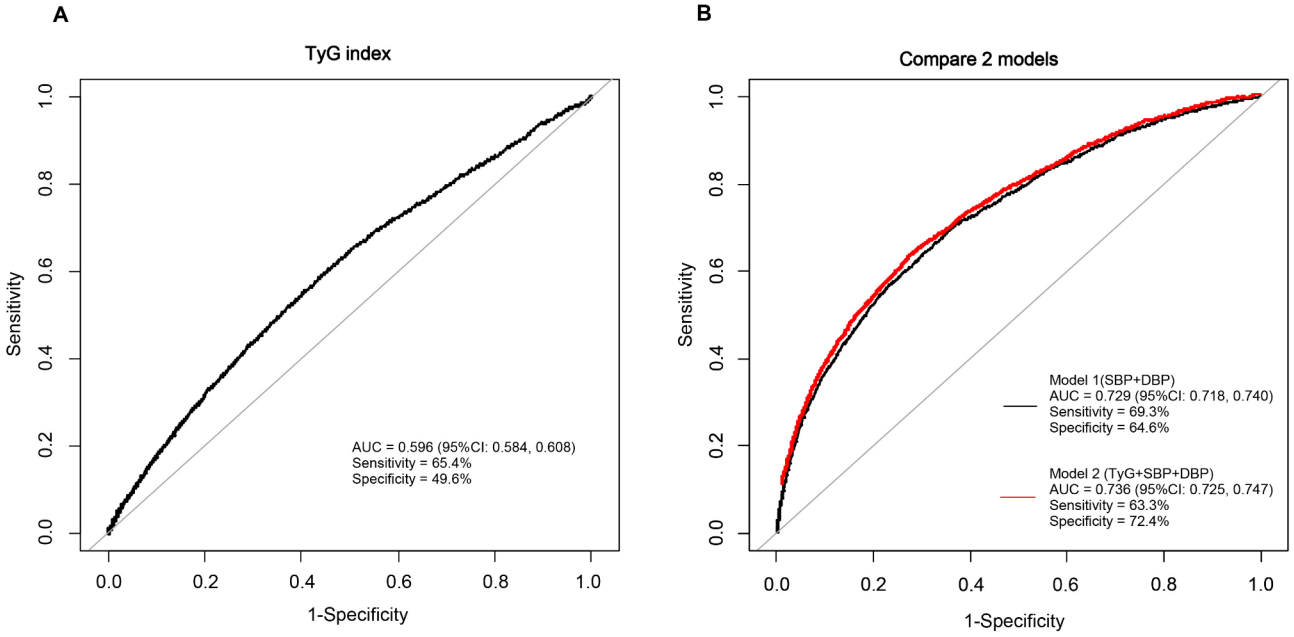

Fig. 4 (**A**) ROC curve of TyG index for predicting the development of PE. (**B**) ROC curve of TyG index combined with SBP and DBP compared to maternal SBP and DBP alone for predicting the development of PE. TyG, triglyceride-glucose index; PE, preeclampsia; ROC, receiver operating characteristic; AUC, the area under the curve; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure

necrosis factor-alpha (TNF-α) and leptin, are secreted in increased amounts in the adipose tissues and placentas of individuals with IR [33]. Both endothelial dysfunction and inflammation can promote the development of PE. Moreover, excessive IR during pregnancy can lead to lipid metabolism disorders, increased oxidative stress, and placental dysfunction, ultimately contributing to the onset and progression of PE [34, 35]. Recent investigations have demonstrated that excessive IR activates the sympathetic nervous system, leading to increased vascular resistance and enhanced distal glomerular sodium reabsorption. These effects ultimately contribute to endothelial dysfunction and the subsequent development of gestational hypertension or PE [24].

The present study revealed the association between the TyG index in early pregnancy and the risk of PE. The stratified fitting curves suggested that TyG levels before 14 weeks have a more significant association with PE compared to the test week between 14 and 20 weeks. Thus, TyG levels during early pregnancy may have greater clinical significance. Clinical monitoring based on specific TyG quartiles in early pregnancy may facilitate risk stratification for PE, enabling appropriate preventive measures such as lifestyle changes and the use of low-dose aspirin for high-risk patients. These interventions are anticipated to lower the risk of adverse pregnancy outcomes for both mothers and their infants.

Strengths and limitations

A key strength of this study was the utilization of large-scale, multicenter clinical and laboratory data, which improved the generalizability of the findings. Additionally, the robustness of the results was further confirmed through multiple sensitivity analyses and subgroup evaluations. Additionally, the exposure factor in the present study was based on routine laboratory measurements available in most hospitals, making it easily accessible and clinically applicable. The TyG index provides a more accurate reflection of maternal IR, offering significant clinical value for the prediction and management of PE. Nevertheless, the current study was not without its limitations. First, while the present findings provide important insights, the retrospective design may have introduced biases such as selection bias and recall bias. Prospective studies are needed to validate the present findings and establish causality more definitively. Second, the present study only analyzed the association between the TyG index in early pregnancy and PE, without considering TyG changes in mid and late pregnancy. This omission may have introduced bias, given that TyG values may fluctuate throughout pregnancy. Future studies should standardize TyG measurement times to better evaluate its predictive value. Third, the study excluded individuals diagnosed with type I diabetes mellitus, type II diabetes mellitus, or metabolic syndrome prior to pregnancy. While this exclusion aimed to minimize the potential influence of metabolic factors on the TyG index, it may have limited the generalizability of the findings.

Lastly, although adjustments were made for numerous potential confounders based on prior research and clinical expertise, certain unmeasured factors, such as dietary patterns and physical activity levels, were not fully evaluated within the current cohort, potentially introducing residual confounding.

Conclusion

The present study demonstrated that a higher TyG index in early pregnancy is independently associated with an elevated risk of PE, irrespective of maternal age, BMI, TyG index test week prior to 20 weeks, and parity. As a straightforward and easily accessible marker of IR, the TyG index may hold promise as a supplementary tool for early risk stratification of PE. Nevertheless, prospective studies are warranted to confirm its predictive value and establish optimal clinical thresholds for its application.

Abbreviations

PE	Preeclampsia
TyG	Triglyceride-glucose
IR	Insulin resistance
Q	Quartile
BMI	Body mass index
ROC	Receiver operating characteristic
AUC	Area under the curve
IVF	In vitro fertilization
LBW	Low birth weight
OR	Odds ratio
CI	Confidence interval
TC	Total cholesterol
FPG	Fasting plasma glucose
ALT	Alanine transaminase
UA	Uric acid
SBP	Systolic blood pressure
DBP	Diastolic blood pressure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02556-z.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

This research has been conducted using data collected from the Obstetrics and Gynecology Hospital affiliated with Fudan University and the First People's Hospital of Chenzhou. All authors thank the physicians, nurses, and scientific staff of the two hospitals.

Author contributions

QL and CYZ contributed to the study design, collected and analyzed the data, interpreted the results, wrote and reviewed the manuscript. ML and ML contributed data. YZ contributed data, interpreted the results and reviewed the manuscript. CYY contributed to the study design, collected and analyzed the data, interpreted the results, and reviewed the manuscript. All authors edited, reviewed, and approved the final version of the manuscript.

Funding

This study was supported by the Xiangnan College-Level Research Project (2024XJ162) and the Pregnancy Cohort of the Scientific Collaboration between the First People's Hospital of Chenzhou and the Tenth People's Hospital of Shanghai (2023-09).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committees of Fudan University Obstetrics and Gynecology Hospital and the ethics committees of Chenzhou First People's Hospital. All participants provided broad informed consent.

Competing interests

The authors declare no competing interests.

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Received: 23 November 2024 / Accepted: 2 April 2025
Published online: 23 April 2025

References

1. Gestational Hypertension and Preeclampsia. ACOG practice bulletin, number 222. Obstet Gynecol. 2020;135:e237–60.
2. Tanner MS, Davey MA, Mol BW, Rolnik DL. The evolution of the diagnostic criteria of preeclampsia-eclampsia. Am J Obstet Gynecol. 2022;226:S835–43.
3. Tsigas EZ. The Preeclampsia Foundation: the voice and views of the patient and her family. Am J Obstet Gynecol 2022;226:S1254-S1264.e1251.
4. Burke SD, Zsengellér ZK, Khankin EV, Lo AS, Rajakumar A, DuPont JJ, McCurley A, Moss ME, Zhang D, Clark CD, et al. Soluble fms-like tyrosine kinase 1 promotes angiotensin II sensitivity in preeclampsia. J Clin Invest. 2016;126:2561–74.
5. Lecarpentier É, Vieillefosse S, Haddad B, Fournier T, Leguy MC, Guibourdenche J, Tsatsaris V. Placental growth factor (PlGF) and sFlt-1 during pregnancy: physiology, assay and interest in preeclampsia. Ann Biol Clin (Paris). 2016;74:259–67.
6. Brands MW, Mizelle HL, Gaillard CA, Hildebrandt DA, Hall JE. The hemodynamic response to chronic hyperinsulinemia in conscious dogs. Am J Hypertens. 1991;4:164–8.
7. Kaaja R, Laivuori H, Laakso M, Tikkanen MJ, Ylikorkala O. Evidence of a state of increased insulin resistance in preeclampsia. Metabolism. 1999;48:892–6.
8. Ong KK, Dunger DB. Birth weight, infant growth and insulin resistance. Eur J Endocrinol. 2004;151(Suppl 3):U131–139.
9. Bai X, Zhu Q, Wang W, Kan S, Hu S, Hao R, Wang S, Shi Z. Second-trimester triglyceride-glucose index to predict adverse outcomes in women with gestational diabetes mellitus: A retrospective multicenter cohort study. J Diabetes Investig. 2024;15:1489–99.
10. Guo Y, Lu J, Bahani M, Ding G, Wang L, Zhang Y, Zhang H, Liu C, Zhou L, Liu X, et al. Triglyceride-glucose index in early pregnancy predicts the risk of gestational diabetes: a prospective cohort study. Lipids Health Dis. 2024;23:87.
11. Park K, Ahn CW, Lee SB, Kang S, Nam JS, Lee BK, Kim JH, Park JS. Elevated TyG index predicts progression of coronary artery calcification. Diabetes Care. 2019;42:1569–73.
12. Won KB, Park EJ, Han D, Lee JH, Choi SY, Chun EJ, Park SH, Han HW, Sung J, Jung HO, Chang HJ. Triglyceride glucose index is an independent predictor for the progression of coronary artery calcification in the absence of heavy coronary artery calcification at baseline. Cardiovasc Diabetol. 2020;19:34.
13. Son DH, Lee HS, Lee YJ, Lee JH, Han JH. Comparison of triglyceride-glucose index and HOMA-IR for predicting prevalence and incidence of metabolic syndrome. Nutr Metab Cardiovasc Dis. 2022;32:596–604.
14. Ye H, Yin BB, Zhang JH, Xi Y, Chen F, Bai YY. Combining the triglyceride-glucose index and glycated hemoglobin A1c to assess the risk of preeclampsia in women with normal glucose tolerance: a cross-sectional study. Eur Rev Med Pharmacol Sci. 2023;27:9279–95.
15. Zhang J, Yin B, Xi Y, Bai Y. Triglyceride-glucose index: A promising biomarker for predicting risks of adverse pregnancy outcomes in Hangzhou, China. Prev Med Rep. 2024;41:102683.

16. Arabzadeh H, Doosti-Irani A, Kamkari S, Farhadian M, Elyasi E, Mohammadi Y. The maternal factors associated with infant low birth weight: an umbrella review. BMC Pregnancy Childbirth. 2024;24:316.
17. Croke L. Gestational hypertension and preeclampsia: A practice bulletin from ACOG. Am Fam Physician. 2019;100:649–50.
18. Swarray-Deen A, Sepenu P, Mensah TE, Osei-Agyapong J, Sefogah PE, Appiah-Sakyi K, Ahmed B, Konje JC. Preterm birth in low-middle income countries. Best Pract Res Clin Obstet Gynecol. 2024;95:102518.
19. Langan SM, Schmidt SA, Wing K, Ehrenstein V, Nicholls SG, Filion KB, Klungel O, Petersen I, Sorensen HT, Dixon WG, et al. The reporting of studies conducted using observational routinely collected health data statement for pharmacoepidemiology (RECORD-PE). BMJ. 2018;363:k3532.
20. Fitchett EJA, Seale AC, Vergnano S, Sharland M, Heath PT, Saha SK, Agarwal R, Ayede AI, Bhutta ZA, Black R, et al. Strengthening the reporting of observational studies in epidemiology for newborn infection (STROBE-NI): an extension of the STROBE statement for neonatal infection research. Lancet Infect Dis. 2016;16:e202–13.
21. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord. 2008;6:299–304.
22. Zhao J, Fan H, Wang T, Yu B, Mao S, Wang X, Zhang W, Wang L, Zhang Y, Ren Z, Liang B. TyG index is positively associated with risk of CHD and coronary atherosclerosis severity among NAFLD patients. Cardiovasc Diabetol. 2022;21:123.
23. Dong W, Gong Y, Zhao J, Wang Y, Li B, Yang Y. A combined analysis of TyG index, SII index, and SIRI index: positive association with CHD risk and coronary atherosclerosis severity in patients with NAFLD. Front Endocrinol (Lausanne). 2023;14:1281839.
24. Pan Y, Zou S, Xu Y, Di R, Gu H, Wang Z, Wei X, Yang C, Zhang G. Is there any association between early trimester Triglyceride-glucose index and incidence of hypertensive disorder of pregnancy and adverse pregnancy outcomes? Front Endocrinol (Lausanne). 2023;14:1093991.
25. Zhao D, Chai S, Yuan N, Sun J, Zhao X, Zhang X. Triglyceride-glycaemic index: insights into predicting fetal macrosomia and its interaction with gestational diabetes mellitus: A cohort study of Chinese pregnant women. Eur J Clin Invest. 2024;54:e14300.
26. Yadav A, Beilin LJ, Huang RC, Newnham JP, White SW, Mori TA. Fetal growth trajectories and measures of insulin resistance in young adults. J Clin Endocrinol Metab. 2023;108:e861–70.
27. Berhe AK, Ilesanmi AO, Aimakhu CO, Mulugeta A. Effect of pregnancy induced hypertension on adverse perinatal outcomes in Tigray regional State, Ethiopia: a prospective cohort study. BMC Pregnancy Childbirth. 2019;20:7.
28. Morrison JL, Duffield JA, Muhlhausler BS, Gentili S, McMillen IC. Fetal growth restriction, catch-up growth and the early origins of insulin resistance and visceral obesity. Pediatr Nephrol. 2010;25:669–77.
29. Sibai BM, Ewell M, Levine RJ, Klebanoff MA, Esterlitz J, Catalano PM, Goldenberg RL, Joffe G. Risk factors associated with preeclampsia in healthy nulliparous women. The calcium for preeclampsia prevention (CPEP) study group. Am J Obstet Gynecol. 1997;177:1003–10.
30. Thadhani R, Stampfer MJ, Hunter DJ, Manson JE, Solomon CG, Curhan GC. High body mass index and hypercholesterolemia: risk of hypertensive disorders of pregnancy. Obstet Gynecol. 1999;94:543–50.
31. Janus A, Szahidewicz-Krupska E, Mazur G, Doroszko A. Insulin Resistance and Endothelial Dysfunction Constitute a Common Therapeutic Target in Cardiometabolic Disorders. Mediators Inflamm 2016;2016:3634948.
32. Jiang ZY, Lin YW, Clemont A, Feener EP, Hein KD, Igarashi M, Yamauchi T, White MF, King GL. Characterization of selective resistance to insulin signaling in the vasculature of obese Zucker (fa/fa) rats. J Clin Invest. 1999;104:447–57.
33. Kirwan JP, Hauguel-De Mouzon S, Lepercq J, Challier JC, Huston-Presley L, Friedman JE, Kalhan SC, Catalano PM. TNF-alpha is a predictor of insulin resistance in human pregnancy. Diabetes. 2002;51:2207–13.
34. Lopez-Jaramillo P, Barajas J, Rueda-Quijano SM, Lopez-Lopez C, Felix C. Obesity and preeclampsia: common pathophysiological mechanisms. Front Physiol. 2018;9:1838.
35. Villalobos-Labra R, Silva L, Subiabre M, Araos J, Salsoso R, Fuenzalida B, Sáez T, Toledo F, González M, Quezada C, et al. Akt/mTOR role in human foetoplacental vascular insulin resistance in diseases of pregnancy. J Diabetes Res. 2017;2017:5947859.

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