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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*], 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 the body' insulin resistance.

Methods The present study included 41,694 singleton pregnant women, comprising 2,308 PE patients and 39,386 healthy controls from three tertiary hospitals in China 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 LBW. Multivariable logistic regression was used to calculate the ORs for the TyG index quartiles comparing to the lowest quartila for the primary and secondary outcomes. Subgroup analyses were conducted to evaluate the effect of age, BMI, parity and TyG test week on these associations.

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 protective association was seen between higher TyG quartiles and preterm birth ($P = 0.0472$ for Q3 and $P = 0.0000$ for Q4), but this association was not significent in Model II after abjusting for confounding factors. Subgroup analysis revealed that age, pre-pregnancy BMI, parity and test week did not influence these associations (interaction $P > 0.05$).

Conclusion The present findings suggested that the TyG index could act as a potential prediction for preeclampsia risk. Clinical evaluation incorporating the TyG index during early pregnancy can help in screening for patients at risk of PE.

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

Background

Preeclampsia (PE) may be a severe complication of pregnancy with an incidence of 5-8% [1]. PE is clinically characterized by the emergence of high blood presure and proteinuria following the 20th week of pregnancy [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 sFlt-1 [4] and 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. Currently, there is a lack of validated, accessible biomarkers that can reliably identify pregnant women at risk of PE during the early pregnancy.

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]. The triglycearide-glucose (TyG) index, deriving from fasting plasma levels of triglyceaides and glucoses, 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 among researchers and is widely applicable in clinical practice. Researches have demonstrated the TyG index is linked to an high risk of gestational diabetes mellitus [9, 10], cardiovascular disease [11, 12], and metabolic syndrome [13]. Nevertheless, there is limited literature exploring the assocciation with the TyG index and PE. A retrospective analysis shows that among pregnant women

with normal glucoses, a high 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, current reseaches about the TyG and PE have some limitations, such as reliance on single-sample sources, insufficient control of confoundingrs, and the acquisition of the TyG index in the mid-to-late stages of pregnancy after the diagnosis of PE. 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 understand in the development of PE.

This study leverages large-scale, multicenter clinical data to examine the TyG index in early pregnancy and the risk of PE. Multivariable regression analyses 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, satisfied by maternal age, body mass index, parity and TyG index test week, to assess whether these variables modify the TyG index and PE. 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. TThe present findings may assist clinical practitioners in offering early monitoring, preventive measures, and treatment

strategies for individuals with elevated TyG values in early pregnant women 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 to 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 HIS and LIS. The inclusion were follows: (1) age more than 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 or type 2 diabetes mellitus, hyparlipidemie 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 comprised, including 2,308 women with PE and 39,386 women without PE. The study process diagram is depicted in Figure 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 Hospital of Chenzhou. It was conduct in according with the principlas set forth in the Helsinki'Declaration. All participants provides broad informed consent upon their first visit.

Variables and measurements

The TyG index was the exposure variable of interest. Clinical and laboratory data were gathered from pregnant women prior to 20 weeks of gestation. Venous samples were obtained after a fasting period of eight hours, and the subsequent laboratory parameters were analyzed using an automated hematology analyzer: triglycerides (mg/dL), total cholesterols (TC, mg/dL), fasting plasma glucoses (FPG, mg/dL), alaenine transeminase (ALT, U/L), uric acids (UA, μmol/L), and creatinine (μmol/L). The TyG index was computed using the formule: TyG = ln[triglycerides (mg/dL) × fasting glucose (mg/dL) / 2]. Data pertaining to both the mothers and their newborns were collected following delivery.

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, DBP, aspirin use, antihypertensive medication use, history of hypertension, tobacco use, alcohol consumption, in vitro fertilization (IVF), ALT, UA, crertinine, TC, FPG, gestational week at testing, adverse pregnancy history, and educational level. BMI was computed by dividing pre-pregnancy weight (kg) by the square of heaght (m^2) and was classified into two categories: lowweight 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 various groups, including postgraduate, bachelor's degree or above, college diploma, high school, and less than junior high school.

Outcomes and measurements

The primary outcome assessed in the study was PE. The diagnostic criteria for PE were besed on the 2020 guidelines established by the ACOG [17]. PE was diagnosed when a patient with normal blood pressure prior to pregnancy developed SBP ≥ 140 mmHg or DBP ≥ 90 mmHg after 20 weeks of gestation, along with proteinuria (+ or higher). PE was also diagnosed if any of the following characteristics were present without proteinuria: pulmonary edema, headache unexplained by other causes, or

visual disturbances.

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

Statistical Analysis

Baseline characteristics were described according to the TyG quartiles (Q1-Q4). Continuousvariables were expressed as means ± standard deviations, and variables was reported as percentage. To assess differencesof covariates among participants, continuous variables were compared using weighted t-tests, and categorical variables were evaluated using weighted chi-square tests.

Multivariable regression analyses was applied investigating the association between the TyG index and the primary and secondary outcomes. The findings were reported as ORs accompanied by 95% CIs. The TyG index was categorized into quartiles, with the lowest quartile (TyG Q1) serving as the reference. Model I not adjusting for any covariate, while Model II adjusted for confounders, including 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 educationa.

To further reveal the relationship between the TyG index and the risk of PE, subgroup analyses were used by stratifying participants according to age (< 35 years or ≥ 35 years), BMI (< 24 kg/m² or ≥ 24 kg/m²), 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 were performed to asses interactions between subgroups.

The statistical analyses were conducted using IBM SPSS (version 21.0, IBM, Armonk, NY) and R statistics packeges (R Fondation, vesion 4.4.1). A significance level of $P < 0.05$ was employed for determining statistical significance.

Results

Baseline characteristics

Table 1 summarizes the baseline characteristics 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. As shown in Table 1, cases with any missing clinical data were excluded to ensure the accuracy and reliability of the results, 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%. Similarly, maternal age, BMI, SBP, DBP, IVF, preterm birth, tobacco, alcohol consumption, adverse pregnancy history, triglycerids, TC, ALT, and FPG all increased with high TyG index value ($P < 0.001$).

Association between the TyG index and PE

As show inTable 2, the TyG index was stratified in quartilas, with the low quartile (TyG index Q1) serving as reference. Multivariate analysis results revealed that, in Model I, compared to TyG index Q1, participants of TyG index Q3 and TyG index Q4 had a high 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 increase in the risk of PE by 25% (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 higher 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, $P = 0.0147$). Fig. 2 illustrate the relationship after adjusting for confoundings.

Subgroup analysis

As detailed in Table 3, subgroup analyses based on age, BMI, parity, and testweek at

testing demonstrated consistent associations between TyGand PE across all strata. After multivariable adjustment for potential confounders, interaction tests indicated no significant effect modification by variables on the TyG and PE association ($P > 0.05$). Figure 3 visually depicts the stratified dose-response relationships across the analyzed subgroups.

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 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 mechanisms 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, uncovering a significant positive correlation. After accounting for all confounder variables, a higher TyG was consistently related to PE. Specifically, women with highest TyG index quartile demonstrated a 31% greater risk of developing PE. A similar positive association was observed in preterm birth. Conversely, an inverse relationship was

noted between the TyG index and LBW. Subgroup analyses revealed maternal age, BMI, and parity did not significantly modify these associations, underscoring the robustness and reliability of the findings.

The TyG index, integrating the effects of blood triglycerides and glucose, has been shown to exhibit higher sensitivity in detecting IR in individuals [19]. While prior research has predominantly concentrated on its association with cardiovascular diseases [20, 21], 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 [22]. A recent retrospective study has discovered that women with normal glucose tolerance and an elevated TyG associated with a high 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 value for PE, preterm birth, and macrosomia, indicating its possible utility as a surrogate marker for these adverse pregnancy outcomes [15]. The present findings agreed with these previous findings. However, these previous studies had methodological limitations, such as single-source samples, small sample sizes, and inadequate consideration of confounding factors. Building on these earlier studies, the present investigation utilized large-scale, multicenter clinical data, that was fully controlled for confounding factors. Duartile stratification analysis of the TyG index demonstrated that elevated levels (Q3 and Q4) were linked to a higher risk of PE, offering enhanced precision for risk stratification based on the TyG index.

The present study identified that only the third quartile (Q3) of the TyG index was associated with a lower risk of LBW (OR = 0.84, 95% CI: 0.74–0.97, P = 0.0147). Associations were not observed for Q2 and Q4. The relationship between TyG and neonatal birth weight has been inconsistent across previous studies [15]. While one study reported a positive rellationship between the TyG index and macrosomia[23], another investigation showed that the TyG index was an risk factor for LBW [22]. 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, 24]. In contrast, excessive IR, which was observed in higher TyG quartiles, could impair placental function and fetal nutrition, leading to adverse outcomes, such as LBW or preterm birth [25, 26]. The quartile-based stratification analysis of the TyG index revealed that only Q3 was negatively correlated with LBW. This finding suggested that different levels of the TyG index may lead to opposite outcomes and should be interpreted objectively in clinical settings when estimating neonatal birth weight.

The underlying mechanisms through which the TyG index impacts PE may be sourced from 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 [27, 28]. IR may contribute to vascular endothelial cell injury by stimulating the release of NO, which in turn can worsen endothelial dysfunction [29, 30]. Inflammatory mediators, such as TNF-α and leptin, are secreted in increased amounts

in the adipose tissues and placentas of individuals with IR [31]. 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 [32, 33]. Recent investigations have demonstrated that excessive IR activates the nervous system, leading to increased vascular and enhanced distal glomerular reabsorption. These effects ultimately contribute to endothelial dysfunction and gestational hypertension or PE [22].

The present study revealed the association between the TyG index and 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 could facilitate risk stratification for PE, enabling appropriate preventive measures such as lifestyle changes and use of aspirin for high-risk patients. These interventions are anticipated to lower adverse pregnancy outcomes for both mother and their infants.

Strengths and limitations

A key strength of the research was the utilization of large-scale, multicenter clinical and laboratory data, which improved the generalizability of the findings. Additionally, the robustness 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. Prospective studies are needed to validate the present findings and establish causality more definitively. Second, the present study only analyzed the association, 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 with type I, type II diabetes mellitus 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 findings demonstrated 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 may hold a tool for early risk prediction of PE. Nevertheless, prospective studies are warranted to confirm its prediction and establish optimal thresholds for its application.

Abbreviations

PE	preeclampsia
TyG	triglyceride-glucose
IR	insulin resistance
Q	quartile

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458 **Table 1** Baseline characteristics of participants.

Characteristic	TyG Q1 n=10399	TyG Q2 n=10440	TyG Q3 n=10427	TyG Q4 n=10428	*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
TC (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	10003 (96.19%)	10004 (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	10096 (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	10060 (96.74%)	10048 (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%)	
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%)	

quartile; IVF, in vitro fertilization.

Table 2 Risk of the primary and the 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 pre-pregnancy BMI, SBP, DBPaspirin, depressor, hypertension history, tobacco, alcohol, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education.

PE, preeclampsiaQ, quartile.

Table 3 Subgroup analysis of the TyG index and preeclampsia.

Subgroup	OR (95% CI)	*P* value	*P* for interaction	Adjust OR (95% CI)	*P*	*P for* interaction
Age (years)			0.7802			0.9164
<35						
Q1	Reference			Reference		
Q2	1.06 (0.91, 1.23)	0.4641		0.94 (0.80, 1.12)	0.4882	
Q3	1.55 (1.35, 1.79)	<0.0001		1.20 (1.02, 1.42)	0.0275	
Q4	2.13 (1.86, 2.44)	<0.0001		1.29 (1.08, 1.55)	0.0044	
≥35						
Q1	Reference			Reference		
Q2	1.29 (0.91, 1.84)	0.1580		1.10 (0.73, 1.65)	0.6538	
Q3	1.79 (1.29, 2.47)	0.0004		1.35 (0.92, 1.97)	0.1277	
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						
Q1	Reference			Reference		
Q2	1.03 (0.88, 1.21)	0.7054		0.91 (0.76, 1.08)	0.2689	
Q3	1.51 (1.29, 1.75)	<0.0001		1.21 (1.02, 1.43)	0.0307	
Q4	1.77 (1.52, 2.06)	<0.0001		1.18 (0.98, 1.43)	0.0887	
≥24						
Q1	Reference			Reference		
Q2	1.14 (0.85, 1.52)	0.3929		1.15 (0.82, 1.62)	0.4252	
Q3	1.38 (1.05, 1.81)	0.0209		1.28 (0.92, 1.77)	0.1395	
Q4	1.79 (1.39, 2.31)	<0.0001		1.53 (1.11, 2.11)	0.0092	
Parity			0.8933			0.9932
Primipara						
Q1	Reference			Reference		
Q2	1.14 (0.98, 1.32)	0.0876		0.96 (0.81, 1.13)	0.5964	
Q3	1.74 (1.52, 2.01)	<0.0001		1.21 (1.03, 1.43)	0.0179	
Q4	2.63 (2.29, 3.01)	<0.0001		1.29 (1.08, 1.53)	0.0041	
Multipara						
Q1	Reference			Reference		
Q2	1.21 (0.79, 1.84)	0.3830		0.98 (0.61, 1.57)	0.9208	
Q3	1.82 (1.24, 2.66)	0.0021		1.29 (0.83, 2.00)	0.2595	
Q4	2.51 (1.76, 3.59)	<0.0001		1.35 (0.87, 2.09)	0.1823	
Test week			0.9676			0.8142
<14						
Q1	Reference			Reference		
Q2	1.10(0.96, 1.27)	0.1738		0.95 (0.81, 1.11)	0.5151	
Q3	1.64 (1.44, 1.87)	<0.0001		1.21 (1.04, 1.41)	0.0159	
Q4	2.31 (2.04, 2.63)	<0.0001		1.24 (1.06, 1.47)	0.0087	
14~20						

Q1	Reference		Reference	
Q2	1.37 (0.50, 3.76)	0.5352	1.51 (0.48, 4.74)	0.4807
Q3	1.80 (0.70, 4.61)	0.2218	1.36 (0.46, 4.06)	0.5817
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, SBP, DBP, aspirin, depressor, hypertension history, tobacco, alcohol, parity, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education.

Model of BMI was adjusted for: age, SBP, DBP,, aspirin, depressor, hypertension history, tobacco, alcohol, parity, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education.

Models of parity and test week were adjusted for age, BMI, SBP, DBP, aspirin, depressor, hypertension history, tobacco, alcohol, IVF, alanine transaminase, uric acid, creatinine, total serum cholesterol, test week, adverse pregnancy history, and education.

PE, preeclampsia; Q, quartile.

Figure legends

Fig. 1 Flowchart illustrating the participant selection process.

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 level were adjusted.

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.