ORIGINAL RESEARCH

Association of Triglyceride-Glucose Index with Risk of Large for Gestational Age: A Prospective Cohort Study

Lihua Lin[1,*], Juan Lin[2,*], Fang Yang[2], Shouzhen Chen[2], Zhaozhen Liu[2]

[1]Department of Healthcare, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou, Fujian Province, People's Republic of China; [2]Department of Obstetrics, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou, Fujian Province, People's Republic of China

*These authors contributed equally to this work

Correspondence: Zhaozhen Liu, Department of Obstetrics, Fujian Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University, 18 Daoshan Road, Fuzhou, Fujian, 350001, People's Republic of China, Tel +86-13515001752, Email fjsfcliuzz@163.com

Background: To evaluate the association of the baseline triglyceride-glucose (TyG) index in the first trimester of pregnancy with the risk of large for gestational age (LGA) in Southeast Chinese pregnant women.

Methods: A prospective birth cohort study recruiting 12,108 pregnant women at their first prenatal visit before 13 gestation weeks was conducted in 2019–2022. Baseline characteristics were collected from medical records or using questionnaires and blood samples were collected in the first trimester. The TyG index was obtained through the formula: ln[triglyceride (mg/dl)×fasting plasma glucose (mg/dl)/2]. The binary logistic regression model was performed to calculate the odds ratio (OR) and 95% confidence intervals (CI) to reveal the relationship between TyG index and LGA. Receiver-operating characteristic curve analysis was conducted to evaluate the ability of the TyG index to predict the risks of LGA.

Results: The overall incidence of LGA in the current study was 11.4% and the incidence of LGA increased with the baseline TyG index increasing. The risk of LGA was 2.05 (1.64, 2.57) for per unit increase in baseline TyG index. The increasing trend was found across the TyG index quartiles and the highest TyG quartiles raised the risk of LGA to 1.86 (95% CI: 1.51, 2.27) compared to the bottom TyG quartiles after full adjustment. The risk of LGA remained positive after stratification analysis. The AUC was 0.584 (95% CI: 0.569~0.600) in the entire subject, and the threshold was 8.34, with a sensitivity of 0.74 and specificity of 0.38.

Conclusion: The findings suggested that a higher TyG index in the first trimester was independently associated with higher risk of LGA and high TyG index in the first trimester may play as a early predictor for LGA.

Keywords: triglyceride-glucose index, large for gestational age, first trimester

Introduction

Large for gestational age (LGA) refers to a birth weight larger than the 90th percentage of the birth weight curve for infant sex and gestational age.[1] Large birth weight has adverse consequences on mothers and infants in the short and long term. For mothers, it is known that LGA is associated with cesarean section, the trauma of the birth canal, prolonged labor, and postpartum hemorrhage.[2,3] For newborn, LGA can increase the risk of shoulder dystocia, hypoglycemia, brachial plexus injury, skeletal injury, clavicular fracture, perinatal asphyxia, and mortality.[4–7] Furthermore, LGA also influences long-term risks of metabolic disease in adult life. Therefore, early prediction and minimization or avoidance of LGA may help to improve adverse pregnancy outcomes.

There has been an increase in the average birth weight and the prevalence of LGA over the past decades in many countries of the world.[8–13] The increase was also found in China,[14,15] which coincided with the increasing prevalence of maternal overweight and obesity, excessive weight gain during pregnancy, high parity, older maternal age, pre-gestational diabetes, and gestational diabetes mellitus after positive socioeconomic change.[9,16] The endocrine and metabolic in the first

trimester of pregnancy is crucial for fetal growth and development. It is well known that LGA is linked with adverse intrauterine exposures, such as maternal high hyperglycemia and abnormal blood lipid level, and suboptimal intrauterine environment could lead to structural and physiological changes that may ultimately affect fetal growth.[9] As early as 1952, the Pedersen hypothesis explained that maternal hyperglycemia due to insulin resistance can lead to fetal hyperglycemia, causing the fetus to overproduce insulin and thus overgrowth can occur.[17] Given the association between adverse intrauterine exposures and fetal development, early identification of pregnant women at risk for fetal overgrowth has become a matter of urgency. Recently, the triglyceride-glucose (TyG) index, calculated as ln[fasting triglycerides (mg/dl) ×fasting blood glucose (mg/dl)/2] has been pushed as a useful indicator of insulin resistance to predict the risk of adverse pregnancy outcomes including gestational diabetes mellitus and LGA[18,19]. However, there were few studies regarding the role of the first trimester TyG index about LGA, especially in the Chinese pregnant population. In this regard, we would like to elucidate the association between the quartiles of TyG index in the first trimester and the risk of LGA, especially among pregnant women in southeast China, using the hospital-based prospective birth cohort study.

Methods

Study Population

The data for analysis was derived from the Fujian Birth Cohort Study, which is a large prospective cohort study carried out in the Fujian Maternity and Child Health Hospital and pregnant women in the first trimester of pregnancy who attended to take regular prenatal visit and delivery in this facility was invited to participate in the study. Women aged less than 18 years old, or with severe liver or kidney disease, cardiovascular disease, psychiatric disorders, autoimmune disease were excluded. Each participant was contacted during pregnancy and required to finish three questionnaires in the first, second and third trimesters as well as blood samples. Detailed clinical information of delivery was collected from the medical records.

Between March 2019 and March 2022, this cohort study recruited 12,789 pregnant women who took their first prenatal visit before 13 gestation weeks and completed all the perinatal care, required questionnaires, and blood samples during the whole pregnancy. We excluded women with pre-pregnancy diabetes, hypertension. We also exclude those who lacked important information on baseline characteristics, delivery outcomes, or multiple births, and those who delivered before 28 weeks of gestation. Finally, 12,108 pregnant women with singleton birth were eligible for the final analysis. The participant flowchart is shown in Figure 1. This study was approved by the Ethics Committee of Fujian Maternity and Child Health Hospital (approval number: 2017KR-030). Written informed consent was obtained from the participants before enrollment.

Data Collection and Definition

Baseline characteristics of maternal age, educational level, marital status, height, pre-pregnancy weight, gravidity, parity, smoking, gestational age, birth weight, delivery way, and infant sex were collected from medical records or using a questionnaire through face-to-face interview. Prepregnancy body mass index (BMI) was calculated as prepregnancy weight/height^2(kg/m^2) and was classified as underweight (BMI<18.5kg/m^2), normal weight (18.5≤BMI<24kg/m^2), overweight and obese (BMI≥24kg/m^2) based on Chinese adult weight standard.[20] Hyperthyroidism and hypothyroidism were defined based on the American thyroid association guideline.[21]

Blood samples were collected in the first trimester at fasting and plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglyceride (TG) were tested. Blood pressure measured in the first trimester using an upper arm oscillometric device was recorded. The TyG index was calculated as ln[fasting triglycerides (mg/dl) ×fasting blood glucose (mg/dl)/2].

Statistical Analysis

Continuous variables are presented as the mean±standard deviation or medians (interquartile ranges), and categorical variables are shown as the numbers and percentages. Characteristics analysis of the participant according to the TyG index quartiles were compared using analysis of variance (ANOVA) for continuous variables with a normal distribution
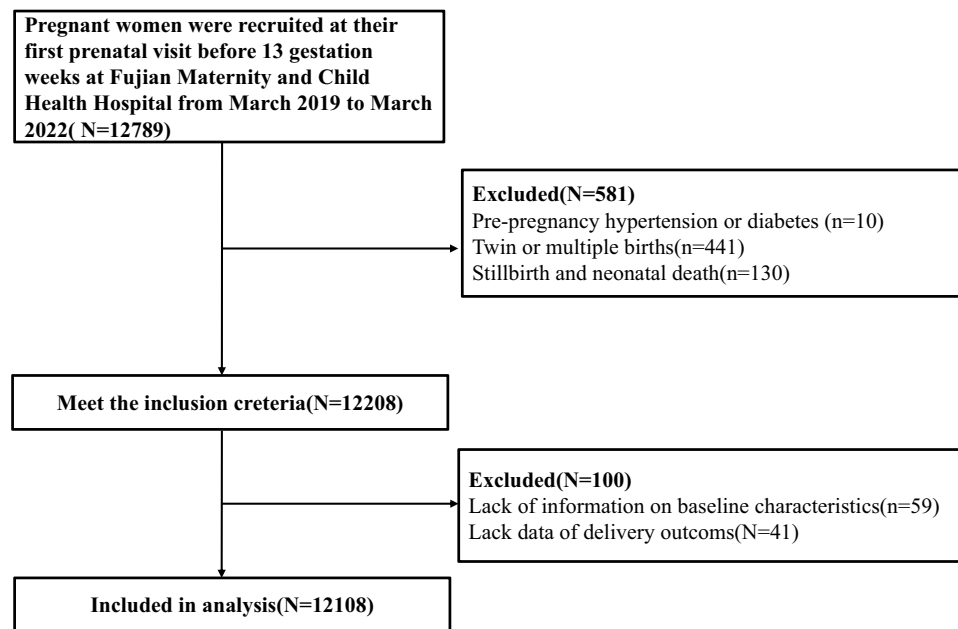
Pregnant women were recruited at their first prenatal visit before 13 gestation weeks at Fujian Maternity and Child Health Hospital from March 2019 to March 2022(N=12789)

Excluded(N=581)
Pre-pregnancy hypertension or diabetes (n=10)
Twin or multiple births(n=441)
Stillbirth and neonatal death(n=130)

Meet the inclusion creteria(N=12208)

Excluded(N=100)
Lack of information on baseline characteristics(n=59)
Lack data of delivery outcomes(N=41)

Included in analysis(N=12108)

Figure 1 Flowchart of subject selection.

or Kruskal–Wallis test with skewed distribution, and Chi-square tests for categorical variables. Logistical regression models were used to estimate the odds ratio (OR) and 95% confidence interval (CI) to determine the association of TyG index level (categorized into quartiles) with the risk of LGA. We adjusted for two models. Model 1 was adjusted for maternal age (continuous variable), education level (college and above, High school or equivalent, and less than high school), marital status (married or never married), gravidity (1,2 and ≥3), parity (primiparous or multiparous), gestational age at delivery (continuous variable), prepregnancy BMI (underweight, normal weight and overweight or obese), infant sex (boy or girl) and smoking status (yes or no); Model 2 was further adjusted for baseline FPG, systolic blood pressure, diastolic blood pressure, HDL-C, LDL-C, TC, and TG.

Subgroup analyses were also conducted according to maternal age (≤35, >35 years), educational level (college and above, High school or equivalent, and Less than high school), gravidity (1, 2, and ≥3), parity (primiparous or multi-parous) and infant sex (boy or girl). Potential modification effects on the LGA risk of these factors were examined by testing the corresponding interaction terms.

Furthermore, Receiver operating characteristic (ROC) curves and areas under the curve (AUCs) were used to assess the ability of the indices to detect LGA infants among different prepregnancy BMI categories. The threshold values of the TyG index were defined as optimal based on the maximizing of the Youden J-index (sensitivity+specificity-1).[22] Finally, to test the robustness of the results, sensitivity analysis was conducted by excluding pregnant women with hyperthyroidism, hypothyroidism, or gestational diabete mellitus (GDM). All analyses were performed using the statistical software package R software, version 4.4.2. Statistical significance was defined as $P<0.05$.

Results

Basic Characteristics of the Study Population

The baseline characteristics of 12,108 participants grouped by TyG index quartiles are provided in Table 1. The average TyG index was 8.46±0.34 and participants with higher TyG index values were more often with lower educational level, married, overweight or obese, high gravidity, and be multiparous (P < 0.001). The overall incidence of GDM was 15.8%, and the incidence for TyG index quartiles rose with the TyG index quartiles increased. The TyG index increased significantly with increasing baseline FPG, LDL-C, and TG but with decreasing baseline HDL-C (all $P<0.001$).

Table 1 Basic Characteristics of the Study Population by Triglyceride-Glucose (TyG) Index Quartile

Variable	Overall	TyG Quartile				P value
	Total (n=12,108)	Q1 (n=3001)	Q2 (n=2997)	Q3 (n=3064)	Q4 (n=3046)	
TYG index	8.46±0.34	<8.23	8.23–8.45	8.45–8.68	≥8.68	
Maternal age (years)	30.16±3.91	29.46±3.71	29.82±3.75*	30.24±3.95*	30.16±3.92*	<0.001
Education level, n(%)						<0.001
College and above	9591(79.2)	2519(83.9)	2403(80.2)*	2417(78.9)*	2252(73.9)*	
High school or equivalent	1565(12.9)	311(10.4)	384(12.8)*	413(13.5)*	457(15.0)*	
Less than high school	952(7.9)	171(5.7)	210(7.0)*	234(7.6)*	337(11.1)*	
Marital status, n(%)						0.002
Married	11,580(95.6)	2842(94.7)	2869(95.7)	2924(95.4)	2945(96.7)*	
Never married	528(4.4)	159(5.3)	128(4.3)	140(4.6)	101(3.3)*	
Pre-pregnancy BMI (kg/m², n(%)						<0.001
Underweight (BMI<18.5)	1923(15.9)	666(22.2)	542(18.1)	462(15.1)*	253(8.3)*	
Normal weight (BMI 18.5~23.9)	8537(70.5)	2139(71.3)	2160(72.1)	2164(70.6)	2074(68.1)*	
Overweight (BMI≥ 24.0)	1648(13.6)	196(6.5)	295(9.8)*	438(14.3)*	719(23.6)*	
Gravidity, n(%)						<0.001
1(%)	5281(43.6)	1589(52.9)	1440(48.0)*	1270(41.4)*	982(32.2)*	
2(%)	3695(30.5)	794(26.5)	891(29.7)*	973(31.8)*	1037(34.0)*	
≥3(%)	3132(25.9)	618(20.6)	666(22.2)	821(26.8)*	1027(33.7)*	
Parity, n(%)						<0.001
Primiparous	7182(59.3)	2073(69.1)	1917(64.0)*	1750(57.1)*	1442(47.3)*	
Multiparous	4926(40.7)	928(30.9)	1080(36.0)*	1314(42.9)*	1604(52.7)*	
Smoking, n(%)						0.491
Yes	240(2.0)	58(1.9)	69(2.3)	54(1.8)	59(1.9)	
No	11,868(98.0)	2943(98.1)	2928(97.7)	3010(98.2)	2987(98.1)	
FPG at first trimester, mmol/L	4.72±0.37	4.60±0.34	4.68±0.31*	4.75±0.34*	4.85±0.445*	<0.001
Systolic blood pressure at first trimester, mm Hg	114.61±10.87	113.02±10.58	113.57±10.79	115.11±10.90	116.71±10.83	0.085
Diastolic blood pressure at first trimester, mm Hg	69.31±8.63	67.79±8.45	68.70±8.52	69.66±8.66	70.86±8.60	0.825
HDL-C at first trimester, mmol/L	1.678±0.30	1.73±0.29	1.71±0.29*	1.68±0.30*	1.59±0.30*	<0.001
LDL-C at first trimester, mmol/L	2.39±0.60	2.14±0.52	2.31±0.53	2.47±0.59	2.63±0.633	<0.001
TC at first trimester, mmol/L	4.63±0.734	4.34±0.65	4.54±0.66	4.71±0.72	4.92±0.77	0.087
TG at first trimester, mmol/L	1.34±0.494	0.864±0.13	1.13±0.10*	1.38±0.13*	1.98±0.50*	<0.001
Delivery						
Gestational age, weeks	39.19±1.48	39.31±1.46	39.24±1.46	39.19±1.40*	39.01±1.57*	0.878
Birth weight, g	3241.58±436.35	3210.68±420.10	3239.21±426.38*	3244.01±429.92*	3271.90±465.27*	<0.001
Cesarean section, n (%)	4506(37.2)	981(32.7)	1028(34.3)	1177(38.4)*	1320(43.3)*	<0.001
Sex of newborn, n (%)						0.008
Boys	6420(53.0)	1652(55.0)	1610(53.7)	1556(50.8)*	1602(52.6)	
Girls	5688(47.0)	1349(45.0)	1387(46.3)	1508(49.2)*	1444(47.4)	
GDM, n(%)						<0.001
Yes	1915(15.8)	253(8.4)	373(12.4)*	493(16.1)*	796(26.1)*	
No	10,193(84.2)	2748(91.6)	2624(87.6)*	2571(83.9)*	2250(73.9)*	

Notes: Date are presented as mean± standard deviation for continuous variables and n(%) for categorical variables. *Different from Q1 group.
Abbreviations: TyG, triglyceride-glucose; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

Association Between Baseline TyG Index and Risk of LGA

Values of the TyG index were divided into quartiles and the lowest quartile was used as the reference group. We performed binary logistic regression analysis to explore the association between the quartiles of the TyG index and the risk of LGA, with adjusting for different potential confounding factors (Table 2). The incidences of LGA of baseline TyG

Table 2 Association of Triglyceride-Glucose (TyG) Index with Large for Gestational Age (LGA)

	TyG (n=12,108) OR (95% CI)	Q1 (n=3001) OR (95% CI)	Q2 (n=2997) OR (95% CI)	Q3 (n=3064) OR (95% CI)	Q4 (n=3046) OR (95% CI)	$P_{for\ trend}$
LGA (%)	1381(11.4)	233(7.8)	315(10.5)	346(11.3)	487(16.0)	<0.001
Unadjusted model	2.35(2.01,2.76)	1(Ref)	1.40(1.17,1.67)	1.51(1.27,1.80)	2.26(1.92,2.67)	<0.001
Model 1[a]	1.62(1.37,1.92)	1(Ref)	1.29(1.09,1.54)	1.31(1.10,1.57)	1.65(1.39,1.96)	<0.001
Model 2[b]	2.05(1.64,2.57)	1(Ref)	1.34(1.12,1.61)	1.36(1.13,1.64)	1.86(1.51,2.27)	<0.001

Notes: [a]Model 1: Adjusted for maternal age, education level, gravidity, parity, gestational age at delivery, prepregnancy BMI, and infant sex, smoking status; [b]Model 2: was further adjusted for first trimester diastolic blood pressure, first trimester high density lipoprotein cholesterol, first trimester low density lipoprotein cholesterol, and first trimester total cholesterol.
Abbreviations: LGA, large for gestational age; OR, odds ratio; CI, confidence interval.

index were 7.8%,10.5%,11.3% and 16.0%, respectively, and the overall incidence was 11.4%. The risk of LGA showed an increasing trend with the increasing of TyG index in the first trimester. The risk of LGA was 2.05 (1.64,2.57) for per unit increase in baseline TyG index. Compared with the lowest TyG index quartiles (Q1,<8.23), the risk of LGA infant in Q2 (8.23≤TyG index<8.45), Q3 (8.45≤TyG index<8.68), Q4 (≥8.68) were 1.34 (95% CI:1.10-1.57), 1.29 (95% CI:1.09–1.54), and 1.65 (95% CI:1.39–1.96), respectively, in the multivariate adjusted model 1(P_{trend}<0.001). After further adjusting confounding factors (baseline FPG, systolic blood pressure, diastolic blood pressure, HDL-C, LDL-C, TC, and TG), the treads of ORs remained.

Stratification Analysis on the Association Between Baseline TyG Index with Risk of LGA

The results of subgroup analyses stratified by advanced age, education level, gravidity, parity, infant sex, and smoking status kept the same with the main results and no significant interactions were observed between all subgroup variables with the baseline TyG index and its quartiles categories on the risk of LGA infant, with adjustment for confounding factors (all $P_{interaction}$>0.05). It is worth noting that the association of baseline TyG index quartile changes with LGA seemed to be somewhat stronger in individuals with age <35 years, educational level less than high school, low gravidity, primiparous, and smokers (Table 3).

Table 3 Stratification Analysis on the Association Between Triglyceride-Glucose (TyG) Index and Large for Gestational Age (LGA)

Subgroup	LGA (%)	TyG Quartile				P_{trend}	$P_{interaction}$
		Q1	Q2 OR (95% CI)[a]	Q3 OR (95% CI)[a]	Q4 OR (95% CI)[a]		
Advanced age							0.967
<35	1157(83.8)	1(Ref)	1.41(1.17,1.71)	1.53(1.27,1.85)	2.24(1.87,2.68)	<0.001	
≥35	224(16.2)	1(Ref)	1.20(0.71,2.01)	1.19(0.73,1.94)	1.78(1.14,2.79)	0.021	
Education level							0.815
College and above	1038(75.2)	1(Ref)	1.42(1.17,1.73)	1.53(1.26,1.86)	2.19(1.81,2.64)	<0.001	
High school or equivalent	194(14.0)	1(Ref)	1.72(1.05,2.82)	1.37(0.83,2.28)	1.98(1.23,3.19)	0.027	
Less than high school	149(10.8)	1(Ref)	0.66(0.33,1.33)	1.407(0.77,2.56)	2.45(1.43,4.20)	<0.001	
Gravidity							0.683
1	434(31.4)	1(Ref)	1.63(1.23,2.16)	1.52(1.13,2.05)	2.40(1.80,3.21)	<0.001	
2	443(32.1)	1(Ref)	1.22(0.89,1.68)	1.43(1.05,1.94)	1.66(1.23,2.23)	0.006	
≥3	504(36.5)	1(Ref)	1.212(0.87,1.68)	1.278(0.94,1.75)	2.012(1.51,2.68)	<0.001	
Parity							0.444
Primiparous	634(45.9)	1(Ref)	1.507(1.19,1.92)	1.57(1.23,2.00)	2.22(1.75,2.82)	<0.001	
Multiparous	747(54.1)	1(Ref)	1.19(0.91,1.55)	1.25(0.97,1.61)	1.80(1.42,2.28)	<0.001	

(Continued)

Table 3 (Continued).

Subgroup	LGA (%)	TyG Quartile				P trend	P interaction
		Q1	Q2 OR (95% CI)[a]	Q3 OR (95% CI)[a]	Q4 OR (95% CI)[a]		
Infant sex							0.891
Girl	683(49.5)	1(Ref)	1.338(1.03,1.71)	1.34(1.05,1.72)	2.16(1.71,2.73)	<0.001	
Boy	698(50.5)	1(Ref)	1.458(1.14,1.87)	1.684(1.32,2.15)	2.35(1.86,2.96)	<0.001	
Smoking							0.536
Yes	36(2.6)	1(Ref)	5.31(1.13,25.04)	5.60(1.15,27.23)	8.71(1.88,40.34)	0.049	
No	1345(97.4)	1(Ref)	1.36(1.14,1.63)	1.48(1.24,1.77)	2.209(1.87,2.61)	<0.001	

Notes: [a]Adjusted for maternal age, education level, gravidity, parity, gestational age at delivery, prepregnancy BMI, and infant sex, smoking status, first trimester diastolic blood pressure, first trimester high density lipoprotein cholesterol, first trimester low density lipoprotein cholesterol, and first trimester total cholesterol.
Abbreviations: LGA, large for gestational age; OR, odds ratio; CI, confidence interval.

ROC Curve Analyses of Baseline TyG Index Predicting LGA

In the Receiver operating characteristic (ROC) curve analyses, the baseline TyG index showed significant areas under the ROC curve (AUCs), and the AUC of the baseline TyG index for LGA was 0.584 (95% CI:0.569~0.600) in the entire study subject. The threshold was 8.34, with a sensitivity of 0.74 and a specificity of 0.38. For prepregnancy BMI categories, the AUCs (95% CI) for underweight, normal weight, and overweight or obese groups were 0.563 (95% CI:0.508~0.618), 0.568 (95% CI:0.549~0.587), 0.554 (95% CI:0.518~0.589), respectively (Table 4).

Sensitivity Analysis

In the sensitivity analyses, consistent results were found after excluding women with hyperthyroidism or/and hypothyroidism, GDM (Table 5). That is, when excluded pregnant women with thyroid dysfunction or GDM, the ORs of LGA in the highest quartile of the TyG index were still significant after adjustment for the confounding factors.

Table 4 Receiver Operating Characteristic (ROC) Analysis of the Triglyceride-Glucose (TyG) Index for Predicting Large for Gestational Age (LGA)

BMI Category	AUC (95% CI)	Threshold	Sensitivity	Specificity	P
All women	0.584(0.569,0.600)	8.34	0.74	0.38	<0.001
Underweight	0.563(0.508,0.618)	8.54	0.37	0.74	<0.001
Normal weight	0.568(0.549,0.587)	8.34	0.72	0.38	<0.001
Overweight	0.554(0.518,0.589)	8.69	0.51	0.59	<0.001

Abbreviations: AUC, areas under the curve; BMI, body mass index; CI, confidence interval.

Table 5 Association of Triglyceride-Glucose (TyG) Index with Large for Gestational Age (LGA)

	TyG OR (95% CI)[a]	Q1 OR (95% CI)	Q2 OR (95% CI)[a]	Q3 OR (95% CI)[a]	Q4 OR (95% CI)[a]
Excluding women with hyperthyroidism (n=201)	2.04(1.62,2.56)	1(Ref)	1.35(1.13,1.62)	1.35(1.12,1.63)	1.85(1.51,2.28)
Excluding women with hypothyroidism (n=405)	2.06(1.64,2.60)	1(Ref)	1.36(1.13,1.64)	1.37(1.13,1.66)	1.80(1.51,2.29)
Excluding women with hyperthyroidism and hypothyroidism (n=606)	2.05(1.63,2.59)	1(Ref)	1.38(1.14,1.66)	1.37(1.13,1.67)	1.87(1.51,2.31)
Excluding women with GDM (n=1915)	2.06(1.60,2.64)	1(Ref)	1.36(1.12,1.64)	1.39(1.14,1.69)	1.86(1.49,2.33)
Excluding women with hyperthyroidism, hypothyroidism and GDM	2.09(1.61,2.71)	1(Ref)	1.39(1.14,1.70)	1.41(1.15,1.73)	1.89(1.51,2.38)

Notes: [a]adjusted for maternal age, education level, gravidity, parity, gestational age at delivery, prepregnancy BMI, and infant sex, smoking status, first trimester diastolic blood pressure, first trimester high density lipoprotein cholesterol, first trimester low density lipoprotein cholesterol, and first trimester total cholesterol.
Abbreviations: OR, odds ratio; CI, confidence interval.

Discussion

As the economy grows and the standard of living rises, the birth weight and the incidence of fetal overgrowth, including macrosomia and LGA raised over the past decades in many countries. The overall incidence of LGA in the current study was 11.4%. In the world, there is a considerable variation in the incidence of LGA, ranging from 5% to 20% in developed countries.[13,23] The incidence of LGA varies in Chinese cities, ranging from 8.2% to 17.7%.[23] This discrepancy in LGA incidence might be due to the application of different standards and characteristics of the study populations. At the same time, we should also realize that in the face of such a severe epidemic trend in birth weight and increased LGA incidence, it is crucial to reduce the incidence of LGA.

Based on this prospective birth cohort study, significant associations were found between the first trimester of pregnancy maternal TyG index with risk of LGA among pregnant women. The results suggest that in the first trimester TyG index and its quartiles change are positively related to the risk of LGA after controlling for maternal age, education level, marital status, gravidity, parity, gestational age at delivery, prepregnancy BMI, infant sex, smoking status, baseline FPG, systolic blood pressure, diastolic blood pressure, HDL-C, LDL-C, TC, and TG. Furthermore, a 1-unit increase in the baseline TyG index increased 105% risk of LGA after the full adjustment. TyG index, as an insulin resistance indicator,[24] could be applied as an indicator for the prediction of pregnancy outcomes among pregnant women. Our finding demonstrated that the baseline TyG index in early pregnancy is a proper predictor of incident LGA, independent of other risk factors among pregnant women in Southeast China.

High levels of triglyceride and glucose are common in pregnant women and are related to birth weight.[18,25,26] Many studies found that women who delivered LGA newborns are accompanied by increasing triglyceride levels.[27] The ratio of triglyceride combines glucose levels could be more stable. The study was in line with previous studies.[18,28] A prospective study carried out in Iran found that the risk of LGA in women with the top tertile of TyG index was 5.3-folds than that in women with the lowest tertile.[29] Liu's research suggested that the TyG in the early trimester of pregnancy was independently related to LGA infant delivery and the TyG values in the highest tertile showed a higher risk of delivering an LGA infant.[28]

TyG index has been widely proven to be the best indicator of insulin resistance in individuals including pregnancies.[30] Some researchers have promoted the TyG index as a surrogate of insulin resistance[31]. Several studies have articulated the predictive ability of the TyG index for pregnancy-related complications.[18,32,33] We focused our work on the power of the first trimester TyG index to predict the possibility of LGA and found that larger neonates and higher incidence of LGA were born in women with higher TyG index. A higher TyG index means an increase in IR, which leads to a decrease in lipoprotein lipase activity. The derived fatty acids enter the umbilical cord blood and are stored in fetal adipose tissue, resulting in accelerated fetal growth and obesity.[34] On the other hand, IR promotes the process of protein synthesis and reduces lipolysis by accelerating the rate of activation of the amino acid transfer system.[35] Since the TyG index has been recognized as an indicator of IR in pregnancies, we also analyzed using ROC curve analysis to detect the power of prediction on LGA infants and found a high sensitivity and specificity in identifying LGA infant delivery. These results suggested the potential clinical utility for predicting the LGA of the TyG index. To the best of our knowledge, the current study is the first effort to elucidate the predictive power of the TyG index in the early trimester of pregnancy on LGA infants in the Southeast China pregnant women.

Furthermore, we found the effect of increased TyG index on LGA risk of was stronger among individuals with age <35 years, educational level less than high school, low gravidity, primiparous, and smokers. The potential explanation for this discrepancy may be partly explained by the higher TyG index in these participants. More studies are warranted to further investigate the reasons and potential mechanisms underlying the relationship between the TyG index and LGA risk in these participants. Research suggests that pre-pregnancy obesity is the independent risk factors for LGA, but the result of ROC found that the sensitivity of TyG in underweight and overweight is lower than overall and normal weight value. The confused results are unknown and deeper research is needed. Healthcare providers and clinical workers should put more effort into these pregnant women to reduce the likelihood of delivering a LGA infant.

Detecting risk factors for pregnancy adverse outcomes in early pregnancy might be of great value in improving pregnancy outcomes. The current study confirmed that the first trimester TyG index could be used as an effective

predictor of LGA in clinical practice. The greatest strength of the current study is the prospective design, with questionnaire data and blood sample collection in the first trimester. Several limitations to this study should be recognized. Firstly, we lacked information on some potential confounding factors, such as gestational weight gain, diet, physical exercise, and serum insulin, which may lead to bias of the results. Secondly, the study population consisted of women who received prenatal visit and delivery in Fujian Maternity and Child Health Hospital, which limits the generalizability to the other population. Thirdly, the level of lipid and glucose in the late trimester were not included in the adjusted models, which might affect the result and cannot fully account for the independent contribution of baseline TyG index to fetal growth. Lastly, only Chinese women were enrolled, our results cannot be generalized to be clinically effective for the western population as the rates of overweight and obese in Western are substantially higher.

Conclusion

In conclusion, in this study, a higher TyG index in the first trimester was independently and significantly associated with a higher risk of LGA, and high TyG index in the first trimester may be the early predictor for LGA. As an easily available index in the early pregnancy, the TyG index can help clinical healthcare providers early identification of high-risk groups and active intervention to improve pregnancy outcomes.

Abbreviations

LGA, large for gestational age; TyG, triglyceride-glucose; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; OR, odds ratio; CI, confidence interval; ROC, receiver operating characteristic; AUC, areas under the curve.

Data Sharing Statement

The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Fujian Maternity and Child Health Hospital and complied with the Declaration of Helsinki. The written informed consent was obtained from every participant before enrollment.

Acknowledgments

The authors thank the perinatal care providers at the department of obstetrics for their professional skills in managing patients.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors report there are no competing interests to declare.

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