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Association between the triglyceride-glucose index in third trimester pregnant women and neonatal birth weight

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ABSTRACT

Objectives: Neonatal birth weight is a pivotal measure of fetal growth and development, with profound implications for an infant's immediate health and long-term well-being. The triglyceride-glucose (TYG) index, a marker of insulin resistance and metabolic health, has become an essential tool for evaluating maternal metabolic status during pregnancy. Recognizing the impact of metabolic abnormalities on fetal development, this study aims to delineate the association between the TYG index in the third trimester and neonatal birth weight.

Material and methods: Our study cohort comprised 475 neonates. We calculated the maternal TYG index in the third trimester and documented neonatal birth weights.

Correlation and multivariate linear regression analyses were conducted to evaluate the association between the TYG index and neonatal weight. Subgroup analyses were further examined using multivariate logistic regression.

Results: A significant positive correlation was observed between the TYG index and neonatal birth weight ($r = 0.314$, $p < 0.001$). The multivariate linear regression analysis substantiated this association, revealing that an increment in the TYG index was associated with an average neonatal weight increase of 227.22 grams (β: 227.22, 95% CI: 148.74 to 305.71, $p < 0.001$). Notably, this correlation was more robust in subgroups without GDM (β: 281.17, $p = 0.002$), among male neonates (β: 213.06, $p = 0.003$) and in mothers over the age of 31 (β: 253.58, $p < 0.001$).

Conclusions: The TYG index during the third trimester of pregnancy is significantly and positively associated with neonatal birth weight, with particularly strong associations in specific subgroups. These insights imply that the TYG index could serve as a predictive biomarker for neonatal weight, offering potential benefits for managing pregnancy and neonatal health.

Keywords: triglyceride-glucose index; neonatal birth weight; gestational diabetes mellitus; insulin resistance

INTRODUCTION

Neonatal birth weight is a critical indicator of fetal growth and development, reflecting the complex interplay of maternal health, nutrition, and genetic factors during pregnancy [1]. It is closely associated with both immediate and long-term health outcomes for the infant. Low birth weight has been linked to an increased risk of neonatal morbidity and mortality [2], while macrosomia (high birth weight) can lead to delivery complications and a higher risk of obesity and metabolic disorders in later life [3]. Metabolic abnormalities during pregnancy, such as insulin resistance and dyslipidemia, have been increasingly recognized for their potential to influence fetal growth and development [4]. These conditions can lead to an altered intrauterine environment, affecting nutrient availability and hormonal signaling, which in turn can

impact the growth trajectory of the fetus [5]. Studies have suggested that maternal metabolic health is not only a reflection of the mother's overall well-being, but also a significant determinant of neonatal birth weight [6, 7]. Specifically, maternal hyperglycemia, a hallmark of insulin resistance, has been linked to macrosomia, while dyslipidemia may affect the partitioning of nutrients to the fetus, potentially leading to variations in birth weight [8].

In recent years, the triglyceride-glucose (TYG) index has gained recognition for its ease of measurement and its correlation with insulin resistance [9]. The TYG index, as an integrative measure of both glycemic and lipid abnormalities [10], offers a unique perspective on the interplay between metabolic health and fetal outcomes. Elevated TYG index values may indicate a pro-inflammatory and pro-thrombotic state, which could further exacerbate the metabolic challenges faced by the developing fetus [11]. Given the profound implications of metabolic health on neonatal birth weight, understanding the nuances of this relationship is crucial for the development of targeted interventions aimed at improving both maternal and neonatal health outcomes.

While there is a growing body of research on the impact of maternal metabolic health on neonatal outcomes [12, 13], the role of the TYG index specifically during the third trimester remains understudied. Furthermore, the influence of maternal factors such as age, fetal gender, and gestational diabetes mellitus (GDM) on the association between the TYG index and neonatal birth weight requires further elucidation.

This study aims to investigate the association between the TYG index in the third trimester of pregnancy and neonatal birth weight. Additionally, the study further explores this association within various subgroups, including the presence of GDM, fetal gender, and maternal age. Consequently, we hope to offer new evidence supporting the TYG index as a potential biomarker for predicting neonatal weight, thereby contributing to the theoretical framework for metabolic monitoring and management during pregnancy.

MATERIAL AND METHODS

Study design and population

This retrospective cohort study was conducted at our hospital from January 2021 to December 2022. The study population comprised pregnant women who delivered singleton neonates during the study period. Inclusion criteria included women with a viable pregnancy at the time of delivery and complete clinical data available for analysis. Exclusion criteria were multiple pregnancies, pre-existing diabetes, and incomplete clinical records. The study was approved by the Changzhou Maternal and Child Health Care Hospital Institutional Review Board (Approval Date: December 30, 2020, Approval Number: 2020081).

Data collection

Data on maternal characteristics, including GDM status, age, pre-pregnancy body mass index (BMI), and other relevant factors, were collected through medical records and standardized interviews.

Fasting triglycerides and glucose levels were obtained from the most recent laboratory tests performed during the third trimester of pregnancy. The TYG index was calculated for each participant using the formula: TYG = ln [fasting triglyceride (mg/dL) × fasting glucose (mg/dL)] / 2 [14]. Neonatal birth weight was recorded immediately following delivery by trained medical staff.

Statistical analysis

All statistical analyses were performed using R version 4.2.3. Measurement data that did not conform to a normal distribution were described using the median and quartile [M, (Q1, Q3)], and differences between any two groups were compared using the Wilcoxon rank sum test. Count data were presented as the number of cases and constituent ratio [n (%)], and group differences were assessed using the chi-square test. Correlation analysis was performed to assess the relationship between the TYG index and neonatal birth weight. Multivariate linear regression models were used to

determine the independent association between the TYG index and neonatal weight. To facilitate the analysis and interpretation of the TYG index's impact on neonatal birth weight, continuous variables (age, HDL, predelivery BMI) were categorized based on the median value. The median of the TYG index for the study population was calculated, and participants were subsequently divided into two groups: those with a TYG index below the median and those with a TYG index at or above the median. This approach allowed for a straightforward comparison between groups with lower and higher levels of insulin resistance and metabolic dysregulation as indicated by the TYG index.

Subgroup analyses were conducted to explore the association within specific groups defined by GDM status, fetal gender, and maternal age. Univariate and multivariate logistic regression was applied for the subgroup analysis adjusting for potential confounders, including GDM status, fental gender, maternal age, pregnancy weight gain, gestational week, BMI, total cholesterol, high density lipoprotein (HDL), and stress hyperglycemia ratio (SHR) [15]. A two-tailed *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Weight distribution of enrolled neonates

In this study, a total of 475 neonates were evaluated, with an average birth weight of 3360.00 grams (Tab. 1). Specifically, neonates delivered via cesarean section had a higher average birth weight (3410.00 grams) compared to those born via eutocia (3310.00 grams), with a statistically significant difference ($p < 0.001$). Male neonates exhibited a higher average birth weight than female neonates (3400.00 grams vs 3330.00 grams, $p = 0.036$). GDM shows no significant differences between newborns of mothers with or without the condition ($p = 0.320$). Furthermore, neonates born to mothers with a higher TYG index had a significantly higher average birth weight (3475.00 grams) compared to those with a lower TYG index (3250.00 grams) ($p < 0.001$). HDL levels and predelivery BMI also showed

significant differences, with higher levels correlating with heavier neonatal weights ($p = 0.012$ and $p < 0.001$, respectively).

Correlation analysis of the TYG index with neonatal weight

The correlation analysis revealed a positive correlation between the TYG index and neonatal birth weight. The correlation coefficient was found to be 0.314 ($p < 0.001$).

Association between neonatal weight and maternal TYG indexes in the third trimester

In the multivariate linear regression analysis, a significant positive correlation was identified between the maternal TYG index in the third trimester and neonatal birth weight, with a β coefficient of 227.22 (95% CI: 148.74 to 305.71, $P < 0.001$). This indicates that for each unit increase in the TYG index, neonatal weight increased by an average of 227.22 grams. Other variables, such as pregnancy weight gain and predelivery BMI, also showed significant associations but did not overshadow the impact of the TYG index.

Association of TYG index with neonatal weight across subgroups

In the unadjusted logistic analysis, a higher TYG index was associated with increased neonatal weight across all patients (β: 226.47, 95% CI: 150.56 to 302.39, $p < 0.001$, Fig. 3).

After adjusting for GDM, gender, age, pregnancies, gestational week, BMI, total cholesterol, HDL, and SHR, the association between the TYG index and neonatal weight remained significant for all patients (β: 144.45, 95% CI: 44.99 to 243.90, $p = 0.005$, Tab. 2). The association between maternal TYG index and neonatal weight was significantly pronounced in subgroups without GDM, among male neonates, and in mothers aged 31 and above. Specifically, in the absence of GDM, a higher TYG index was linked to a substantial increase in neonatal weight (β: 281.17, $p = 0.002$). Male neonates also exhibited a notable weight increase with higher TYG index values (β:

213.06, p = 0.003). Furthermore, in mothers over 31 years, a higher TYG index was associated with a significant neonatal weight gain (β: 253.58, p < 0.001).

DISCUSSION

The present study reveals a significant positive correlation between the maternal TYG index during the third trimester of pregnancy and neonatal birth weight, with particularly strong associations in pregnant woman without GDM, among male neonates, and in mothers aged 31 and above. This finding underscores the potential of the TYG index as a predictive biomarker for birth weight, and suggests that maternal metabolic health, as reflected by the TYG index, plays a critical role in fetal growth and development.

Our findings align with recent studies that emphasize the importance of maternal metabolic status in determining neonatal outcomes [16, 17]. Previous research has established that insulin resistance and lipid metabolism are key factors influencing fetal development during pregnancy [18, 19]. The TYG index, a surrogate marker for insulin resistance, has been increasingly recognized in various contexts, including its role in predicting the risk of diabetes and cardiovascular diseases [20, 21]. However, its specific impact on pregnancy and neonatal outcomes has not been extensively studied until recently. A study by Liu et al. [22] demonstrated that higher maternal TYG index values in maternal first-trimester were associated with an increased risk of large-for-gestational-age (LGA) infants, corroborating our findings that elevated TYG index correlates with greater neonatal birth weight. Similarly, Zawiejska A. et al. [23] reported that maternal insulin resistance was related to adverse neonatal outcomes, including higher birth weights. The biological plausibility of our findings may be explained by the role of insulin resistance in altering the placental transport of nutrients and the subsequent metabolic programming of the fetus [24]. Elevated levels of insulin resistance could lead to increased lipolysis and reduced lipid clearance, resulting in higher levels of circulating free fatty acids that are preferentially transferred to the fetus, promoting adipose tissue development and weight gain [25,

26].

The subgroup analysis in our study reveals that the association between the TYG index and neonatal birth weight is more pronounced in certain groups. Specifically, the correlation was stronger among neonates born to mothers without GDM, male neonates, and mothers aged 31 years or older. This suggests that the TYG index may have differential effects based on maternal and fetal characteristics. The absence of GDM in mothers appears to amplify the relationship between the TYG index and neonatal birth weight. This could be because in non-GDM pregnancies, the TYG index more accurately reflects underlying metabolic disturbances that directly influence fetal growth. In contrast, GDM pregnancies may involve more complex metabolic interactions that could attenuate the direct effect of the TYG index on birth weight [27]. Gender differences in the association between the TYG index and birth weight also emerged, with male neonates showing a stronger correlation. This finding is consistent with literature suggesting that male fetuses are more sensitive to maternal metabolic conditions, possibly due to differences in placental function or fetal growth patterns [28, 29]. Lastly, the stronger association observed in mothers aged 31 years or older may reflect age-related metabolic changes that influence both the TYG index and fetal growth [30, 31]. As maternal age increases, so does the risk of insulin resistance and other metabolic disorders, which could explain the heightened impact of the TYG index on neonatal birth weight in this subgroup.

The TYG index could serve as a useful tool for identifying pregnancies at risk for abnormal fetal growth, particularly in populations without GDM or in older mothers. Early identification of high-risk pregnancies could allow for targeted interventions aimed at optimizing maternal metabolic health and improving neonatal outcomes. Moreover, the TYG index could be integrated into routine prenatal care as part of a comprehensive metabolic assessment, enabling healthcare providers to better monitor and manage metabolic risks during pregnancy.

Our study boasts several key strengths. The large cohort of 475 neonates ensures our findings are statistically robust. We utilized multivariate regression to isolate the

impact of the TYG index, controlling for confounding variables like maternal age and GDM status. Subgroup analyses uncovered specific associations that could guide clinical interventions. Moreover, our results have clear clinical relevance, suggesting the TYG index could be a valuable tool in prenatal care for predicting neonatal weight. However, this study has several limitations that should be acknowledged. First, the observational nature of the study precludes the establishment of a causal relationship between the TYG index and neonatal birth weight. Second, the study population was relatively homogeneous, which may limit the generalizability of the findings to more diverse populations. Future research should aim to replicate these findings in larger and more diverse cohorts, as well as explore the underlying mechanisms by which the TYG index influences fetal growth.

CONCLUSION

In conclusion, this study highlights the significant role of the maternal TYG index in predicting neonatal birth weight, particularly in specific subgroups. The TYG index may offer a valuable addition to prenatal care, providing insights into maternal metabolic health and its impact on neonatal outcomes.

Article information and declarations

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical statement

The study was approved by the Changzhou Maternal and Child Health Care Hospital Institutional Review Board (approval date: December 30, 2020, approval number: 2020081). The studies were conducted in accordance with the local legislation and institutional requirements.

Author contributions

SJ participated in writing the manuscript. WL and KC conduct the study design. FW provides clinical information and data. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary material

None.

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Table 1. Weight distribution of the enrolled neonates

Variable	n (%)	Birthweight (g)	Statistic	p value
Total	475 (100)	3360.00 (3100.00, 3630.00)		
GDM			Z = 0.99	0.320
No	106 (22.32)	3310.00 (3075.00, 3590.00)		
Yes	369 (77.68)	3380.00 (3100.00, 3640.00)		
Para			Z = 6.99	0.136
One	296 (62.32)	3350.00 (3090.00, 3600.00)		
Two	154 (32.42)	3400.00 (3115.00, 3627.50)		
Three	23 (4.84)	3640.00 (3250.00, 3900.00)		
Four	1 (0.21)	3530.00 (3530.00, 3530.00)		
Five	1 (0.21)	3770.00 (3770.00, 3770.00)		
Delivery mode			Z = 16.60	< 0.001
Eutocia	251 (52.84)	3310.00 (3050.00, 3560.00)		
Cesarean	198 (41.68)	3410.00 (3172.50, 3770.00)		
Cesarean section following labor	26 (5.47)	3515.00 (3365.00, 3932.50)		
Neonata gender			Z = 2.09	0.036
Male	261 (55.06)	3400.00 (3130.00, 3680.00)		
Female	213 (44.94)	3330.00 (3050.00, 3580.00)		
Neonatal hypoglycemia			Z = 1.20	0.232
No	428 (90.11)	3350.00 (3087.50, 3632.50)		
Yes	47 (9.89)	3440.00 (3190.00, 3615.00)		
TYG index			Z = 5.94	< 0.001
< 2.06	223 (49.89)	3250.00 (3025.00, 3500.00)		

Variable	n (%)	Birthweight (g)	Statistic	p value
≥ 2.06	224 (50.11)	3475.00 (3245.00, 3800.00)		
HDL, mmol/L			Z = 2.52	0.012
< 1.99	220 (49.22)	3415.00 (3150.00, 3712.50)		
≥ 1.99	227 (50.78)	3330.00 (3045.00, 3575.00)		
Predelivery BMI, kg/m^2			Z = 6.92	< 0.001
< 27.68	237 (49.89)	3250.00 (3020.00, 3480.00)		
≥ 27.68	238 (50.11)	3490.00 (3242.50, 3800.00)		
Age, years			Z = 0.79	0.428
< 31	232 (48.84)	3350.00 (3075.00, 3605.00)		
≥ 31	243 (51.16)	3400.00 (3110.00, 3645.00)		

BMI — body mass index; GDM — gestational diabetes mellitus; HDL — high density lipoprotein; TYG — triglyceride-glucose

Table 2. Association of triglyceride-glucose with neonatal weight across subgroups

Variables	n (%)	Lower TYG (< 2.06)	Higher TYG (≥ 2.06)	β (95% CI)	p
All patients	447 (100.00)	3279.64 ± 371.76	3506.12 ± 443.83	144.45 (44.99–243.90)	0.005
GDM					
NO	106 (22.32)	3280.55 ± 386.67	3503.64 ± 303.69	281.17 (111.69–450.64)	0.002
YES	369 (77.68)	3279.20 ± 365.60	3506.54 ± 464.40	93.98 (–29.07–217.03)	0.136
Gender					
Male	261 (55.06)	3296.64 ± 370.07	3557.32 ± 451.81	213.06 (75.30–350.81)	0.003

Female	213 (44.94)	3257.96 ± 374.68	3440.20 ± 428.53	7.82 (–133.34–148.98)	0.914
Age					
< 31	232 (48.84)	3320.85 ± 381.06	3463.60 ± 466.77	38.56 (–113.45–190.56)	0.620
≥ 31	243 (51.16)	3234.15 ± 357.49	3540.40 ± 423.22	253.58 (122.18–384.99)	< 0.001

GDM subgroup — adjust for gender, age, pregnancies, gestational week, BMI, total cholesterol, HDL, SHR; gender subgroup — adjust for GDM, age, pregnancies, gestational week, BMI, total cholesterol, HDL, SHR; age subgroup — adjust for GDM, gender, pregnancies, gestational week, BMI, total cholesterol, HDL, SHR

BMI — body mass index; CI — confidence interval; GDM — gestational diabetes mellitus; HDL — high density lipoprotein; SHR — stress hyperglycemia ratio; TYG — triglyceride-glucose

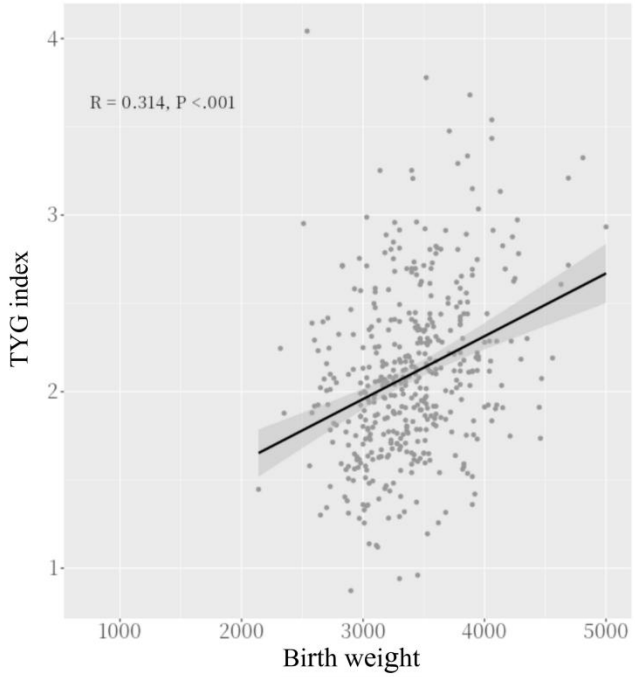

Figure 1. Correlation analysis between triglyceride-glucose index in the third trimester pregnant women and neonatal weight

TYG — triglyceride-glucose

Variables	β (95%CI)	P
TYG index	227.22 (148.74 ~ 305.71)	<0.001
HDL	-63.09 (-155.29 ~ 29.10)	0.180
Gender		
Male	Reference	
Female	-74.90 (-147.27 ~ -2.52)	0.043
Pregnancy weight gain	6.55 (1.36 ~ 11.74)	0.014
Predelivery BMI	25.53 (15.80 ~ 35.27)	<0.001

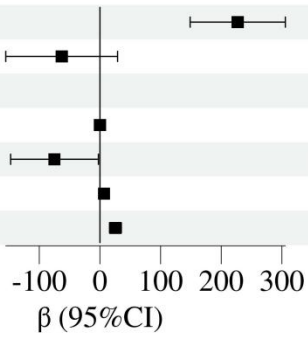

Figure 2. Association between neonatal weight and maternal triglyceride-glucose indexes in the third trimester using multivariate linear regression

BMI — body mass index; CI — confidence interval; HDL — high density lipoprotein; TYG — triglyceride-glucose

Variables	n (%)	Lower TYG	Higher TYG	β (95% CI)	P
All patients	447 (100.00)	3279.64 ± 371.76	3506.12 ± 443.83	226.47 (150.56 ~ 302.39)	<0.001
GDM					
NO	106 (22.32)	3280.55 ± 386.67	3503.64 ± 303.69	223.09 (73.78 ~ 372.40)	0.004
YES	369 (77.68)	3279.20 ± 365.60	3506.54 ± 464.40	227.34 (136.72 ~ 317.97)	<0.001
Gender					
Male	261 (55.06)	3296.64 ± 370.07	3557.32 ± 451.81	260.68 (157.96 ~ 363.39)	<0.001
Female	213 (44.94)	3257.96 ± 374.68	3440.20 ± 428.53	182.24 (70.03 ~ 294.45)	0.002
Age					
< 31	232 (48.84)	3320.85 ± 381.06	3463.60 ± 466.77	142.75 (29.92 ~ 255.57)	0.014
≥ 31	243 (51.16)	3234.15 ± 357.49	3540.40 ± 423.22	306.25 (204.02 ~ 408.49)	<0.001

Figure 3. Association between triglyceride-glucose index and neonatal weight across subgroups (no adjust)

CI — confidence interval; GDM — gestational diabetes mellitus; TYG — triglyceride-glucose