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ORIGINAL RESEARCH

Early Pregnancy Triglyceride to HDL-C Ratio Predicts Gestational Diabetes Mellitus and Neonatal Hypoglycemia: A Retrospective Cohort Study

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Objective: This study aimed to investigate the independent association between the early pregnancy triglyceride to high density lipoprotein cholesterol (TG/HDL-C) ratio and the risks of gestational diabetes mellitus (GDM) and neonatal hypoglycemia (NH), with a focus on its dose-response relationship and mediating pathways.

Methods: This retrospective cohort study included 17,056 women with singleton pregnancies who were registered and delivered at our hospital. Early pregnancy fasting lipid profiles were collected, and the TG/HDL-C ratio was calculated. Propensity score matching (PSM) was applied to balance baseline characteristics. Logistic regression, restricted cubic spline models, and mediation analysis were employed to assess associations, nonlinear relationships, and potential mediating pathways. Subgroup analyses were conducted to explore effect heterogeneity across populations with different clinical features.

Results: After PSM, balanced cohorts were obtained (10,131 cases for GDM analysis and 2,123 cases for NH analysis). A significant dose-response relationship was observed between increasing TG/HDL-C ratio quartiles and GDM risk. In the fully adjusted model after matching, the adjusted odds ratios (aORs) for Q2–Q4 were 1.20, 1.44, and 1.69, respectively (all $P < 0.05$). A nonlinear relationship was identified, with a threshold inflection point at 2.91; below this value, the risk increased more steeply. In contrast, the TG/HDL-C ratio was associated with NH only at the highest quartile (Q4: aOR = 1.39, $P < 0.05$), with no clear dose-response trend. Mediation analysis revealed that 11.14% of the effect of the TG/HDL-C ratio on NH was mediated through GDM, while the mediating effect of GH was minimal (1.41%).

Conclusion: An elevated TG/HDL-C ratio in early pregnancy is an independent risk factor for GDM, demonstrating a significant dose-response relationship with a nonlinear threshold. The inflection point of 2.91 may serve as a practical reference for early risk stratification. The association with NH is modest and partially mediated through GDM. Monitoring the TG/HDL-C ratio at the initial prenatal visit may facilitate early identification of high-risk individuals, enabling targeted interventions to reduce GDM incidence and potentially lower the risk of neonatal hypoglycemia through improved GDM management.

Keywords: triglyceride to HDL-C ratio, gestational diabetes mellitus, gestational hypertension, neonatal hypoglycemia, perinatal period

Introduction

Pregnancy involves continuous metabolic changes throughout the body. During the first trimester, a mother's lipid metabolism begins to adapt in preparation for the later stages of fetal growth.[1] The initial prenatal visit, typically scheduled in early pregnancy, offers an important opportunity to evaluate the mother's baseline metabolic health. Among the routine tests performed, the lipid profile is a key component. In non-pregnant individuals, the triglyceride to high-

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density lipoprotein cholesterol (TG/HDL-C) ratio is widely regarded as a sensitive indicator of insulin resistance and atherogenic dyslipidemia.[2,3] However, the clinical significance of this ratio when measured in early pregnancy—during the distinct physiological state of pregnancy—is not yet well understood. While some studies have reported associations between the TG/HDL-C ratio and adverse outcomes, findings remain inconsistent, likely due to variations in study design, gestational timing of measurements, and inadequate control for confounding factors.[4,5] Most existing studies focus on lipid changes in the second or third trimester and their link to pregnancy complications, often overlooking how early pregnancy metabolic patterns may influence the later course of pregnancy.[6] Clarifying the predictive role of the TG/HDL-C ratio in early gestation could aid in earlier identification and tailored management of pregnancy-related complications.

In recent years, a number of studies have examined the relationship between the TG/HDL-C ratio in early pregnancy and various pregnancy outcomes. However, their findings are inconsistent. Some prospective research indicates that a higher TG/HDL-C ratio in early pregnancy is an independent risk factor for gestational diabetes mellitus (GDM), with some suggesting it may have better predictive value than fasting glucose alone. For instance, a Chinese cohort study found a significant link between an elevated TG/HDL-C ratio measured at 8–14 weeks' gestation and a subsequently increased risk of GDM.[7] Conversely, other studies have failed to demonstrate a significant independent association after multivariable adjustment, suggesting that the relationship may be confounded by factors such as maternal obesity or that the predictive value of the TG/HDL-C ratio varies across different populations.[8,9] These studies have largely relied on standard multivariable adjustment to control for confounders, which may not fully account for the complex interplay among factors such as maternal age, pre-pregnancy BMI, parity, use of assisted reproductive technology, and socioeconomic status, leaving room for residual confounding. While existing literature recognizes that pre-pregnancy metabolic status can influence lipid metabolism during gestation, few studies have performed adequate stratification or interaction analyses when assessing the clinical relevance of the TG/HDL-C ratio.[10] In contrast, research on the association between this ratio and neonatal hypoglycemia (NH) remains scarce and inconsistent. Although maternal hypertriglyceridemia has been linked to an increased risk of NH, studies specifically examining the direct relationship between early-pregnancy TG/HDL-C ratios and NH are notably lacking.[11] More importantly, current studies tend to analyze pregnancy complications such as GDM and gestational hypertension (GH) —which is positioned in the present study as a potential secondary mediator rather than a primary outcome— in isolation. There is a lack of comprehensive research that systematically compares the predictive performance of the TG/HDL-C ratio for different pregnancy complications within the same cohort. A 2018 review highlighted the need for further studies to determine which metabolic biomarkers have specific predictive value for particular pregnancy outcomes.[12] Furthermore, the pathways connecting maternal and neonatal outcomes are not fully understood. Neonatal hypoglycemia can arise from fetal hyperinsulinemia in response to maternal hyperglycemia, but the role of maternal lipids in this process is less clear. The placenta plays a critical role in both glucose and lipid transfer; maternal dyslipidemia may alter the intrauterine metabolic environment, influencing fetal pancreatic development and metabolic programming. Evidence remains very limited as to whether early-pregnancy metabolic disturbances—particularly dyslipidemia—contribute to an altered intrauterine metabolic environment and thereby increase the risk of neonatal metabolic complications such as hypoglycemia. This represents a significant gap in current knowledge.

The present study aims to address these critical gaps by offering several novel contributions. First, unlike previous investigations that have primarily focused on GDM as an isolated outcome, this study systematically examines the association between the early-pregnancy TG/HDL-C ratio and both GDM and neonatal hypoglycemia within the same large cohort, thereby elucidating potential intergenerational metabolic links.[13] Second, by employing rigorous analytical approaches—including propensity score matching to minimize confounding and mediation analysis to explore underlying pathways—this study provides a more robust assessment of the independent predictive value of the TG/HDL-C ratio than has been previously possible. Third, this study specifically focuses on the early pregnancy window, a period when routine prenatal visits occur and when interventions could be implemented to mitigate subsequent risks. This focus addresses a significant limitation of studies that measure lipids later in gestation, when metabolic adaptations are already advanced.

To address these research gaps, the present study utilized a large retrospective obstetric cohort and employed multiple robust analytical approaches to investigate whether an elevated early-pregnancy TG/HDL-C ratio independently

increases the risk of GDM and whether this effect extends into the neonatal period. From a clinical and public health perspective, establishing the early-pregnancy TG/HDL-C ratio as a practical risk marker has substantial implications. Given the rising global burden of GDM and associated neonatal complications—particularly in middle-income countries undergoing rapid nutritional transitions—a simple, inexpensive biomarker measurable at the initial prenatal visit could facilitate early risk stratification. This would enable targeted metabolic monitoring and timely lifestyle interventions for high-risk individuals, potentially reducing the incidence of GDM and its neonatal sequelae. Such an approach aligns with the growing emphasis on preventive obstetric care and has the potential to improve maternal and neonatal outcomes on a population scale. Through this systematic exploration, we aim to clarify the association between the early-pregnancy TG/HDL-C ratio and both GDM and NH. The findings are expected to position the early-pregnancy TG /HDL-C ratio as a valuable, comprehensive early-risk marker. Such a marker could facilitate the identification of high-risk individuals in the initial stages of pregnancy, allowing for targeted metabolic monitoring and early intervention, ultimately contributing to better maternal and neonatal health outcomes.

Methods

The Study Population

This retrospective study was based on a cohort of 17,056 women with singleton pregnancies and cephalic presentation, who were registered and gave birth at our hospital between January 2022 and December 2024. Within this cohort, GDM was diagnosed in 3,389 women during the second or third trimester, and NH was identified in 710 newborns. The process of participant selection is outlined in Figure 1, which illustrates the stepwise process from initial eligibility assessment to the formation of the final analytical cohort. GDM was diagnosed according to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria, based on a 75-g oral glucose tolerance test performed at 24–28 weeks of gestation, with at least one value meeting or exceeding the following thresholds: fasting plasma glucose

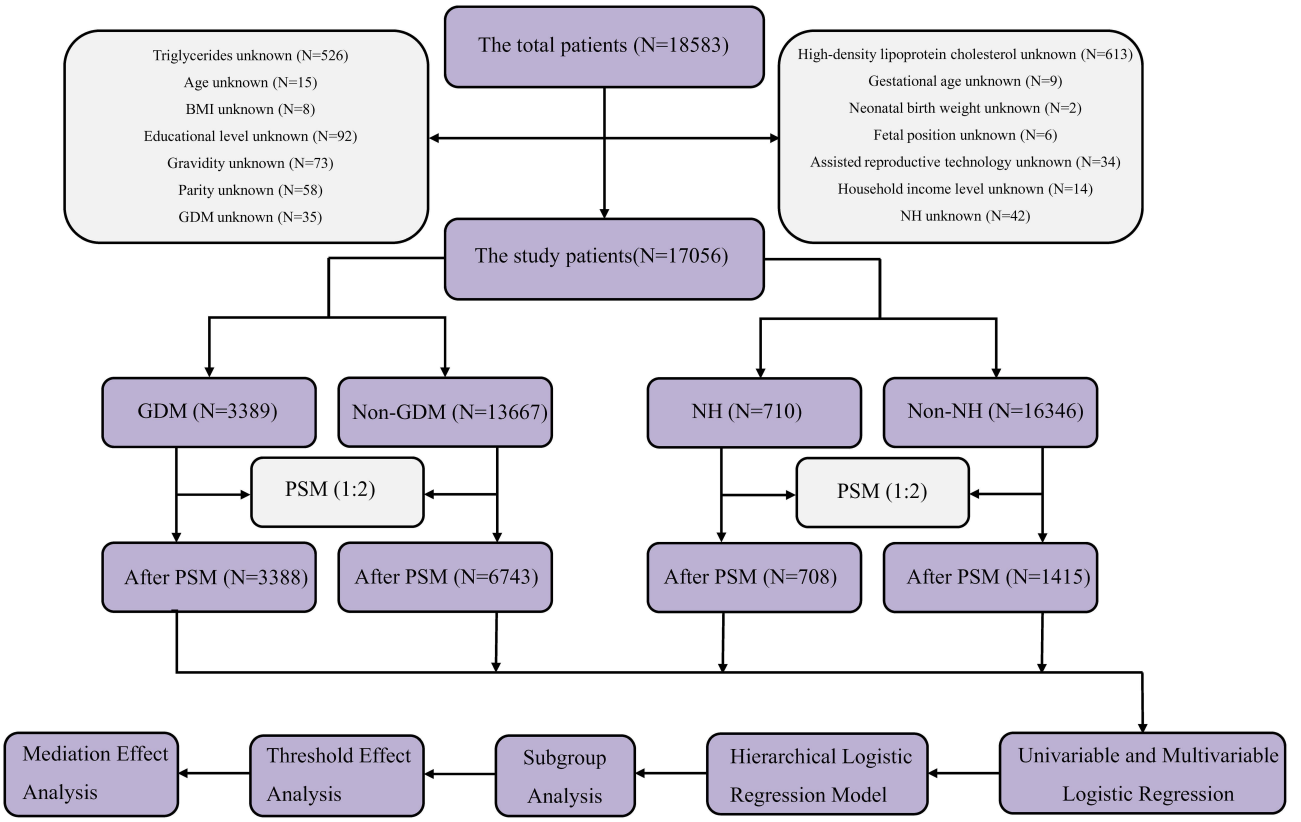

Figure 1 Flowchart of participant selection and analytical workflow. The diagram illustrates the inclusion and exclusion criteria, the 1:2 propensity score matching (PSM) process for both the Gestational Diabetes Mellitus (GDM) and Neonatal Hypoglycemia (NH) cohorts, and the subsequent statistical analyses performed.

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≥5.1 mmol/L, 1-hour plasma glucose ≥10.0 mmol/L, or 2-hour plasma glucose ≥8.5 mmol/L.[14] NH was defined as a plasma glucose level <2.6 mmol/L within the first 24 hours after birth, based on the clinical practice guidelines of the American Academy of Pediatrics.[15]

Data Collection

We conducted a retrospective analysis of clinically routine data extracted from the His electronic medical record system and nursing documentation to examine maternal and neonatal baseline characteristics. All lipid profiles were measured at the initial prenatal visit, which occurred at 8–12 weeks of gestation. Blood samples were collected after an overnight fast of at least 8 hours and analyzed using standard methods. The extracted variables included maternal age, body mass index (BMI), gravidity, parity (primiparous vs. multiparous), educational level, family economic status, reproductive method (assisted vs. natural conception), fetal position (cephalic vs. non-cephalic), gestational age, neonatal birth weight, infant sex, diagnosis of GDM, diagnosis of gestational hypertension (GH), diagnosis of NH, and the initial lipid metabolic profile at registration (triglycerides and high density lipoprotein cholesterol). All lipid measurements were obtained from a single blood sample collected at the initial prenatal visit. We acknowledge that this reliance on a single measurement limits our ability to capture dynamic changes in lipid metabolism throughout pregnancy. For the variable of family economic status, enrollment in a single-room special-care service during pregnancy was used as the criterion. This proxy was chosen based on the institutional context where this service represents a discretionary, out-of-pocket expenditure that is not covered by standard medical insurance, thereby reflecting the family's financial capacity to afford enhanced care. In the absence of direct income data in the medical records, this indicator served as a pragmatic proxy for above-average economic status. This service, involving specialized care from registration through delivery, incurs higher costs compared with standard maternity care. Participants who did not receive this service were categorized as having "average or below-average" economic status, while those who received it were classified as having "above-average" economic status. We recognize that using enrollment in a single-room special-care service as a proxy for family economic status may not fully capture the multidimensional nature of socioeconomic status. This approach represents an institutional proxy that reflects ability to pay for enhanced services, but it does not directly measure key socioeconomic dimensions such as household income, educational attainment, occupational status, or neighborhood-level deprivation indices. Future studies would benefit from incorporating more comprehensive and validated socioeconomic indicators to better account for economic diversity and reduce potential residual confounding. To ensure data accuracy and completeness, all extracted data underwent a standardized two-step quality control process. First, a resident physician and a midwife independently reviewed and extracted data from the electronic medical records, with any discrepancies between their extractions flagged for resolution. Second, a senior obstetrician and a senior midwife independently verified a random sample of 10% of the extracted records against the original source documentation; any systematic errors identified during this verification prompted a full review of the affected data fields. This process ensured a high level of data accuracy while maintaining feasibility for a large cohort. Given the relatively low proportion of missing data and its random distribution across key variables, a complete-case analysis approach was employed; records with any missing variables were excluded from the final analysis. Baseline characteristics were comparable between included and excluded participants, suggesting that the exclusion is unlikely to have introduced significant bias. Furthermore, due to the standardized data collection protocols at our institution, the overall completeness of the medical records was high, supporting the appropriateness of this analytical approach.

Statistical Analysis

Comprehensive descriptive analyses were conducted for all study participants. Continuous variables are presented as mean ± standard deviation (SD) and were compared using *t*-tests, while categorical variables are expressed as percentages and were analyzed using chi-square tests. To enhance statistical power and minimize bias in this observational study, we performed propensity score matching (PSM) using a 1:2 nearest-neighbor algorithm with a caliper width of 0.05.[16,17] Following matching, we assessed balance between groups using standardized mean differences (SMD), where an absolute SMD below 10% indicated acceptable balance of baseline characteristics. Univariable and multivariable logistic regression analyses were performed both before and after PSM to examine the associations between the

TG/HDL-C ratio and GDM, as well as NH. Restricted cubic spline analysis was further applied to explore potential linear and nonlinear relationships. Threshold effect analysis was conducted for associations exhibiting nonlinear patterns. Subgroup analyses were carried out based on all relevant covariates, including maternal age, BMI, gestational age, parity, and gravidity. We employed Bayesian mediation analysis, a method widely used in observational studies to enhance statistical power and reduce bias.[18,19] A p-value less than 0.05 was considered statistically significant. All statistical analyses were performed using R software, version 4.4.1.

Results

Overview of Key Findings

This study yielded several important findings regarding the association between the early-pregnancy TG/HDL-C ratio and adverse pregnancy outcomes. First, a significant and robust dose-response relationship was observed between elevated TG/HDL-C ratios and increased GDM risk, which persisted across multiple adjustment models and after rigorous confounding control. Second, nonlinear threshold effects were identified, revealing that the relationship between TG/HDL-C ratio and GDM risk is not linear and that risk increases vary across different ranges of the ratio. Third, the association between TG/HDL-C ratio and neonatal hypoglycemia was more modest and primarily mediated through GDM, with mediation analysis demonstrating that GDM accounts for approximately 11% of this relationship. Fourth, subgroup analyses identified BMI as a significant effect modifier, with stronger GDM risk associations observed in overweight and obese women.

Balance of Baseline Characteristics Before and After PSM in the Study Cohort

Table 1 presents a comparison of baseline characteristics between GDM and non-GDM groups before and after PSM. Before matching, significant differences ($P < 0.05$) were observed in several variables between the two groups. Specifically, the GDM group consisted of older women (≥35 years: 20.92% vs. 11.97%), had a higher proportion with a pre-pregnancy BMI ≥24 kg/m^2 (83.03% vs. 81.28%), exhibited higher gravidity (≥3 pregnancies: 34.52% vs. 26.36%) and parity (multiparous: 42.20% vs. 35.76%), and had a greater prevalence of assisted reproductive technology (ART) use (7.20% vs. 5.47%). However, the distributions of educational level and household income were comparable between groups ($P > 0.05$). Following 1:2 nearest-neighbor matching with a caliper of 0.05, which successfully matched 3,389 GDM cases with 6,743 non-GDM controls, all baseline variables—including age, BMI, obstetric history, and ART use—showed no statistically significant differences between the matched groups (all $P > 0.05$). Table 2 presents a comparison of baseline characteristics between groups with and without NH before and after PSM. Before matching, significant differences ($P < 0.05$) were observed in multiple covariates. The NH group had a higher proportion of advanced maternal age (≥35 years: 19.30% vs. 13.51%), higher gravidity (≥3 pregnancies: 34.65% vs. 27.69%) and parity (multiparous: 40.85% vs. 36.88%), and a lower proportion of high household income (8.87% vs. 14.33%). More importantly, the NH group exhibited significantly higher rates of comorbid GDM (29.72% vs. 19.44%) and GH (6.76% vs. 4.69%), as well as higher incidences of non-cephalic presentation (8.73% vs. 3.96%), preterm birth (≤37 weeks: 18.87% vs. 4.74%), and low birth weight (<2.5 kg: 13.94% vs. 3.69%). After PSM, a balanced cohort consisting of 708 infants with NH and 1,415 infants without NH was obtained. Figure 2 presents balance assessment results before and after PSM for different outcomes. Figure 2A displays the distribution of the TG/HDL-C ratio in relation to GDM before and after matching, while Figure 2B shows the SMD. Figure 2C illustrates the distribution of the TG/HDL-C ratio in relation to NH before and after matching, and Figure 2D presents the corresponding SMD. After matching, the distributions of the two groups largely overlapped, and all SMD values were below 0.1, indicating adequate balance of baseline characteristics between the matched groups and effective control of potential confounding bias.

Logistic Regression Analysis of the Triglyceride to HDL-C Ratio with GDM and NH: Univariate and Multivariate Models

Table 3 presents the logistic regression analysis of the association between the early-pregnancy TG/HDL-C ratio and GDM. Before PSM, univariate analysis indicated that multiple potential covariates, including age, BMI, obstetric history,

Table 1 Baseline Characteristics Before and After Propensity Score Matching in the Analysis of Triglyceride-to-HDL-C Ratio and Gestational Diabetes Mellitus

Variable	Before PSM				After PSM			
	Total (n = 17056)	Non-GDM (n = 13667)	GDM (n = 3389)	*P*	Total (n = 10131)	Non-GDM (n = 6743)	GDM (n = 3388)	*P*
Age, n (%)				<0.05				0.637
<35 years	14711 (86.25)	12,031 (88.03)	2680 (79.08)		8041 (79.37)	5361 (79.50)	2680 (79.10)	
≥35 years	2345 (13.75)	1636 (11.97)	709 (20.92)		2090 (20.63)	1382 (20.50)	708 (20.90)	
BMI, n (%)				<0.05				0.964
<24 kg/m^2	3134 (18.37)	2559 (18.72)	575 (16.97)		1714 (16.92)	1140 (16.91)	574 (16.94)	
≥24 kg/m^2	13922 (81.63)	11,108 (81.28)	2814 (83.03)		8417 (83.08)	5603 (83.09)	2814 (83.06)	
Gravidity, n (%)				<0.05				0.782
<3	12,283 (72.02)	10,064 (73.64)	2219 (65.48)		6654 (65.68)	4435 (65.77)	2219 (65.50)	
≥3	4773 (27.98)	3603 (26.36)	1170 (34.52)		3477 (34.32)	2308 (34.23)	1169 (34.50)	
Parity, n (%)				<0.05				0.766
Primipara	10738 (62.96)	8779 (64.24)	1959 (57.80)		5834 (57.59)	3876 (57.48)	1958 (57.79)	
Multipara	6318 (37.04)	4888 (35.76)	1430 (42.20)		4297 (42.41)	2867 (42.52)	1430 (42.21)	
Educational Level, n (%)				0.838				0.989
Below bachelor's degree	13369 (78.38)	10,717 (78.42)	2652 (78.25)		7928 (78.25)	5277 (78.26)	2651 (78.25)	
Bachelor's degree or higher	3687 (21.62)	2950 (21.58)	737 (21.75)		2203 (21.75)	1466 (21.74)	737 (21.75)	
Household Income Level, n (%)				0.872				0.741
Average	14650 (85.89)	11,742 (85.91)	2908 (85.81)		8709 (85.96)	5802 (86.04)	2907 (85.80)	
Above average	2406 (14.11)	1925 (14.09)	481 (14.19)		1422 (14.04)	941 (13.96)	481 (14.20)	
ART, n (%)				<0.05				0.460
No	16064 (94.18)	12,919 (94.53)	3145 (92.80)		9431 (93.09)	6286 (93.22)	3145 (92.83)	
Yes	992 (5.82)	748 (5.47)	244 (7.20)		700 (6.91)	457 (6.78)	243 (7.17)	

Abbreviations: CI, confidence intervals; OR, odds ratios; Quartiles, Q1 (0–25%), Q2 (25–50%), Q3 (50–75%), Q4 (75–100%); PSM, propensity score matching; GDM, Gestational Diabetes Mellitus; ART, Assisted reproductive technology.

Table 2 Baseline Characteristics Before and After Propensity Score Matching in the Analysis of Triglyceride-to-HDL-C Ratio and Neonatal Hypoglycemia

Variable	Before PSM				After PSM			
	Total (n = 17056)	Non-NH (n = 16346)	NH (n = 710)	*P*	Total (n = 2123)	Non-NH (n = 1415)	NH (n = 708)	*P*
Age, n (%)				<0.05				0.486
<35 years	14711 (86.25)	14,138 (86.49)	573 (80.70)		1697 (79.93)	1125 (79.51)	572 (80.79)	
≥35 years	2345 (13.75)	2208 (13.51)	137 (19.30)		426 (20.07)	290 (20.49)	136 (19.21)	
BMI, n (%)				0.103				0.741
<24 kg/m^2	3134 (18.37)	3020 (18.48)	114 (16.06)		334 (15.73)	220 (15.55)	114 (16.10)	
≥24 kg/m^2	13922 (81.63)	13,326 (81.52)	596 (83.94)		1789 (84.27)	1195 (84.45)	594 (83.90)	
Gravidity, n (%)				<0.05				0.813
<3	12,283 (72.02)	11,819 (72.31)	464 (65.35)		1381 (65.05)	918 (64.88)	463 (65.40)	
≥3	4773 (27.98)	4527 (27.69)	246 (34.65)		742 (34.95)	497 (35.12)	245 (34.60)	
Parity, n (%)				<0.05				0.746
Primipara	10738 (62.96)	10,318 (63.12)	420 (59.15)		1246 (58.69)	827 (58.45)	419 (59.18)	
Multipara	6318 (37.04)	6028 (36.88)	290 (40.85)		877 (41.31)	588 (41.55)	289 (40.82)	
Educational Level, n (%)				0.329				0.915
Below bachelor's degree	13369 (78.38)	12,802 (78.32)	567 (79.86)		1697 (79.93)	1132 (80.00)	565 (79.80)	
Bachelor's degree or higher	3687 (21.62)	3544 (21.68)	143 (20.14)		426 (20.07)	283 (20.00)	143 (20.20)	

(*Continued*)

Table 2 (Continued).

Variable	Before PSM				After PSM			
	Total (n = 17056)	Non-NH (n = 16346)	NH (n = 710)	*P*	Total (n = 2123)	Non-NH (n = 1415)	NH (n = 708)	*P*
Household Income Level, n (%)				<0.05				0.874
Average	14650 (85.89)	14,003 (85.67)	647 (91.13)		1937 (91.24)	1292 (91.31)	645 (91.10)	
Above average	2406 (14.11)	2343 (14.33)	63 (8.87)		186 (8.76)	123 (8.69)	63 (8.90)	
ART, n (%)				0.055				0.586
No	16064 (94.18)	15,407 (94.26)	657 (92.54)		1979 (93.22)	1322 (93.43)	657 (92.80)	
Yes	992 (5.82)	939 (5.74)	53 (7.46)		144 (6.78)	93 (6.57)	51 (7.20)	
GDM, n (%)				<0.05				0.217
No	13667 (80.13)	13,168 (80.56)	499 (70.28)		1456 (68.58)	958 (67.70)	498 (70.34)	
Yes	3389 (19.87)	3178 (19.44)	211 (29.72)		667 (31.42)	457 (32.30)	210 (29.66)	
GH, n (%)				<0.05				0.806
No	16242 (95.23)	15,580 (95.31)	662 (93.24)		1975 (93.03)	1315 (92.93)	660 (93.22)	
Yes	814 (4.77)	766 (4.69)	48 (6.76)		148 (6.97)	100 (7.07)	48 (6.78)	
Fetal Position, n (%)				<0.05				0.615
Cephalic presentation	16346 (95.84)	15,698 (96.04)	648 (91.27)		1952 (91.95)	1304 (92.16)	648 (91.53)	
Non−cephalic presentation	710 (4.16)	648 (3.96)	62 (8.73)		171 (8.05)	111 (7.84)	60 (8.47)	
Gestational Age, n (%)				<0.05				0.638
<=37 weeks	909 (5.33)	775 (4.74)	134 (18.87)		384 (18.09)	252 (17.81)	132 (18.64)	
>37 weeks	16147 (94.67)	15,571 (95.26)	576 (81.13)		1739 (81.91)	1163 (82.19)	576 (81.36)	
Infant Sex, n (%)				0.520				0.507
Male infant	8855 (51.92)	8478 (51.87)	377 (53.10)		1149 (54.12)	773 (54.63)	376 (53.11)	
Female infant	8201 (48.08)	7868 (48.13)	333 (46.90)		974 (45.88)	642 (45.37)	332 (46.89)	
Birth Weight, n (%)				<0.05				0.336
<2.5 kg	702 (4.12)	603 (3.69)	99 (13.94)		270 (12.72)	173 (12.23)	97 (13.70)	
≥2.5 kg	16354 (95.88)	15,743 (96.31)	611 (86.06)		1853 (87.28)	1242 (87.77)	611 (86.30)	

Abbreviations: CI, confidence intervals; OR, odds ratios; Quartiles, Q1 (0–25%), Q2 (25–50%), Q3 (50–75%), Q4 (75–100%); PSM, propensity score matching; GDM, Gestational Diabetes Mellitus; GH, Gestational Hypertension; ART, Assisted reproductive technology; NH, Neonatal Hypoglycemia.

and use of ART, were associated with GDM risk (all $P < 0.05$). In the multivariate model, parity was no longer significantly associated with GDM risk ($P > 0.05$). Both univariate and multivariate models consistently showed a significant and robust dose-response relationship between an elevated early-pregnancy TG/HDL-C ratio and GDM risk. In the multivariate-adjusted model, the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for Q2–Q4 were 1.21 (1.08–1.36), 1.45 (1.30–1.63), and 1.72 (1.54–1.92), respectively (all $P < 0.05$). After PSM, compared with the Q1 (lowest) group, the Q2, Q3, and Q4 groups exhibited significantly increased GDM risk, with a consistent dose-response trend and ORs increasing across quartiles, peaking in Q4. In the multivariate-adjusted model after matching, the aORs and 95% CIs for Q2–Q4 were 1.20 (1.06–1.36), 1.44 (1.28–1.63), and 1.69 (1.50–1.91), respectively (all $P < 0.05$). Table 4 presents the logistic regression analysis of the association between the early-pregnancy TG/HDL-C ratio and NH. Before PSM, univariate analysis showed that several potential covariates, including maternal age, obstetric history, household income status, pregnancy complications, fetal position, gestational age, and birth weight, were associated with NH risk (all $P < 0.05$). In the multivariate model, maternal age and parity were no longer significantly associated with NH risk ($P > 0.05$). Both univariate and multivariate analyses indicated that only the highest quartile (Q4) of the TG/HDL-C ratio was significantly associated with NH risk (univariate: OR = 1.51, 95% CI: 1.23–1.86; multivariate: aOR = 1.31, 95% CI: 1.06–1.63; both $P < 0.05$), with no evidence of a dose-response relationship across quartiles, suggesting a threshold effect rather than a graded association. After PSM, the association between Q4 of the TG/HDL-C ratio and NH remained significant (univariate: OR = 1.33, 95% CI: 1.03–1.71; multivariate: aOR = 1.39, 95% CI: 1.07–1.80; both $P < 0.05$), while Q2 and Q3 showed no statistically significant associations. These findings indicate that the association between TG/HDL-C ratio and NH is modest in magnitude and primarily driven by extreme elevations of the ratio.

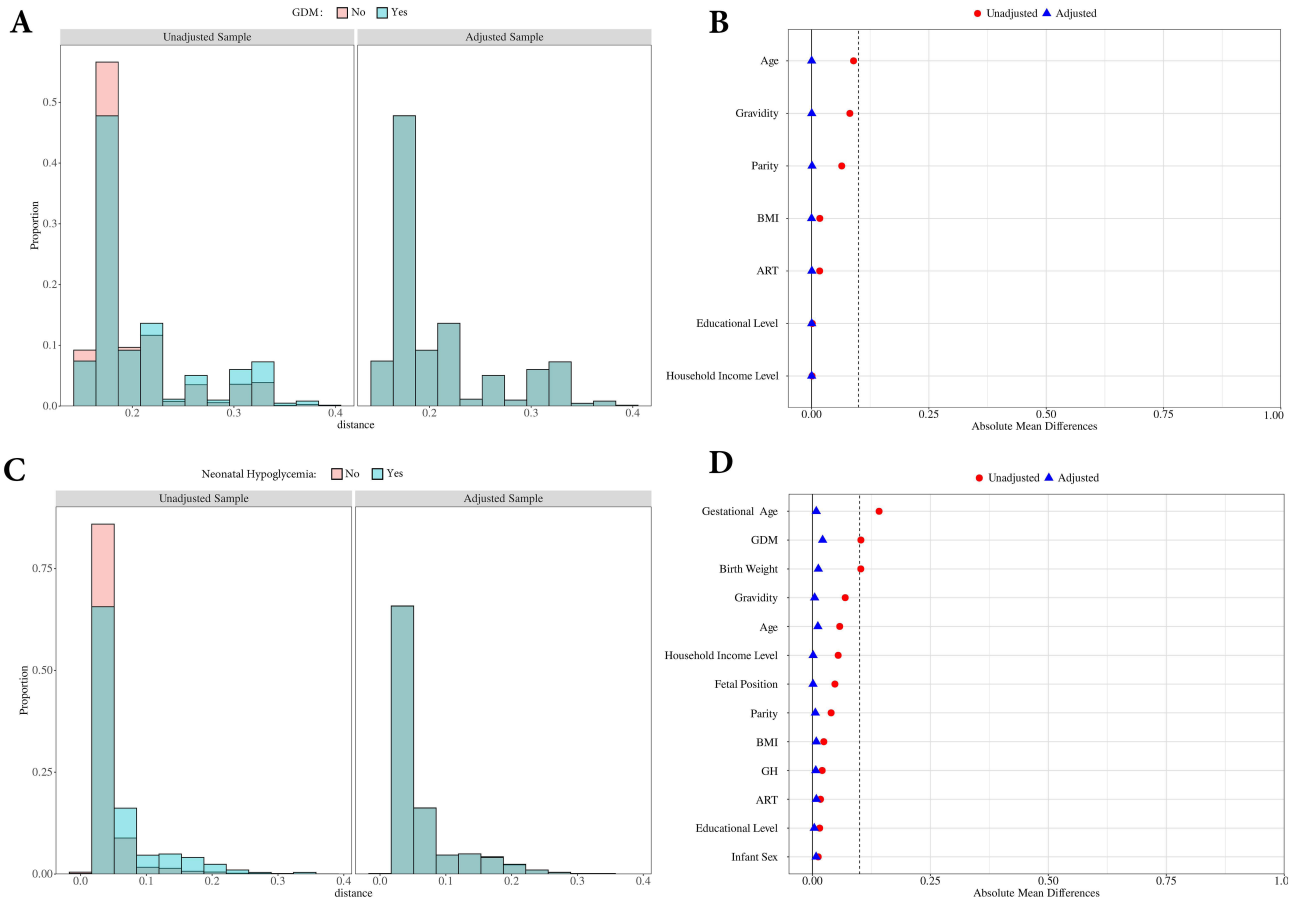

Figure 2 Balance assessment before and after propensity score matching (PSM). (**A**) Distribution of propensity scores for GDM vs. non-GDM groups before and after PSM. (**B**) Standardized mean differences (SMD) of baseline variables for the GDM analysis; SMD < 0.1 indicates good balance. (**C**) Distribution of propensity scores for NH vs. non-NH groups before and after PSM. (**D**) SMD of baseline variables for the NH analysis.

Hierarchical Regression Analysis of the Triglyceride to HDL-C Ratio with GDM and NH

Figure 3 presents stratified regression analysis results of the association strength between the early-pregnancy TG/HDL-C ratio and GDM as well as NH under different adjustment models. For GDM, in the unadjusted crude model (Model 1), increasing quartiles of the TG/HDL-C ratio were significantly associated with a dose-response-like increase in

Table 3 Univariate and Multivariate Logistic Regression Analysis of the Association Between TG/HDL-C Ratio and Gestational Diabetes Mellitus

Variable	Before PSM				After PSM			
	Univariate Logistic		Multivariable Logistic		Univariate Logistic		Multivariable Logistic	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age								
<35 years	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥35 years	1.95 (1.76 ~ 2.14)	<0.05	1.70 (1.53 ~ 1.89)	<0.05	1.02 (0.93 ~ 1.13)	0.637	1.01 (0.90 ~ 1.13)	0.870
BMI								
<24 kg/m^2	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥24 kg/m^2	1.13 (1.02 ~ 1.25)	<0.05	1.02 (0.92 ~ 1.13)	0.735	1.00 (0.89 ~ 1.11)	0.964	0.95 (0.85 ~ 1.06)	0.352

(*Continued*)

Table 3 (Continued).

Variable	Before PSM				After PSM			
	Univariate Logistic		Multivariable Logistic		Univariate Logistic		Multivariable Logistic	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Gravidity								
<3	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥3	1.47 (1.36 ~ 1.60)	<0.05	1.28 (1.15 ~ 1.43)	<0.05	1.01 (0.93 ~ 1.10)	0.782	1.02 (0.91 ~ 1.14)	0.775
Parity								
Primipara	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Multipara	1.31 (1.21 ~ 1.42)	<0.05	0.99 (0.89 ~ 1.10)	0.855	0.99 (0.91 ~ 1.07)	0.766	0.94 (0.84 ~ 1.06)	0.311
Educational Level								
Below bachelor's degree	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Bachelor's degree or higher	1.01 (0.92 ~ 1.11)	0.838	0.86 (0.78 ~ 0.95)	<0.05	1.00 (0.91 ~ 1.11)	0.989	0.98 (0.88 ~ 1.09)	0.675
Household Income Level								
Average	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Above average	1.01 (0.91 ~ 1.12)	0.872	1.09 (0.97 ~ 1.22)	0.137	1.02 (0.91 ~ 1.15)	0.741	1.04 (0.92 ~ 1.18)	0.520
ART								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.34 (1.15 ~ 1.56)	<0.05	1.20 (1.03 ~ 1.40)	<0.05	1.06 (0.90 ~ 1.25)	0.460	1.00 (0.85 ~ 1.18)	0.962
TG/HDL-C								
Q1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Q2	1.24 (1.10 ~ 1.39)	<0.05	1.21 (1.08 ~ 1.36)	<0.05	1.19 (1.06 ~ 1.35)	<0.05	1.20 (1.06 ~ 1.36)	<0.05
Q3	1.51 (1.35 ~ 1.69)	<0.05	1.45 (1.30 ~ 1.63)	<0.05	1.43 (1.27 ~ 1.61)	<0.05	1.44 (1.28 ~ 1.63)	<0.05
Q4	1.82 (1.63 ~ 2.03)	<0.05	1.72 (1.54 ~ 1.92)	<0.05	1.66 (1.48 ~ 1.87)	<0.05	1.69 (1.50 ~ 1.91)	<0.05

Abbreviations: CI, confidence intervals; OR, odds ratios; Quartiles, Q1 (0–25%), Q2 (25–50%), Q3 (50–75%), Q4 (75–100%); PSM, propensity score matching; ART, Assisted reproductive technology; TG/HDL-C, Triglyceride to High-Density Lipoprotein Cholesterol Ratio.

Table 4 Univariate and Multivariate Logistic Regression Analysis of the Association Between TG/HDL-C Ratio and Neonatal Hypoglycemia

Variable	Before PSM				After PSM			
	Univariate Logistic		Multivariable Logistic		Univariate Logistic		Multivariable Logistic	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age								
<35 years	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥35 years	1.53 (1.26 ~ 1.85)	<0.05	1.22 (0.98 ~ 1.51)	0.073	0.92 (0.73 ~ 1.16)	0.486	0.92 (0.72 ~ 1.18)	0.518
BMI								
<24 kg/m^2	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥24 kg/m^2	1.18 (0.97 ~ 1.45)	0.104	1.14 (0.92 ~ 1.40)	0.237	0.96 (0.75 ~ 1.23)	0.741	0.94 (0.73 ~ 1.21)	0.642
Gravidity								
<3	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥3	1.38 (1.18 ~ 1.62)	<0.05	1.28 (1.04 ~ 1.58)	<0.05	0.98 (0.81 ~ 1.18)	0.813	0.99 (0.77 ~ 1.27)	0.936
Parity								
Primipara	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Multipara	1.18 (1.01 ~ 1.38)	<0.05	0.95 (0.78 ~ 1.17)	0.655	0.97 (0.81 ~ 1.17)	0.746	0.98 (0.76 ~ 1.25)	0.839
Educational Level								
Below bachelor's degree	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Bachelor's degree or higher	0.91 (0.76 ~ 1.10)	0.329	0.77 (0.63 ~ 0.93)	<0.05	1.01 (0.81 ~ 1.27)	0.915	1.02 (0.81 ~ 1.29)	0.857
Household Income Level								
Average	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Above average	0.58 (0.45 ~ 0.76)	<0.05	0.65 (0.50 ~ 0.85)	<0.05	1.03 (0.75 ~ 1.41)	0.874	1.05 (0.76 ~ 1.45)	0.778

(*Continued*)

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Table 4 (Continued).

Variable	Before PSM				After PSM			
	Univariate Logistic		Multivariable Logistic		Univariate Logistic		Multivariable Logistic	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
ART								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.32 (0.99 ~ 1.76)	0.056	1.08 (0.80 ~ 1.45)	0.627	1.10 (0.77 ~ 1.57)	0.586	1.11 (0.77 ~ 1.59)	0.578
GDM								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.47 (1.09 ~ 1.99)	<0.05	1.30 (0.95 ~ 1.77)	0.096	0.88 (0.73 ~ 1.08)	0.218	0.87 (0.71 ~ 1.07)	0.186
GH								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.75 (1.48 ~ 2.07)	<0.05	1.57 (1.32 ~ 1.86)	<0.05	0.96 (0.67 ~ 1.37)	0.806	0.92 (0.64 ~ 1.32)	0.656
Fetal Position								
Cephalic presentation	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Non−cephalic presentation	2.32 (1.77 ~ 3.04)	<0.05	1.69 (1.27 ~ 2.24)	<0.05	1.09 (0.78 ~ 1.51)	0.615	1.06 (0.76 ~ 1.48)	0.727
Gestational Age								
<=37 weeks	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
>37 weeks	0.21 (0.17 ~ 0.26)	<0.05	0.33 (0.25 ~ 0.44)	<0.05	0.95 (0.75 ~ 1.19)	0.638	1.00 (0.75 ~ 1.33)	0.996
Infant Sex								
Male infant	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Female infant	0.95 (0.82 ~ 1.11)	0.520	0.95 (0.82 ~ 1.11)	0.524	1.06 (0.89 ~ 1.27)	0.507	1.08 (0.90 ~ 1.29)	0.435
Birth Weight								
<2.5 kg	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥2.5 kg	0.24 (0.19 ~ 0.30)	<0.05	0.59 (0.43 ~ 0.82)	<0.05	0.88 (0.67 ~ 1.15)	0.337	0.91 (0.66 ~ 1.27)	0.595
TG/HDL-C								
Q1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Q2	0.98 (0.78 ~ 1.24)	0.879	0.94 (0.75 ~ 1.19)	0.628	1.08 (0.83 ~ 1.40)	0.571	1.09 (0.84 ~ 1.42)	0.510
Q3	1.15 (0.92 ~ 1.43)	0.228	1.05 (0.84 ~ 1.31)	0.686	1.02 (0.79 ~ 1.32)	0.881	1.04 (0.80 ~ 1.35)	0.772
Q4	1.51 (1.23 ~ 1.86)	<0.05	1.31 (1.06 ~ 1.63)	<0.05	1.33 (1.03 ~ 1.71)	<0.05	1.39 (1.07 ~ 1.80)	<0.05

Abbreviations: CI, confidence intervals; OR, odds ratios; Quartiles, Q1 (0–25%), Q2 (25–50%), Q3 (50–75%), Q4 (75–100%); PSM, propensity score matching; GDM, Gestational Diabetes Mellitus; GH, Gestational Hypertension; ART, Assisted reproductive technology; TG/HDL-C, Triglyceride to High-Density Lipoprotein Cholesterol Ratio.

risk (pre-PSM Q2–Q4 ORs: 1.24, 1.51, 1.82; post-PSM: 1.19, 1.43, 1.66; all $P < 0.05$). After adjustment for demographic and obstetric factors (Model 2: age, BMI, gravidity, parity), the association remained highly significant though slightly attenuated (pre-PSM Q2–Q4 ORs: 1.21, 1.45, 1.70; post-PSM: 1.20, 1.44, 1.69; all $P < 0.05$). Further adjustment for socioeconomic and reproductive-related factors (Model 3: adding education level, household income, and assisted reproductive technology) yielded stable results (pre-PSM Q2–Q4 ORs: 1.21, 1.45, 1.72; post-PSM: 1.20, 1.44, 1.69; all $P < 0.05$), indicating that the association was robust across models and not confounded by the aforementioned covariates. For neonatal hypoglycemia, in the crude model (Model 1), only the highest quartile (Q4) was associated with increased risk (pre-PSM OR = 1.51, $P < 0.05$; post-PSM OR = 1.33, $P < 0.05$), with no dose-response trend. In both the partially adjusted (Model 2) and fully adjusted (Model 3) models, the Q4 group remained significantly associated (Model 2: pre-PSM OR = 1.42, post-PSM OR = 1.36, $P < 0.05$; Model 3: pre-PSM OR = 1.31, post-PSM OR = 1.39, $P < 0.05$), whereas no significant associations were observed for the Q2 and Q3 groups.

Threshold Effect Analysis Before and After Propensity Score Matching

Figure 4 illustrates the dose-response relationship and threshold effect between the early-pregnancy TG/HDL-C ratio and GDM risk using restricted cubic spline models. Before matching (Figure 4A), a significant nonlinear association was observed between the TG/HDL-C ratio and GDM risk (overall $P < 0.001$, nonlinear $P < 0.001$), with a threshold identified at 1.21. Below this threshold, risk increased sharply (OR = 1.79, 95% CI: 1.41–2.27, $P < 0.05$); above it, the association

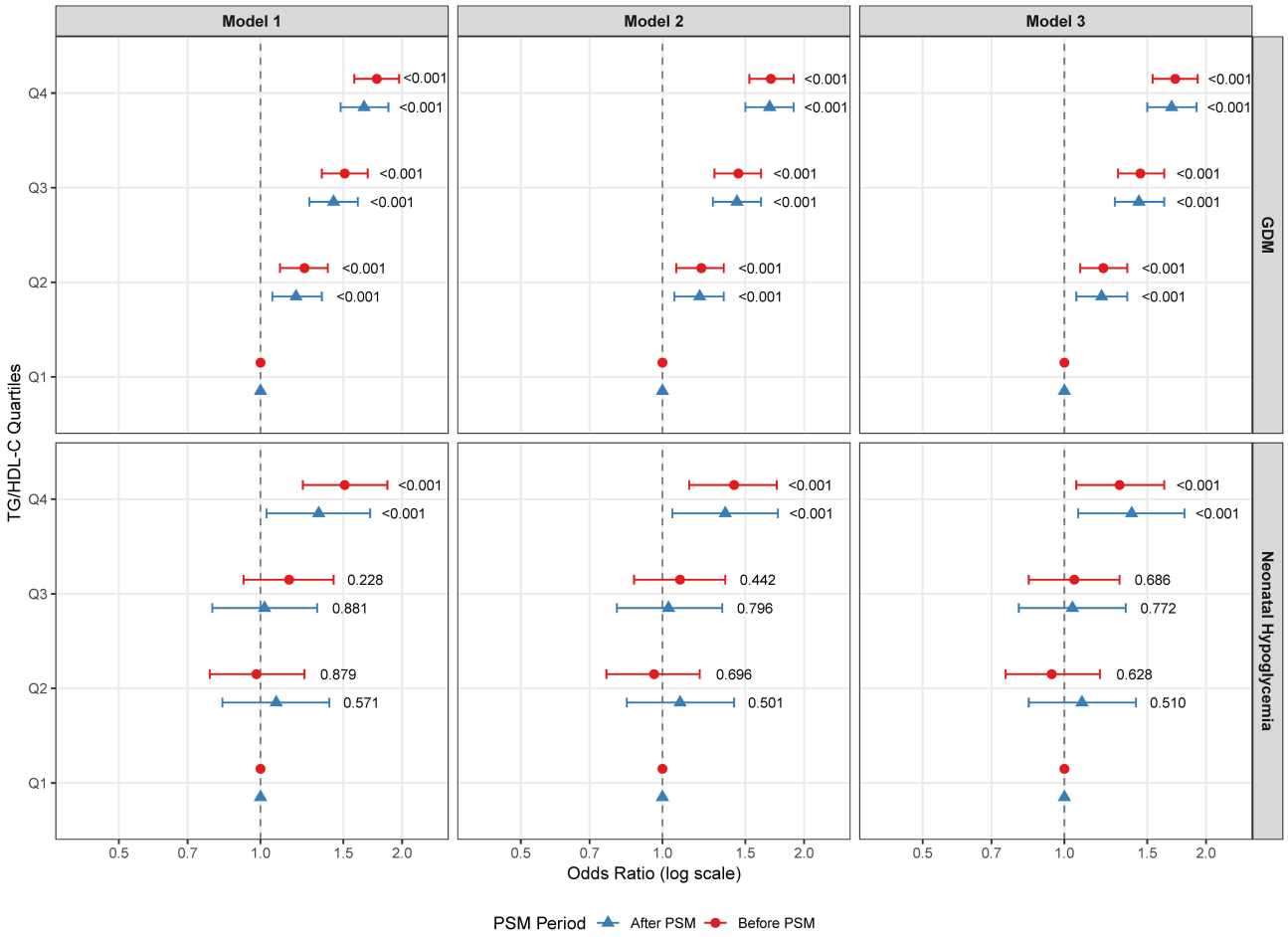

Figure 3 Association of TG/HDL-C quartiles with GDM and NH across different adjustment models. Odds ratios (ORs) with 95% confidence intervals for (Top) GDM and (Bottom) NH according to TG/HDL-C quartiles (Q1 as reference), before and after PSM. Model 1 (unadjusted); Model 2 (adjusted for age, BMI, gravidity, and parity); Model 3 (further adjusted for educational level, household income, and assisted reproductive technology). (Bottom panel) Odds ratios for neonatal hypoglycemia before and after PSM across the same quartiles and models: Model 1 (unadjusted); Model 2 (adjusted for age, BMI, gravidity, parity, educational level, household income, and assisted reproductive technology); Model 3 (fully adjusted for the variables in Model 2 plus gestational hypertension, gestational diabetes, fetal po-sition, gestational age, neonatal birth weight, and infant sex). The consistent dose-response trend for GDM contrasts with the weaker, quartile-specific association for NH.

remained significant but was notably attenuated (OR = 1.14, 95% CI: 1.07–1.21, $P < 0.05$). After matching (Figure 4B), the nonlinear association remained significant (overall $P < 0.001$, nonlinear $P = 0.002$), but the threshold shifted to 2.91. A significant positive association with GDM risk was observed only when the ratio was below this threshold (OR = 1.34, 95% CI: 1.24–1.44, $P < 0.05$); above 2.91, the association was no longer significant (OR = 1.03, 95% CI: 0.86–1.23, $P > 0.05$). These results indicate a nonlinear dose-response relationship between the early-pregnancy TG/HDL-C ratio and GDM risk, which is influenced by confounding factors. After controlling for confounders, the risk effect was mainly concentrated in the moderate-to-low range of the ratio (below 2.91), suggesting that this value may serve as a potential reference threshold for clinical risk assessment.

Mediation Effect Analysis

Figure 5 presents the results of a mediation analysis examining the role of GDM and GH in the association between early pregnancy lipid parameters and NH. Both GDM and GH were found to act as mediators in the relationship between the TG/HDL-C ratio and NH, but the strength of their mediating effects differed significantly. GDM emerged as the more important mediating factor. In the association between the TG/HDL-C ratio and NH (Figure 5A), the proportion mediated by GDM was 11.143% (indirect effect = 0.0063, $P < 0.05$). Similarly, when examining individual lipid components, GDM accounted for 10.042% (indirect effect = 0.0039, $P < 0.05$) of the association between triglycerides (TG) and NH (Figure 5B) and for

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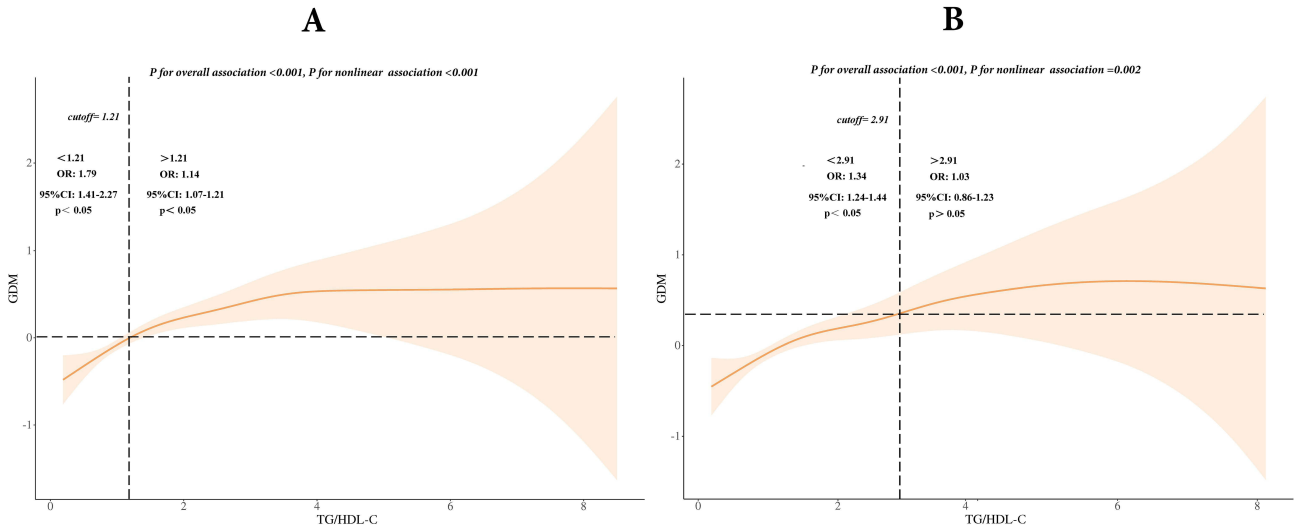

Figure 4 Nonlinear dose-response relationship and threshold effect analysis between TG/HDL-C ratio and GDM risk using restricted cubic splines, before and after PSM. (**A**) Before PSM: The overall association (P < 0.001) and nonlinear association (P < 0.001) were significant. A threshold was identified at TG/HDL-C = 1.21, below which the risk increased sharply (P < 0.05) and above which the increase was attenuated (P < 0.05). (**B**) After PSM: The overall (P < 0.001) and nonlinear (P = 0.002) associations remained significant. The threshold shifted to TG/HDL-C = 2.91, with a significant positive association below this point (P < 0.05) and no significant association above it (P > 0.05).

21.005% of the association between HDL-C and NH (Figure 5C). In contrast, the mediating role of GH was minimal. In the three respective pathways described above (Figures 5D–F), the proportions mediated by GH were only 1.413%, 1.468%, and 3.960%. These findings suggest that the increased risk of neonatal hypoglycemia associated with elevated TG/HDL-C ratio and TG levels in early pregnancy is partly mediated through the development of GDM, underscoring the significant role of GDM as a mediator, while the contribution of GH remains limited. Importantly, these results indicate that the association between TG/HDL-C ratio and NH is predominantly indirect, acting through GDM, rather than a direct effect. This explains the modest and inconsistent direct associations observed in the primary analyses and highlights that GDM is the key intermediate pathway linking maternal dyslipidemia to neonatal metabolic outcomes.

Subgroup Analyses Before and After PSM

Figure 6 illustrates the results of subgroup analyses examining the association between the early-pregnancy TG/HDL-C ratio and GDM risk across different populations, separately before (Figure 6A) and after (Figure 6B) PSM. In the overall population before PSM (n = 17,056), each one-unit increase in the TG/HDL-C ratio was associated with a 49% increase in GDM risk (OR = 1.49, 95% CI: 1.38–1.61, P < 0.001). This association persisted in most subgroups, with particularly pronounced effects in women who were overweight/obese (BMI > 24 kg/m^2; OR = 1.57, P < 0.05) and those who underwent assisted reproductive technology (ART; OR = 1.75, P < 0.05). Notably, no significant association was observed in the subgroup with BMI ≤ 24 kg/m^2 (OR = 1.13, P = 0.18). Interaction tests indicated that BMI was a significant effect modifier (P for interaction = 0.002). After PSM (n = 10,131), the overall association remained highly significant though slightly attenuated (OR = 1.41, 95% CI: 1.30–1.53, P < 0.001). Subgroup trends were largely consistent with those observed before matching: significant associations were maintained in women with BMI > 24 kg/m^2 (OR = 1.49) and those who underwent ART (OR = 1.52), while no significant association was found in the BMI ≤ 24 kg/m^2 subgroup (OR = 1.08, P = 0.463). The modifying effect of BMI remained significant after matching (P for interaction = 0.005), further confirming its role in modulating the association. Other factors, including obstetric history, educational level, and household income, did not show significant effect modification (all interaction P > 0.05). Figure 7 presents subgroup analyses exploring variations in the association between the early-pregnancy TG/HDL-C ratio and NH across different clinical characteristics. Before matching (Figure 7A, n = 17,056), a higher TG/HDL-C ratio was significantly associated with increased NH risk in the overall population (OR = 1.34, 95% CI: 1.15–1.56, P < 0.001). This association persisted across several subgroups, including women aged > 35 years, those with BMI > 24 kg/m^2, primiparous women, women

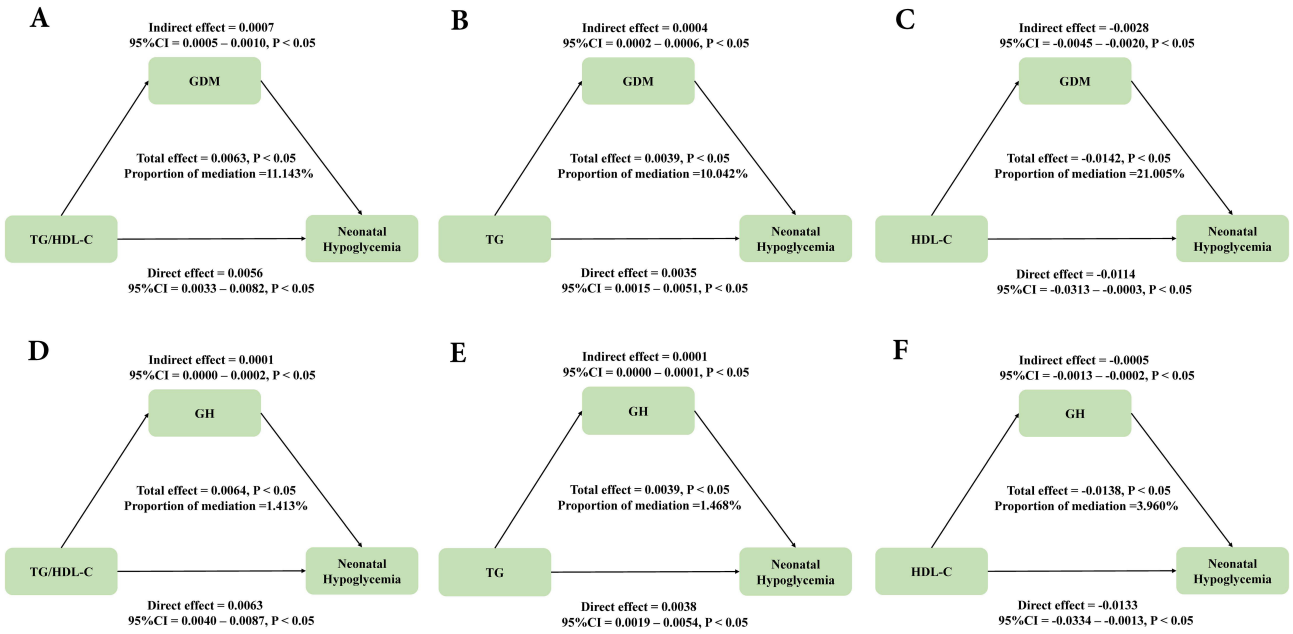

Figure 5 Mediation analysis of the TG/HDL-C-NH association by gestational diabetes mellitus (GDM) and gestational hypertension (GH). Path diagrams display the direct, indirect (mediated), and total effects, with the proportion of mediation. (**A**–**C**) show GDM as a significant mediator for the effects of TG/HDL-C, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) on NH. (**D**–**F**) show the minimal mediating role of GH. The findings indicate that the association between TG/HDL-C and NH is modest and primarily mediated through GDM.

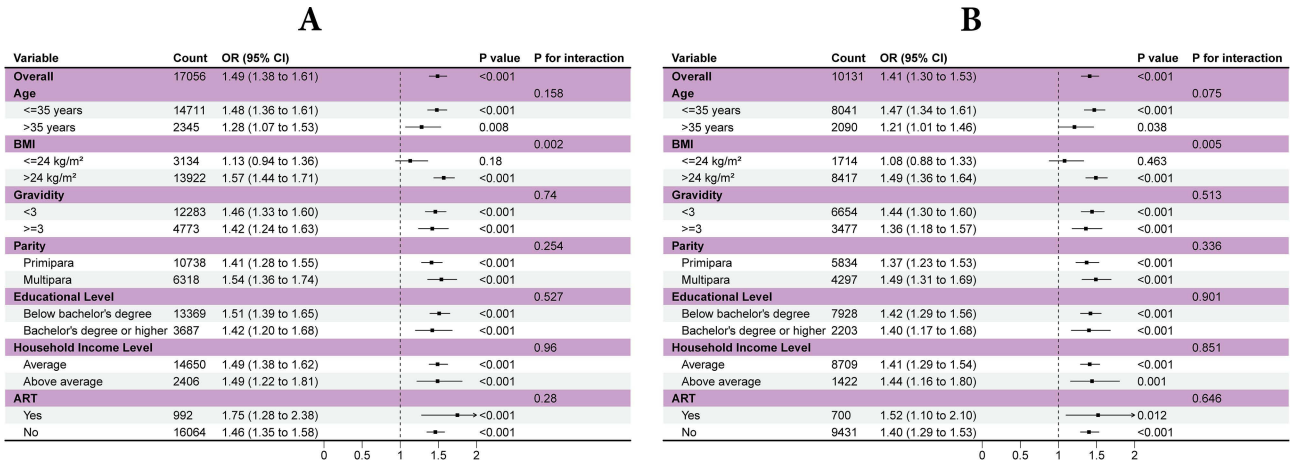

Figure 6 Subgroup analysis of the association between the TG/HDL-C ratio and GDM before and after PSM. (**A**) Forest plot showing odds ratios (OR) and 95% confidence intervals for the association between the TG/HDL-C ratio and GDM across various subgroups before PSM. (**B**) Forest plot showing ORs and 95% confidence intervals for the same association after PSM.

with fewer than three pregnancies, and mothers of male infants. However, no statistically significant associations were observed in subgroups such as women with BMI ≤ 24 kg/m^2, higher education levels, higher household income, those who underwent ART, non-cephalic fetal presentation, or preterm delivery. After matching (Figure 7B, n = 2,132), the association was no longer significant in the overall population (OR = 1.12, 95% CI: 0.81–1.34, P = 0.214), and most subgroup associations were either attenuated or disappeared. Significant positive associations were retained only in two subgroups: male infants (OR = 1.28, 95% CI: 1.00–1.65, P = 0.048) and low birth weight (<2.5 kg; OR = 1.70, 95% CI: 1.03–2.81, P < 0.05). These findings underscore the modest and inconsistent nature of the association between TG/HDL-C ratio and NH across different populations, particularly after rigorous confounding control.

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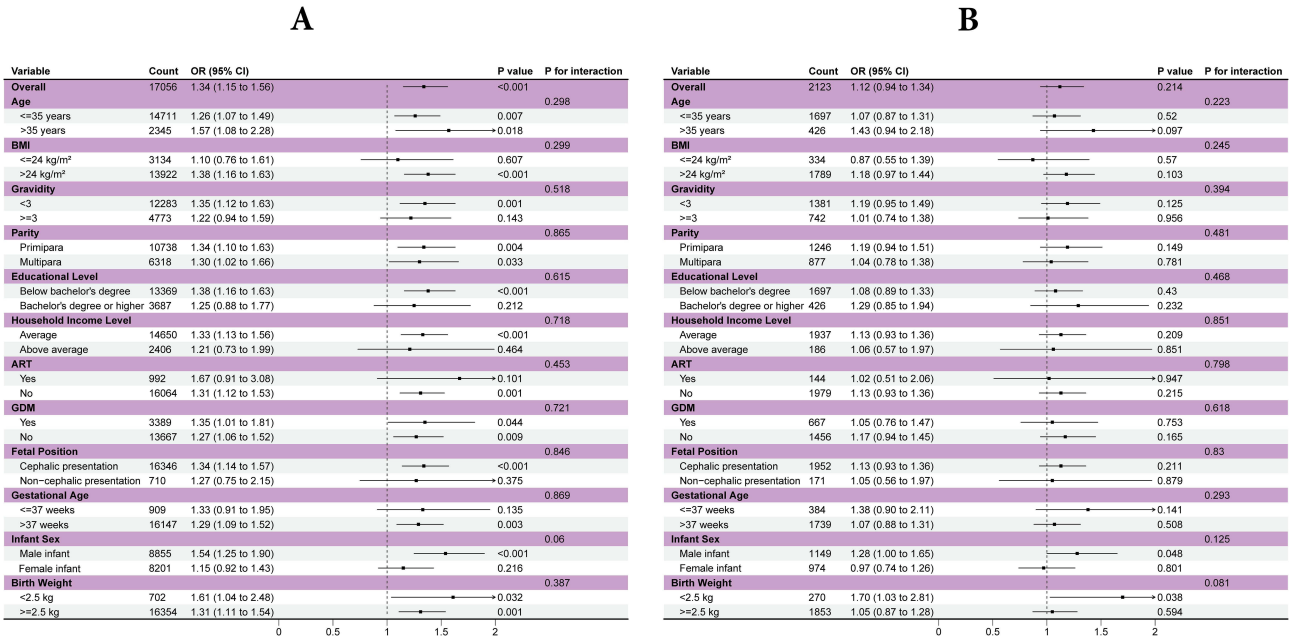

Figure 7 Subgroup analysis of the association between the TG/HDL-C ratio and neonatal hypoglycemia before and after PSM. (**A**) Forest plot showing odds ratios (OR) and 95% confidence intervals for the association between the TG/HDL-C ratio and neonatal hypoglycemia across various subgroups before PSM. (**B**) Forest plot showing ORs and 95% confidence intervals for the same association after PSM.

Discussion

This study confirms that an elevated early-pregnancy TG/HDL-C ratio independently increases the risk of GDM, demonstrating both a clear dose–response relationship and a nonlinear threshold effect. This robust finding represents the primary contribution of our study and offers a useful serological marker for the early detection of metabolic disturbances in pregnancy. From a pathophysiological standpoint, a raised TG/HDL-C ratio reflects concurrent dysregulation of lipid metabolism and insulin resistance. Early-pregnancy dyslipidemia can worsen insulin resistance through several mechanisms. Elevated free fatty acids, for example, can interfere with insulin signaling and reduce glucose uptake in peripheral tissues. Additionally, ectopic lipid deposition may disrupt the normal secretion of adipokines, further impairing glucose homeostasis.[20–22] Beyond these established mechanisms, the TG/HDL-C ratio may also serve as a marker of systemic inflammation and oxidative stress, both of which contribute to pancreatic β-cell dysfunction and impaired insulin secretion.[23] Furthermore, emerging evidence suggests that an elevated TG/HDL-C ratio reflects lipoprotein particle size and composition abnormalities—specifically, an abundance of small, dense LDL particles and reduced large buoyant HDL particles—which may independently affect placental function and nutrient transfer. These pathophysiological insights position the TG/HDL-C ratio not merely as a correlate of insulin resistance but as an integrative marker of metabolic health with direct implications for the intrauterine environment.[24]

Our subgroup analysis indicates that the association between the TG/HDL-C ratio and GDM risk is particularly strong in women who are overweight or obese (BMI > 24 kg/m^2), while no significant association was observed in those with normal weight. This result aligns with earlier research.[25] Overweight status is itself linked to chronic low-grade inflammation and insulin resistance; the additional metabolic burden of early-pregnancy dyslipidemia may therefore amplify the overall risk. The nonlinear pattern identified through restricted cubic spline modeling suggests that GDM risk rises substantially as the TG/HDL-C ratio increases up to a threshold of 2.91, beyond which the risk appears to plateau. While this plateau may indicate the activation of compensatory metabolic pathways, this explanation remains speculative and requires further investigation through mechanistic studies.[26] In contrast to the robust GDM findings, the relationship between the TG/HDL-C ratio and NH was more complex and should be interpreted with caution. Given the modest nature of this association and the lack of a graded relationship, these findings should be considered exploratory and hypothesis-generating rather than definitive. Unlike GDM, only the highest quartile (Q4) of the TG/HDL-C ratio was

independently associated with NH risk, without a clear dose–response pattern. This difference may reflect the multifactorial nature of NH. Neonatal glucose regulation depends not only on the maternal metabolic milieu but also on fetal insulin secretion, placental glucose transfer efficiency, and birth-related stress.[27] Our mediation analysis offered a mechanistic explanation: the impact of the TG/HDL-C ratio on NH was largely indirect, mediated through GDM, which accounted for approximately 11.14% of the total effect. This finding suggests that the primary pathway linking maternal dyslipidemia to neonatal hypoglycemia operates through the development of GDM, rather than through a direct effect of lipids on neonatal glucose regulation. This is consistent with earlier studies suggesting that maternal hyperglycemia can cross the placenta, stimulate fetal β-cell proliferation, and lead to neonatal hyperinsulinemia and subsequent hypoglycemia.[28] Notably, GH played only a minor mediating role (mediation proportion < 4%), indicating that while GH and GDM share some pathophysiological overlap, disturbances in glucose metabolism likely represent a more direct pathway affecting neonatal glucose homeostasis.[29] Subgroup analysis also showed that after matching, the association between the TG/HDL-C ratio and NH was generally attenuated but remained statistically significant in male infants and in those with low birth weight. These exploratory findings suggest that fetal sex and growth status may modify the observed relationship, but they require validation in larger, dedicated studies before any clinical recommendations can be made.[30]

The unique contribution of this study compared with previous research lies in its simultaneous elucidation of dose-response relationships, nonlinear threshold effects, and mediating pathways linking early-pregnancy dyslipidemia to both maternal and neonatal outcomes within a single large cohort. While previous systematic reviews have comprehensively summarized the association between maternal metabolic factors and GDM risk,[31] and large-scale epidemiologic studies have established the global burden of GDM and its adverse pregnancy outcomes,[32] this study provides deeper mechanistic insights. Specifically, it demonstrates that the relationship with neonatal hypoglycemia is primarily indirect and mediated through GDM, and it identifies a specific threshold value of 2.91 that may inform clinical risk stratification. This integrated approach—examining dose-response, threshold, and mediation effects simultaneously—extends beyond the scope of prior research and positions the TG/HDL-C ratio not only as a predictor of GDM but also as a marker with implications for downstream neonatal outcomes. From a clinical translational perspective, the identification of 2.91 as a potential cutoff value offers a practical reference point for early pregnancy risk assessment. For example, women with a TG/HDL-C ratio approaching or exceeding this threshold at their initial prenatal visit could be flagged for closer metabolic monitoring, receive targeted lifestyle counseling, and undergo earlier oral glucose tolerance testing. Integrating this simple, inexpensive biomarker into routine antenatal screening pathways could enhance risk stratification without adding significant burden to clinical workflows. However, this threshold requires external validation in diverse populations before it can be recommended for widespread clinical implementation. By using propensity score matching, we effectively minimized baseline confounding. Additionally, stratified regression and mediation analysis contributed multidimensional evidence to support a mechanistic understanding. Integrating the TG/HDL-C ratio—an easily accessible marker—into early-pregnancy GDM risk assessment could improve the timely identification and management of high-risk individuals.[33] However, the NH findings, while novel, should be viewed as preliminary and requiring confirmation in future studies.

As a single-center retrospective study, several limitations should be acknowledged. First, the single-center design limits the generalizability of our findings to other populations and clinical settings, underscoring the need for external validation in multicenter cohorts across diverse geographic regions and ethnic groups. Second, lipid levels were measured only once at the early pregnancy registration visit, preventing an assessment of dynamic lipid changes across gestation and their potential impact on pregnancy outcomes. Third, although we adjusted for multiple known confounders, unmeasured lifestyle factors such as dietary patterns, physical activity levels, and socioeconomic variables could still introduce residual confounding. Fourth, the lack of data on pre-pregnancy metabolic status limits our ability to distinguish whether the observed associations reflect pre-existing conditions versus pregnancy-induced metabolic changes. Fifth, differences in diagnostic criteria and monitoring practices for neonatal hypoglycemia may exist across clinical settings.[34] Sixth, the modest and inconsistent nature of the NH findings, particularly after propensity score matching, underscores the need for cautious interpretation and further validation. Future research should prioritize the following directions: (1) validating the threshold effect of 2.91 using large, multicenter prospective cohorts across diverse

populations to establish generalizability and, if needed, population-specific cutoffs; (2) conducting prospective cohort studies with serial lipid measurements throughout pregnancy to examine how dynamic changes in the TG/HDL-C ratio relate to GDM development and neonatal outcomes; (3) designing randomized controlled trials to assess whether early interventions guided by the TG/HDL-C ratio—such as lifestyle modification, dietary counseling, or pharmacotherapy—can effectively reduce GDM incidence and improve perinatal outcomes; and (4) exploring the biological mechanisms underlying the observed associations through multi-omics approaches, including genomics, metabolomics, and proteomics, to identify novel therapeutic targets.[35] Moreover, combining these approaches could help clarify the molecular mechanisms linking dyslipidemia to pregnancy-related metabolic disorders and may uncover new targets for personalized prevention and treatment.

Conclusion

The results of this study demonstrate that a high TG/HDL-C ratio in early pregnancy independently predicts GDM, showing both a clear dose–response pattern and nonlinear threshold effects. In contrast, the association with neonatal hypoglycemia was more modest and largely indirect, mediated primarily through GDM rather than a direct effect. The key contribution of this study is the simultaneous elucidation of dose-response relationships, threshold effects, and mediating pathways linking early-pregnancy dyslipidemia to both maternal and neonatal outcomes. These findings position the TG/HDL-C ratio as a practical early-pregnancy marker for identifying women at elevated GDM risk. The identified threshold of 2.91 may serve as a reference point for risk stratification in similar populations, though validation in diverse settings is warranted. Incorporating TG/HDL-C measurement into routine early-pregnancy screening could facilitate timely identification of high-risk individuals, enabling targeted interventions to reduce GDM incidence and potentially lower the risk of neonatal hypoglycemia through improved GDM management. Future prospective studies are needed to confirm whether this risk stratification approach effectively improves perinatal outcomes.

Abbreviations

GDM, gestational diabetes mellitus; BMI, body mass index; CI, confidence intervals; OR, odds ratios; Quartiles, Q1 (0-25%), Q2 (25-50%), Q3 (50-75%), Q4 (75-100%); PSM, propensity score matching; GH, gestational hypertension; ART, assisted reproductive technology; NH, neonatal hypoglycemia; PSM, propensity score matching; TG/HDL-C, triglyceride to high-density lipoprotein cholesterol ratio.

Data Sharing Statement

Relevant data from this study can be obtained from the corresponding author.

Ethics Statement

This retrospective study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Shaoxing Maternal and Child Health Hospital (IRB-AF/35-2.0). The research involved analysis of anonymized medical records and did not include human participants or animal trials. The ethics committee waived the requirement for informed consent given the retrospective nature of the study. All data were handled in compliance with institutional guidelines and regulations for patient data confidentiality.

Author Contributions

Lingxiang Jiang: Data Curation, Methodology, Formal Analysis, Visualization, Writing - Original Draft, Writing - Review & Editing; Hui Shao: Data Curation, Investigation, Visualization,Writing - Original Draft; Xiujuan Wang: Data Curation, Methodology, Writing - Original Draft; Junjiang Wu: Data Curation, Investigation, Writing - Original Draft; Fen Dong: Conceptualization, Methodology, Resources, Supervision, Funding Acquisition, Writing - Review & Editing. All authors 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.

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Disclosure

No conflict of interests is declared.

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