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# Association Between Total Cholesterol–to–High-Density Lipoprotein Ratio and Gestational Hypertension: A Case-Control Study

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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**Background:** While dyslipidemia has been implicated in gestational hypertension (GH), individual lipid parameters show inconsistent associations. The total cholesterol to high-density lipoprotein cholesterol (TC/HDL-C) ratio may better reflect this association. This study assessed the association between the TC/HDL-C ratio and GH.

**Material/Methods:** This case-control study included 307 women with GH and 307 normotensive pregnant women as controls in China (2021-2024). Blood samples were collected after 20 weeks of gestation. The TC/HDL-C ratio was calculated and categorized into quintiles. Multivariable logistic regression models were used to examine the association between TC/HDL-C ratio and GH, adjusting for potential confounders. Restricted cubic splines (RCS) were employed to assess non-linear associations. Subgroup analyses were performed to evaluate whether this association varied among participants with different characteristics.

**Results:** Higher TC/HDL-C ratio was positively associated with GH (odds ratio [OR]: 1.44, 95% confidence interval [CI]: 1.11-1.88, *P*=0.006), consistent across 3 models. The odds of GH progressively increased with rising quintiles of TC/HDL-C ratio. RCS curves revealed a linear relationship, with higher ratios associated with increased GH odds. Subgroup analyses showed that this association exhibited significant variations among subgroups stratified by hematocrit (HCT) and triglycerides (TG).

**Conclusions:** We found a positive association between TC/HDL-C ratio and GH; however, body mass index (BMI) was not available in this study, and this association may partly reflect underlying metabolic status, including adiposity, rather than a direct lipid-mediated effect.

**Keywords:** Case-Control Studies • Cholesterol, HDL • Hypertension, Pregnancy-Induced • Risk Factors

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## Introduction

Gestational hypertension (GH) is defined as a systolic blood pressure of 140 to 160 mmHg and/or a diastolic blood pressure of 90 to 110 mmHg occurring after 20 weeks of pregnancy in women who previously had normal blood pressure and no proteinuria [1]. GH affects approximately 5% to 15% of pregnant women worldwide [2-5]. This condition remains a leading cause of maternal and perinatal morbidity and mortality [6,7]. Despite advances in prenatal care, its etiology is multifactorial and not fully elucidated. Therefore, identifying factors associated with GH is important for generating hypotheses regarding early prevention and intervention.

Lipid metabolism has been related to various physiological and pathological processes, including normal pregnancy and GH [8,9]. Physiologically, normal pregnancy is characterized by progressive elevations in total cholesterol (TC) and triglycerides (TG) to support fetal development, while high-density lipoprotein cholesterol (HDL-C) remains relatively stable [10]. In contrast, women with GH exhibit pathological dyslipidemia, marked by exaggerated increases in TC, TG, and low-density lipoprotein cholesterol (LDL-C), coupled with reduced HDL-C levels [11]. These pathological alterations can impair vascular endothelial function, trigger chronic inflammatory responses, and elevate oxidative stress [12-14], and have been implicated in GH.

Unlike individual lipid parameters, the TC/HDL-C ratio captures the balance between pro-atherogenic and anti-atherogenic lipid fractions, offering a more integrated reflection of lipid metabolism [15]. Beyond lipid profiling, this ratio has been shown to be correlates with insulin resistance, oxidative stress, and systemic inflammation [16,17], which are pathophysiological pathways that are also implicated in hypertensive disorders of pregnancy. These properties suggest that the TC/HDL-C ratio could serve as a composite marker of metabolic disturbance relevant to GH, but whether it reflects lipid-specific effects or broader metabolic dysregulation (including adiposity) remains unclear. Previous research has documented lipid abnormalities in women with GH, but these studies have primarily examined discrete lipid components such as TC, HDL-C, LDL-C, and triglycerides [18]. The TC/HDL-C ratio, which captures the balance between atherogenic and protective lipoproteins, has received limited attention in the context of GH. Whether this composite marker has a stronger or more consistent association with GH than individual lipid parameters remains unclear.

This study aimed to examine the association between the TC/HDL-C ratio and GH through a single-center retrospective case-control design. We further evaluated whether this association varies across different age groups and demographic characteristics. By providing insight into this relationship, our findings may generate hypotheses for future prospective studies and contribute to understanding the role of metabolic status in GH.

## Material and Methods

### Ethics Statement

This study was approved by the Ethics Committee of Guilin Maternal and Child Health Hospital (Approval Number: 2025-048KY). The need for informed consent was waived due to the retrospective nature of this study and the use of de-identified data from electronic medical records.

### Study Design and Population

This was a single-center case-control study conducted at Guilin Maternal and Child Health Hospital, Guilin, China, between January 2021 and December 2024. GH is defined as a systolic blood pressure (BP) ≥140 and <160 mmHg and/or a diastolic BP of ≥90 and <110 mmHg on at least 2 separate occasions at least 4 hours apart after 20 weeks' gestation, in a woman who previously had normal blood pressure and without evidence of significant proteinuria (urine protein <300 mg in a 24-hour urine collection) [19]. All diagnoses were confirmed by obstetricians according to these criteria through systematic review of prenatal records, including documented blood pressure measurements and laboratory results. To ensure a homogeneous study population focused exclusively on gestational hypertension, we excluded cases with preeclampsia-eclampsia, chronic hypertension (hypertension present before pregnancy or diagnosed before 20 weeks of gestation), and preeclampsia superimposed on chronic hypertension. The present study exclusively encompassed singleton pregnancies confirmed by ultrasonography. Patients with previously known secondary hypertension (eg, chronic kidney disease, primary aldosteronism, Cushing's syndrome), autoimmune disease, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy, severe infection, multiple organ injury, cancer, and incomplete clinical records were excluded from this study. Secondary causes of hypertension were ruled out by reviewing electronic medical records for documented clinical assessments, relevant laboratory findings, and imaging results obtained during routine prenatal care.

### Demographic Characteristics Collection

Electronic medical record systems were used to obtain clinical features, such as age, white blood cells (WBC), red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), platelets (PLT), neutrophils, lymphocytes, monocytes, red cell distribution width (RDW), total cholesterol (TC), triglycerides (TG),





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high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and TC/HDL-C ratios. Data extraction was performed by querying the system with each patient's unique hospital ID number to retrieve laboratory results and clinical records. Blood samples were collected after 20 weeks of gestation. Hematological parameters were measured using the Mindray BC-6800Plus automated hematology analyzer (Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). Biochemical parameters were analyzed using the HITACHI LABOSPECT 008 AS automated chemistry analyzer (Hitachi, Ltd). Reference ranges for laboratory parameters in our institution are as follows: WBC (3.5-9.5)×$10^9$/L, RBC (3.8-5.1)×$10^{12}$/L, HGB (115-150) g/L, HCT (35-45)%, PLT (125-350)×$10^9$/L, neutrophils (1.8-6.3)×$10^9$/L, lymphocytes (1.1-3.2)×$10^9$/L, monocytes (0.1-0.6)×$10^9$/L, RDW (11.5-14.5)%, TC <5.18 mmol/L, TG <1.17 mmol/L, HDL-C (1.29-1.55) mmol/L, and LDL-C <3.37 mmol/L. These reference ranges are established based on the manufacturer's recommendations and validated for the local population. Women with documented preconception hypercholesterolemia or those receiving lipid-lowering therapy before pregnancy were excluded to minimize confounding from pre-existing dyslipidemia. Altogether, a total of 307 patients with GH and 307 age-matched normotensive pregnancy controls (1: 1) were enrolled in this study.

### Study Variables

In the present investigation, factors that may have an impact on the connection between GH and the TC/HDL-C ratio were regarded as covariates. Covariates such as age, WBC, RBC, HGB, HCT, PLT, neutrophils, lymphocytes, monocytes, RDW, TG, and LDL-C were considered. We recognize that body mass index (BMI) is a potential upstream confounder, as it influences both lipid metabolism (including TC/HDL-C ratio) and GH. However, BMI data were not systematically recorded in our electronic medical records during the study period and thus could not be included in the analysis. This is a limitation of the study, as residual confounding from unmeasured adiposity cannot be excluded. To avoid multicollinearity, variance inflation factor (VIF) analysis was performed for all candidate covariates. Variables with VIF >5 (WBC, RBC, and HGB) were excluded from the final multivariable model.

### Statistical Analysis

Data were checked for completeness, and no missing values were identified for the variables included in the analysis. Normality of continuous variables was assessed using the Shapiro-Wilk test. Demographic and clinical characteristics were compared between groups based on the presence of GH. Categorical variables were presented as counts (weighted percentages) and compared using Chi-square test. Continuous variables were presented as median (1st quartile, 3rd quartile) for skewed distributed variables and compared using Mann-Whitney U tests. Univariate and multivariate logistic regression models were employed to evaluate the association between the TC/HDL-C ratio and GH, with odds ratios (ORs) and 95% confidence intervals (CIs) being reported. The modeling strategy involved a hierarchical approach with 3 progressively adjusted models to assess the robustness of the association across different levels of covariate control. Model 1 was unadjusted; Model 2 was adjusted for age as a fundamental demographic confounder; and Model 3 included comprehensive adjustment for age, HCT, PLT, neutrophils, lymphocytes, monocytes, RDW, TG, and LDL-C. Variables with VIF >5 were excluded from Model 3 to minimize multicollinearity. The goodness-of-fit of the multivariable logistic regression models was evaluated using the Hosmer-Lemeshow test, with $P>0.05$ indicating acceptable model calibration. We acknowledge that TG and LDL-C in Model 3 may lie on the causal pathway between the TC/HDL-C ratio and GH, potentially leading to overadjustment. However, we included these variables to provide a comprehensive assessment of the association independent of other lipid parameters and to evaluate the robustness of the findings under maximal adjustment. Restricted cubic spline (RCS) analysis was performed to examine potential non-linear associations between TC/HDL-C ratio and GH. Four knots were positioned at the 5th, 35th, 65th, and 95th percentiles of the TC/HDL-C distribution, following standard practice for RCS modeling. The median TC/HDL-C value was used as the reference point. Non-linearity was assessed using the likelihood ratio test. RCS curves were generated for Model 1 (unadjusted), Model 2 (adjusted for age), and Model 3 (fully adjusted) to examine whether the association pattern changed with progressive covariate adjustment. Furthermore, the multiple logistic regression models incorporated both continuous and categorical models. The TC/HDL-C was divided into quintiles, after which the linear trends were conducted by considering the median value of every subgroup as the continuous variable. To explore potential effect modification, subgroup analyses were performed stratified by the covariates included in Model 3 (age, HCT, PLT, neutrophils, lymphocytes, monocytes, RDW, TG, and LDL-C). These analyses aimed to assess whether the association between TC/HDL-C ratio and GH varied across different levels of these clinical and demographic characteristics. Interaction terms were tested to evaluate statistical evidence for effect modification. For continuous covariates, quartile-based categorization was used, a standard approach in epidemiological research for examining exposure-response relationships and facilitating clinical interpretation. These subgroup analyses should be considered exploratory, as no correction for multiple comparisons was applied, and the findings require confirmation in independent studies. All statistical analyses in this study were performed using R (v4.5.1), along with Zstats v1.0 (www.zstats.net). A 2-sided $P$ value of less than 0.05 was considered statistically significant.







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**Table 1.** Baseline characteristics of study participants by GH status.

| Variables | Total (n=614) | Normotensive pregnancy (n=307) | GH (n=307) | *P* values |
|---|---|---|---|---|
| Age, years | 32.0 (28.0, 35.0) | 32.0 (27.0, 34.5) | 32.0 (28.0, 36.0) | 0.118 |
| WBC, ×10$^9$/L | 8.50 (7.29, 9.92) | 8.24 (6.91, 9.61) | 8.88 (7.51, 10.21) | <0.001 |
| RBC, ×10$^{12}$/L | 4.26 (4.01, 4.54) | 4.18 (3.95, 4.46) | 4.35 (4.10, 4.64) | <0.001 |
| HGB, g/L | 126.00 (118.00, 133.00) | 123.00 (116.00, 131.00) | 127.00 (118.00, 135.00) | <0.001 |
| HCT,% | 36.65 (34.40, 38.77) | 35.90 (33.90, 37.80) | 37.50 (35.50, 39.50) | <0.001 |
| PLT, ×10$^9$/L | 252.00 (214.25, 293.75) | 242.00 (211.00, 290.50) | 260.00 (219.00, 294.50) | 0.039 |
| Neutrophils, ×10$^9$/L | 6.10 (5.12, 7.40) | 5.84 (4.77, 7.25) | 6.46 (5.36, 7.54) | <0.001 |
| Lymphocytes, ×10$^9$/L | 1.72 (1.41, 2.06) | 1.67 (1.38, 2.00) | 1.76 (1.46, 2.10) | 0.013 |
| Monocytes, ×10$^9$/L | 0.43 (0.35, 0.52) | 0.42 (0.34, 0.52) | 0.44 (0.37, 0.52) | 0.065 |
| RDW | 13.00 (12.60, 13.60) | 13.00 (12.25, 13.65) | 13.00 (12.60, 13.60) | 0.156 |
| TC, mmol/L | 4.61 (4.10, 5.23) | 4.55 (4.04, 5.19) | 4.65 (4.12, 5.28) | 0.135 |
| TG, mmol/L | 1.59 (1.22, 2.11) | 1.58 (1.25, 2.00) | 1.60 (1.17, 2.20) | 0.675 |
| HDL-C, mmol/L | 1.39 (1.20, 1.63) | 1.43 (1.21, 1.70) | 1.36 (1.19, 1.58) | 0.014 |
| LDL-C, mmol/L | 2.41 (2.00, 2.89) | 2.35 (1.98, 2.75) | 2.47 (2.07, 2.97) | 0.005 |
| TC/HDL-C | 3.36 (2.92, 3.79) | 3.22 (2.77, 3.71) | 3.42 (3.06, 3.88) | <0.001 |

Data are presented as median (1st quartile, 3rd quartile) for skewed variables. The Mann-Whitney U test was used to compare differences between groups. Abbreviations: GH, gestational hypertension; WBC, white blood cells; RBC, red blood cells; HGB, hemoglobin; HCT, hematocrit; PLT, platelets; RDW, red cell distribution width; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

## Results

### Baseline Characteristics of Participants

A total of 614 participants were included in this study, with 307 in the GH group and 307 in the normotensive pregnancy group (**Table 1**). Women with GH had significantly higher TC/HDL-C ratios compared to normotensive controls (*P*<0.001). They also exhibited higher levels of WBC, RBC, HGB, HCT, PLT, neutrophils, lymphocytes, and LDL-C, alongside lower HDL-C levels (all *P*<0.05).

### Association Between TC/HDL-C Ratio and GH

We used logistic regression to examine the relationship between TC/HDL-C ratio and GH (**Table 2**). The TC/HDL-C ratio was positively associated with GH in all models. In the fully adjusted Model 3 (adjusted for age, HCT, PLT, neutrophils, lymphocytes, monocytes, RDW, TG, and LDL-C), each unit increase in TC/HDL-C ratio was associated with 44% higher odds of GH (OR: 1.44, 95% CI: 1.11-1.88, *P*=0.006, **Table 2**). It should be noted, however, that BMI was not included in the adjustment set due to data unavailability; as BMI is closely related to both lipid levels and blood pressure in pregnancy, residual confounding by adiposity cannot be ruled out, and this OR should not be interpreted as an independent effect of lipid imbalance. When categorized into quintiles, a monotonic increase in GH odds was observed across TC/HDL-C quintiles, with higher quintiles showing progressively greater odds of GH compared to the lowest quintile (Q1). The ORs for Q2 through Q5 ranged from 2.12 to 2.89 in Model 3, all statistically significant (*P* for trend=0.006, **Table 2**). However, given that BMI was unavailable for adjustment, this gradient may partly or substantially reflect differences in adiposity across quintiles rather than being a direct effect of lipid imbalance, and should therefore be interpreted as an observed trend rather than evidence of a biologically meaningful dose–response relationship.

### Dose–Response Relationship Between TC/HDL-C Ratio and GH

**Figure 1** illustrates the association between TC/HDL-C ratio and GH across the continuous range of values, estimated using restricted cubic spline logistic regression. We found no





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**Table 2.** Association between TC/HDL-C ratio and GH: logistic regression models and trend tests.

| TC/HDL-C | GH OR (95% CI) | | | | | |
|---|---|---|---|---|---|---|
| | Model 1 | *P* value | Model 2 | *P* value | Model 3 | *P* value |
| Continuous | 1.46 (1.18~1.80) | <0.001 | 1.46 (1.18~1.80) | <0.001 | 1.44 (1.11~1.88) | 0.006 |
| Quantile | | | | | | |
| Q1 | 1.00 (Reference) | | 1.00 (Reference) | | 1.00 (Reference) | |
| Q2 | 2.11 (1.25~3.57) | 0.005 | 2.07 (1.22~3.50) | 0.007 | 2.12 (1.21~3.74) | 0.009 |
| Q3 | 2.72 (1.62~4.57) | <0.001 | 2.62 (1.56~4.42) | <0.001 | 2.89 (1.62~5.15) | <0.001 |
| Q4 | 2.33 (1.38~3.92) | 0.001 | 2.32 (1.38~3.91) | 0.002 | 2.14 (1.18~3.58) | 0.012 |
| Q5 | 2.73 (1.62~4.60) | <0.001 | 2.71 (1.61~4.56) | <0.001 | 2.82 (1.48~5.37) | 0.002 |
| *P* for trend | | <0.001 | | <0.001 | | 0.006 |

**Model 1:** unadjusted. **Model 2:** adjusted for age. **Model 3:** adjusted for age, HCT, PLT, neutrophils, lymphocytes, monocytes, RDW, TG, and LDL-C. Abbreviations: GH, gestational hypertension; OR, odds ratio; CI, confidence interval; HCT, hematocrit; PLT, platelets; RDW, red cell distribution width; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol.

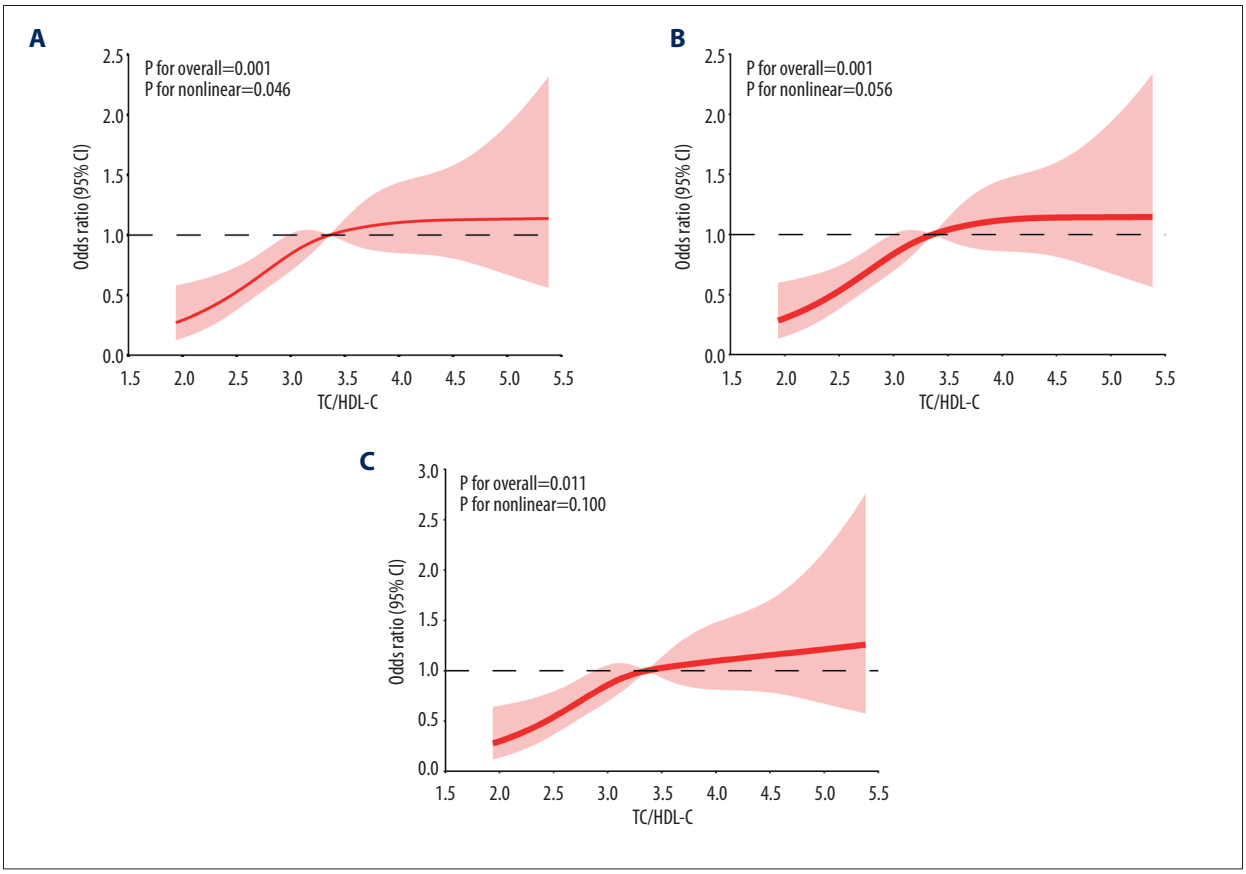


**Figure 1.** Dose–response relationship between TC/HDL-C ratio and GH assessed by RCS analysis. RCS curves illustrate the association between TC/HDL-C ratio and GH across 3 adjustment models. (**A**) Model 1 was adjusted for none. (**B**) Model 2 was adjusted for age. (**C**) Model 3 was adjusted for Age, HCT, PLT, Neutrophils, Lymphocytes, Monocytes, RDW, TG, and LDL-C. Abbreviations: GH, gestational hypertension; RCS, restricted cubic spline; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; HCT, hematocrit; PLT, platelets; RDW, red cell distribution width; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol.







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**Figure 2.** Subgroup analysis of the association between TC/HDL-C ratio and GH stratified by clinical characteristics. Forest plot displays OR and 95% CI for the association between TC/HDL-C ratio and GH across different subgroups defined by baseline clinical and laboratory parameters. *P* values for interaction tests are shown to assess effect modification. Abbreviations: GH, gestational hypertension; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; HCT, hematocrit; PLT, platelets; RDW, red cell distribution width; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; CI, confidence interval.





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strong evidence of non-linearity between TC/HDL-C ratio and GH. The magnitude of the observed association was found to be statistically significant in the unadjusted model 1 (**Figure 1**). However, when Model 3 was incrementally adjusted for age, HCT, PLT, neutrophils, lymphocytes, monocytes, RDW, TG, and LDL-C, the association displayed linearity (**Figure 1**). As BMI was not available for adjustment, the possibility that this linear trend is driven by residual confounding from adiposity or related metabolic factors cannot be excluded.

### Subgroup Analysis

We performed exploratory subgroup analyses with interaction tests to examine whether the association between TC/HDL-C ratio and GH varied across clinical characteristics. Statistical interactions were observed for HCT (*P* for interaction=0.025) and TG (*P* for interaction=0.007). Higher TC/HDL-C ratios were associated with greater odds of GH among participants with higher HCT levels (Q3-Q4) and lower TG levels (≤1.71 mmol/L). These subgroup analyses are exploratory in nature and are highly susceptible to residual confounding, particularly by unmeasured BMI. Sensitivity analysis adjusting for BMI could not be performed, as these data were not collected in this study. The observed interactions should not be interpreted as evidence of true biological effect modification, as differential distribution of unmeasured confounders (eg, adiposity and related metabolic factors) across subgroups may explain these findings. Detailed subgroup results are provided in **Figure 2**.

## Discussion

This case-control study examined the relationship between the TC/HDL-C ratio and GH in 614 singleton pregnancies from 2021 to 2024. We found a statistically significant positive association between the TC/HDL-C ratio and GH across all 3 analytical models. A monotonic increase in GH odds was observed across TC/HDL-C ratio quintiles, and RCS analysis indicated a linear trend across the continuous range of values; however, as discussed below, this pattern may partly reflect residual confounding by adiposity, given that BMI was unavailable for adjustment. Exploratory subgroup analyses stratified by HCT and TG yielded statistical interactions, but these findings should be interpreted with caution. Because BMI and other metabolic variables were unavailable for subgroup-specific adjustment, the observed heterogeneity may reflect differential distribution of unmeasured confounders (particularly adiposity) across subgroups rather than true biological effect modification.

Existing evidence suggests that abnormal lipid metabolism is associated with the development of GH. Numerous previous studies have reported the relationship between blood lipid levels and hypertensive disorders complicating pregnancy. For instance, Jin et al [20] found that the serum levels of TC, TG, and LDL-C in GH patients were significantly higher than those of the control group, while the level of serum HDL-C was significantly decreased in GH patients compared to the control group. Several case-control studies also reported that the levels of serum TC, TG, and LDL-C were significantly elevated, while HDL-C was lower among women with pregnancy-induced hypertension, such as preeclampsia, eclampsia, GH, chronic hypertension in pregnancy, compared to normotensive pregnant women [21-24]. A recent systematic review and meta-analysis by Qin et al [18] further confirmed these findings, demonstrating that patients with GH and preeclampsia had significantly lower HDL levels and elevated LDL, TC, and TG levels compared to healthy pregnant women. Recent studies have demonstrated that elevated levels of TC, TG and LDL-C were associated with PE and GH [25-27]. Our findings align with these previous reports, as we observed significantly higher LDL-C and lower HDL-C levels in women with GH compared to normotensive controls. In summary, this evidence suggests that abnormal lipid metabolism is associated with GH, but the temporal sequence and causal nature of this relationship remain to be established.

Although individual lipid parameters (TC, LDL-C, HDL-C) have been associated with GH as described above, the TC/HDL-C ratio may provide complementary clinical information. The TC/HDL-C ratio is considered a composite lipid marker that integrates both atherogenic and protective components, potentially providing a more accurate reflection of disease odds than isolated lipid parameters. Unlike single measurements, the ratio reflects the net balance between pro-atherogenic and anti-atherogenic forces. For instance, a woman with only mildly elevated TC but markedly reduced HDL-C may have a substantially elevated TC/HDL-C ratio, identifying her as higher odds despite unremarkable TC levels alone. Thus, the ratio may capture metabolic imbalance that isolated parameters overlook. Notably, Egeland et al. [28] reported in a large prospective cohort study that a preconception TC/HDL-C ratio >5 was associated with both gestational hypertension and preeclampsia, highlighting the clinical relevance of this threshold. Our findings are consistent with this observation, as we found that each unit increase in TC/HDL-C ratio was associated with 44% higher odds of GH (OR: 1.44, 95% CI: 1.11-1.88) after adjusting for multiple confounders. Nevertheless, this estimate should be interpreted cautiously, as it may partly reflect the influence of maternal adiposity given that BMI was not measured in the present study. The linear trend observed in our RCS analysis and the monotonic gradient across quintiles are consistent with a positive association, but should be regarded as descriptive findings; whether this pattern reflects a true lipid-mediated relationship or is substantially attributable to unmeasured adiposity and related metabolic factors cannot be determined from the present data. Previous studies have shown that elevated TC/HDL-C ratio







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is positively associated with metabolic syndrome, stroke, coronary artery disease, and diabetes [29-32], conditions that share pathophysiological features with GH. An elevated TC/HDL-C ratio has been linked to systemic inflammation, endothelial injury, and atherosclerosis in other cardiovascular conditions [33-35], and similar processes have been implicated in the pathophysiology of GH; however, whether these mechanisms are relevant to the observed association in our study cannot be established given the cross-sectional design and the absence of BMI adjustment. Whether elevated TC/HDL-C ratio precedes and contributes to GH development, or whether it represents a metabolic consequence of the hypertensive state itself, cannot be determined from our cross-sectional case-control design. Therefore, the present findings suggest that an elevated TC/HDL-C ratio is associated with GH, but this association may reflect the ratio serving as a surrogate marker of broader metabolic status rather than a direct lipid-mediated effect. Prospective studies with serial lipid measurements beginning in early pregnancy and mandatory BMI assessment are needed to clarify the temporal sequence of this relationship, distinguish lipid-specific from adiposity-related effects, and determine whether this marker has potential clinical implications.

The present study has several strengths. We observed a positive association between the TC/HDL-C ratio and GH in a Chinese population using a moderately sized sample with adjustment for multiple laboratory covariates. Restricted cubic spline models and exploratory subgroup analyses provided further insights into this relationship, but these findings should be interpreted with caution given their hypothesis-generating nature. However, several important limitations must be acknowledged. Most critically, BMI data were unavailable in this study. BMI is a well-established determinant of both lipid metabolism and blood pressure regulation in pregnancy, and its absence from the adjustment set means that the observed association between TC/HDL-C ratio and GH may, at least in part, reflect underlying adiposity rather than a direct lipid-mediated effect. In particular, the monotonic increase in GH odds across TC/HDL-C quintiles may reflect a gradient in unmeasured BMI or related metabolic factors rather than a biologically meaningful dose–response effect. Accordingly, the reported OR of 1.44 should not be interpreted as an independent association, and the possibility of substantial residual confounding by BMI cannot be dismissed. Additionally, other potentially important confounding variables were not available in our dataset, including parity, smoking status, gestational age at blood sampling, and socioeconomic factors. These unmeasured confounders may have influenced the observed associations. While these variables may also contribute to residual confounding, their impact is secondary to that of BMI. Second, this was a single-center case-control study conducted in a specific regional population in China, which may limit the external generalizability of our findings to other populations with different genetic backgrounds, dietary patterns, and healthcare systems. Therefore, our results should be validated through multicenter studies in diverse populations. Third, the case-control design with cross-sectional lipid measurements precludes determination of temporal relationships. We cannot distinguish whether the elevated TC/HDL-C ratio is a cause or consequence of GH. Prospective cohort studies with serial lipid measurements from early pregnancy, mandatory BMI assessment, standardized measurement protocols, and comprehensive covariate collection are needed to confirm these findings and establish temporal relationships.

## Conclusions

This study observed a positive association between the TC/HDL-C ratio and GH in women with singleton pregnancy, with higher ratios corresponding to increased odds of GH. However, the absence of BMI data is a critical limitation, and the observed association may reflect the TC/HDL-C ratio functioning as a surrogate marker of broader metabolic status, including unmeasured adiposity and related metabolic disturbances, rather than an independent lipid-mediated effect. Given the retrospective case-control design, temporal relationships and causality cannot be established from our data. These findings are hypothesis-generating and warrant validation in prospective cohort studies with comprehensive metabolic characterization, including mandatory BMI assessment, to determine whether elevated TC/HDL-C ratios precede GH onset, clarify the underlying mechanisms, and to evaluate whether this marker has clinical applicability when interpreted within the context of overall metabolic assessment.

### Ethics Statement

This study was approved by Guilin Maternal and Child Health Hospital Ethics Committee (Approval Number: 2025-048KY).

### Acknowledgements

During the preparation of this manuscript, the authors used AI-based language tools (including ChatGPT-5.2) for English language editing, grammar checking, and improving the clarity and readability of the text. These tools were used solely for language refinement and formatting purposes. All scientific content, including study design, data collection, statistical analysis, interpretation of results, and conclusions, was developed entirely by the authors.

### Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.





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