Postprint: Prevalence of Gestational Dyslipidemia and Early Predictive Value of Lipid Levels

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Abstract

Background: Elevated dyslipidemia during pregnancy can adversely affect maternal and fetal health, not only increasing the risks of preeclampsia, gestational diabetes mellitus (GDM), hypertriglyceridemia-induced pancreatitis, late miscarriage, preterm birth, and macrosomia, but also significantly elevating the risk of postpartum cardiovascular diseases in both mother and child.

Objective: To analyze the distribution characteristics of dyslipidemia in early, middle, and late pregnancy and the predictive value of early pregnancy lipid levels for dyslipidemia in middle and late pregnancy.

Methods: This study was a single-center retrospective study that included singleton pregnant women who established prenatal care and delivered at the Department of Obstetrics, Beijing Obstetrics and Gynecology Hospital, Capital Medical University from January 2018 to June 2019. Clinical data and lipid data from early, middle, and late pregnancy [total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)] were collected. The reference range for blood lipids during pregnancy at Beijing Obstetrics and Gynecology Hospital, Capital Medical University was used as the diagnostic criterion for dyslipidemia, including hypercholesterolemia, hypertriglyceridemia, low high-density lipoprotein cholesterolemia, and high low-density lipoprotein cholesterolemia. Binary logistic regression was used to analyze the correlation between early pregnancy lipid levels and dyslipidemia in middle and late pregnancy, receiver operating characteristic (ROC) curves were plotted to obtain the area under the curve (AUC), the predictive value of early pregnancy lipid levels for dyslipidemia in middle and late pregnancy was evaluated, and optimal cutoff values were determined based on sensitivity and specificity.

Results: A total of 8,511 singleton pregnant women were included in the study, with a mean age of (31.7$\pm$3.9)$years and a mean pre-$

pregnancyBMIof(21.7±$3.2) kg/m2, including 988 (11.6%) underweight, 5,568 (65.4%) normal weight, 1,271 (14.9%) overweight, and 366 (4.3%) obese women before pregnancy. There were 1,415 (16.7%) women with GDM and 650 (7.6%) women with hypertensive disorders of pregnancy (HDP). The levels of TC, TG, and LDL-C in middle and late pregnancy were higher than those in early pregnancy ($P<0.05$), while HDL-C level in late pregnancy was higher than that in early pregnancy but lower than that in middle pregnancy ($P<0.05$). The prevalence of dyslipidemia in early pregnancy was 23.4% (1,990/8,511), and the prevalence of dyslipidemia in middle and late pregnancy was lower than that in early pregnancy ($P<0.05$). The prevalence of dyslipidemia in early pregnancy was higher in overweight and obese women before pregnancy than in normal weight women before pregnancy, but there was no statistically significant difference in the prevalence of dyslipidemia in late pregnancy ($P>0.05$). The prevalence of dyslipidemia in early and middle pregnancy was higher in the GDM group than in the non-GDM group, and the prevalence of dyslipidemia in early, middle, and late pregnancy was higher in women with HDP than in those without HDP ($P<0.05$). After excluding pregnancy complications that might affect blood lipids, the optimal cutoff values for early pregnancy predicting dyslipidemia in middle pregnancy were TC 4.485 mmol/L (AUC=0.854), TG 1.325 mmol/L (AUC=0.864), HDL-C 1.275 mmol/L (AUC=0.908), and LDL-C 2.265 mmol/L (AUC=0.823), respectively. The optimal cutoff values for early pregnancy predicting dyslipidemia in late pregnancy were TC 4.485 mmol/L (AUC=0.809), TG 1.145 mmol/L (AUC=0.833), HDL-C 1.285 mmol/L (AUC=0.851), and LDL-C 2.195 mmol/L (AUC=0.766), respectively.

Conclusion: The prevalence of dyslipidemia during pregnancy did not increase, there were significant differences in the prevalence of dyslipidemia during pregnancy among women with different pre-pregnancy BMI, GDM versus non-GDM, and HDP versus non-HDP, and early pregnancy lipid levels were helpful for predicting the occurrence of dyslipidemia in middle and late pregnancy.

Full Text

Prevalence of Dyslipidemia in Pregnancy and Early Predictive Value of Blood Lipid Levels

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Abstract

Background: Elevated dyslipidemia during pregnancy can adversely affect maternal and child health, increasing the risk of preeclampsia, gestational diabetes mellitus (GDM), hypertriglyceridemic pancreatitis, late abortion, preterm delivery, and macrosomia, while also significantly increasing the risk of postnatal cardiovascular disease in both mother and child.

Objective: To analyze the distributional characteristics of dyslipidemia across the first, second, and third trimesters of pregnancy and evaluate the predictive value of early lipid levels for dyslipidemia in later pregnancy.

Methods: This single-center retrospective study included singleton pregnant women who enrolled for antenatal care and delivered at the Department of Obstetrics, Beijing Obstetrics and Gynecology Hospital, Capital Medical University between January 2018 and June 2019. Clinical data and lipid profiles [total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)] were collected during each trimester. The hospital's pregnancy-specific lipid reference ranges served as diagnostic criteria for dyslipidemia, including hypercholesterolemia, hypertriglyceridemia, low HDL-C, and high LDL-C. Binary logistic regression analyzed associations between first-trimester lipid levels and dyslipidemia in later pregnancy. Receiver operating characteristic (ROC) curves were constructed to obtain area under the curve (AUC) values, evaluate predictive value, and determine optimal cutoff values based on sensitivity and specificity.

Results: Among 8,511 singleton pregnant women with a mean age of (31.7$±3.9)$yearsandmeanpre - pregnancyBMIof(21.7±3.2)kg/m^{2}$$, 988 (11.6%) were underweight, 5,568 (65.4%) had normal weight, 1,271 (14.9%) were overweight, and 366 (4.3%) were obese pre-pregnancy. GDM occurred in 1,415 women (16.7%) and hypertensive disorders of pregnancy (HDP) in 650 (7.6%). TC, TG, and LDL-C levels were significantly higher in the second and third trimesters compared to the first ($P<0.05$). HDL-C in the third trimester was higher than in the first but lower than in the second ($P<0.05$). The prevalence of dyslipidemia was 23.4% (1,990/8,511) in the first trimester, with significantly lower rates in the second and third trimesters ($P<0.05$). Overweight and obese women had higher first-trimester dyslipidemia prevalence than normal-weight women, but no significant difference was observed in the third trimester ($P>0.05$). GDM women showed higher dyslipidemia prevalence in the first and second trimesters compared to non-GDM women, while HDP women had higher prevalence across all three trimesters ($P<0.05$). After excluding pregnancy complications that might affect lipids, optimal first-trimester cutoff values for predicting second-trimester dyslipidemia were: TC 4.485 mmol/L (AUC=0.854), TG 1.325 mmol/L (AUC=0.864), HDL-C 1.275 mmol/L (AUC=0.908), and LDL-C 2.265 mmol/L (AUC=0.823). For predicting third-trimester dyslipidemia, cutoffs were: TC 4.485 mmol/L (AUC=0.809), TG 1.145 mmol/L (AUC=0.833), HDL-C 1.285 mmol/L (AUC=0.851), and LDL-C 2.195 mmol/L (AUC=0.766).

Conclusion: Dyslipidemia prevalence did not increase during pregnancy and was actually lower in the second and third trimesters compared to the first. Significant differences existed in dyslipidemia prevalence based on pre-pregnancy BMI, GDM status, and HDP status. First-trimester lipid levels demonstrated good predictive value for dyslipidemia in later pregnancy, with AUCs ranging from 0.747 to 0.908.

Keywords: Pregnancy; Pregnant women; Dyslipidemias; Prevalence; Gestational diabetes mellitus; Hypertensive disorders in pregnancy; Cut-off value

Introduction

Dyslipidemia refers to elevated cholesterol and/or triglyceride levels in serum and can be classified as hypercholesterolemia, hypertriglyceridemia, mixed hyperlipidemia, or low HDL-cholesterolemia. To meet fetal growth and development needs and support postpartum lactation, maternal lipid metabolism undergoes significant physiological changes during pregnancy. The two major changes in gestational lipid metabolism are early pregnancy fat accumulation and later development of hyperlipidemia. While physiological elevation of lipids during pregnancy is essential for meeting maternal-fetal nutritional demands and ensuring postpartum milk production, abnormal lipid elevation can adversely affect maternal and child health. Studies have shown that gestational dyslipidemia increases the risk of preeclampsia, gestational diabetes mellitus (GDM), hypertriglyceridemic pancreatitis, late abortion, preterm delivery, and macrosomia, while also significantly elevating postpartum cardiovascular disease risk for both mother and child. With socioeconomic development, urbanization, and population aging, the prevalence of dyslipidemia in China has been increasing. The "three-child" policy has led to more advanced maternal age pregnancies and increased incidence of GDM and preeclampsia, yet reports on the prevalence of gestational dyslipidemia remain limited. This retrospective study analyzes the distribution characteristics of dyslipidemia during pregnancy and establishes early predictive cutoff values to provide a theoretical basis for prevention and control of gestational dyslipidemia.

Methods

Study Subjects

Data were derived from the Beijing Birth Cohort Study (registered as ChiCTR220058395). Singleton pregnant women aged 18-45 years who enrolled for antenatal care and delivered at Beijing Obstetrics and Gynecology Hospital, Capital Medical University between January 2018 and June 2019 were included.

All participants had complete lipid data for early (5-14 weeks), second (24-28 weeks), and third (32-34 weeks) trimesters. Exclusion criteria included use of medications affecting lipid metabolism during pregnancy such as corticosteroids, diuretics, or beta-blockers. The study was approved by the hospital's Ethics Committee (2018-ky-009-01). As a retrospective non-interventional study, informed consent was waived.

Data Collection

This single-center retrospective study collected maternal age, pre-pregnancy BMI [weight (kg)/height $(m)^2$], last menstrual period, parity, conception method, medical history (including diabetes, hypertension, polycystic ovary syndrome [PCOS], thyroid disease), and pregnancy complications [including GDM, hypertensive disorders of pregnancy (HDP), intrahepatic cholestasis, acute fatty liver of pregnancy, cardiac and renal disease, thyroid disease]. Lipid profiles were obtained during each trimester.

Diagnostic Criteria

Currently, no unified diagnostic criteria exist for gestational dyslipidemia. This study applied pregnancy-specific reference ranges from Beijing Obstetrics and Gynecology Hospital as diagnostic standards: (1) Hypercholesterolemia: TC $ $5.38 mmol/L (first trimester), $ $7.56 mmol/L (second), $ $8.20 mmol/L (third); (2) Hypertriglyceridemia: TG $ $1.81 mmol/L (first), $ $3.49 mmol/L (second), $ $4.63 mmol/L (third); (3) Low HDL-C: HDL-C $ $1.12 mmol/L (first), $ $1.33 mmol/L (second), $ $1.24 mmol/L (third); (4) High LDL-C: LDL-C $ $2.98 mmol/L (first), $ $4.36 mmol/L (second), $ 4.92mmol/L(third).Pre − pregnancyBMIcategorieswere : underweight(< 18.5kg/m{2}), normalweight(18.5 − 24.0kg/m{2}), overweight(24.0 − 28.0kg/m{2}), andobese(28.0kg/m{2}$).

Lipid Measurement

Fasting venous blood samples were collected after an overnight fast of at least 8 hours during 5-14 weeks, 24-28 weeks, and 32-34 weeks of gestation. Serum TC, TG, LDL-C, and HDL-C levels were measured using an ARCHITECT ci16200 automated biochemical analyzer (Abbott Park, IL, USA).

Statistical Analysis

SPSS 25.0 software was used for statistical analysis. Normally distributed continuous variables were expressed as mean ± standard deviation; non-normally distributed variables as median (P25, P75). Comparisons across time points used generalized estimating equations. Categorical variables were expressed as frequencies and percentages, with intergroup comparisons using ^{2} tests and Bonferroni correction for multiple comparisons. Binary logistic regression analyzed associations between first-trimester lipid levels and dyslipidemia in later pregnancy. ROC curves were constructed to obtain AUC values and evaluate predictive value, with optimal cutoff values determined based on sensitivity and specificity. Pregnancy comorbidities and complications that might affect lipids were excluded in sensitivity analyses. Statistical significance was defined as P<0.05.

Results

General Characteristics

The study included 8,511 singleton pregnant women with mean age (31.7\$±3.9)$yearsandmeanpre - pregnancyBMI(21.7\pm3.2)kg/m$^{2}\$. Pre-pregnancy BMI data were missing for 318 women (3.7%). Among the remainder, 988 (11.6%) were underweight, 5,568 (65.4%) normal weight, 1,271 (14.9%) overweight, and 366 (4.3%) obese. Multiparous women accounted for 2,437 (28.6%), assisted conception for 466 (5.5%), pregestational diabetes for 27 (0.3%), pregestational hypertension for 64 (0.8%), and PCOS for 448 (5.3%). GDM occurred in 1,415 women (16.7%) and HDP in 650 (7.6%), comprising gestational hypertension (673, 7.9%), mild preeclampsia (156, 1.8%), severe preeclampsia (170, 2.0%), chronic hypertension (26, 0.3%), and chronic hypertension with superimposed preeclampsia (1).

Comparison of Lipid Levels Across Trimesters

Compared to the first trimester, TC, TG, HDL-C, and LDL-C levels all increased significantly in the second trimester (P<0.05). In the third trimester, TC, TG, and LDL-C levels increased further, exceeding both early and mid-pregnancy values (P<0.05). TC increased by a mean of 41.7% in the second trimester and 53.3% in the third. TG increased by 113.8% in the second trimester and 196.8% in the third. LDL-C increased by 49.9% in the second trimester and 65.5% in the third. HDL-C increased from early to mid-pregnancy but declined in the third trimester, remaining higher than early pregnancy levels with a mean increase of 26.5% (P<0.05) .

Prevalence of Dyslipidemia Across Trimesters

Regardless of whether pregnancy complications were excluded, the prevalence of overall dyslipidemia, hypertriglyceridemia, low HDL-C, and high LDL-C differed significantly across trimesters (P<0.05), with lower prevalence in the second and third trimesters compared to the first (P<0.05) .

By Pre-pregnancy BMI Pre-pregnancy BMI groups showed no significant difference in third-trimester dyslipidemia prevalence (P>0.05), but significant differences existed for other trimesters and dyslipidemia types (P<0.05). Underweight women had lower prevalence of hypertriglyceridemia and low HDL-C across all trimesters but higher prevalence of hypercholesterolemia and high LDL-C in the third trimester compared to normal-weight women

(P<0.05). Overweight and obese women had higher first-trimester prevalence of hypercholesterolemia and high LDL-C than normal-weight women, but lower prevalence in the second and third trimesters (P<0.05). Overweight women had higher hypertriglyceridemia prevalence across all trimesters, while obese women had higher hypertriglyceridemia in early and mid-pregnancy compared to normal-weight women, though no significant difference existed in the third trimester (P>0.05) .

GDM vs Non-GDM Women In the first trimester, GDM women had higher prevalence of overall dyslipidemia and all dyslipidemia types compared to non-GDM women (P<0.05). In the second and third trimesters, GDM women maintained higher prevalence of hypertriglyceridemia and low HDL-C but showed lower prevalence of hypercholesterolemia and high LDL-C (P<0.05) .

HDP vs Non-HDP Women HDP women had higher prevalence of overall dyslipidemia and all types in the first and second trimesters compared to non-HDP women (P<0.05). In the third trimester, HDP women continued to show higher prevalence of overall dyslipidemia, hypercholesterolemia, hypertriglyceridemia, and low HDL-C (P<0.05), though high LDL-C prevalence showed no significant difference (P>0.05) .

Predictive Cutoff Values

Binary logistic regression and ROC curve analysis revealed optimal first-trimester cutoff values for predicting second-trimester dyslipidemia: TC 4.485 mmol/L (AUC=0.854), TG 1.325 mmol/L (AUC=0.864), HDL-C 1.275 mmol/L (AUC=0.908), and LDL-C 2.265 mmol/L (AUC=0.823). For predicting third-trimester dyslipidemia, cutoffs were: TC 4.485 mmol/L (AUC=0.809), TG 1.145 mmol/L (AUC=0.833), HDL-C 1.285 mmol/L (AUC=0.851), and LDL-C 2.195 mmol/L (AUC=0.766) [Figure 1: see original paper], [Figure 2: see original paper], , .

Discussion

Physiological insulin resistance and increased estrogen secretion during pregnancy induce adaptive changes in maternal lipid metabolism. Increased food intake and intestinal lipid synthesis in early and mid-pregnancy promote maternal fat deposition, while enhanced lipolytic activity and decreased lipoprotein lipase activity in late pregnancy reduce adipose tissue uptake of circulating TG, leading to decreased or ceased fat deposition. All lipid components and lipoprotein levels increase during pregnancy, with normal pregnancy associated with 25-40% elevation in serum TC and 200-400% elevation in TG. This study found mean TC increases of 41.7% in the second trimester and 53.3% in the third; TG increases of 113.8% in the second and 196.8% in the third; LDL-C increases of 49.9% in the second and 65.5% in the third; and HDL-C increases of 26.5% from first to third trimester, following a pattern of early-to-mid pregnancy increase with a slight late-pregnancy decline.

Currently, only small-scale hospital-based studies exist, and no unified reference standards for gestational lipids and lipoproteins have been established. Large-scale multicenter epidemiological studies are needed to develop standardized diagnostic criteria for gestational dyslipidemia.

This study found a 23.4% prevalence of dyslipidemia in early pregnancy, comprising hypercholesterolemia (6.5%), hypertriglyceridemia (8.6%), low HDL-C (9.4%), and high LDL-C (8.7%). Notably, dyslipidemia prevalence did not increase in later pregnancy, with lower rates in the second and third trimesters. A Cameroonian hospital-based cross-sectional study using metabolic syndrome criteria (pre-pregnancy BMI>30 kg/m^2, TG$ 150mg/dL, HDL − C < 50mg/dL, bloodpressure 130/85mmHg, fastingglucose $100 mg/dL) reported a 17.88% prevalence (95%CI: 15.03-21.14), with low HDL-C (66.23%) and hypertriglyceridemia (28%) being the most common components. However, that study included women across all trimesters without gestational age-specific diagnostic criteria.

Dyslipidemia is a complication of obesity, with higher hyperlipidemia prevalence in obese pregnant women. This study found significantly higher early-pregnancy dyslipidemia prevalence in overweight and obese women compared to underweight and normal-weight women, but no significant difference in the third trimester, possibly due to dietary and lifestyle management throughout pregnancy in overweight/obese women.

Lipid metabolism disorders can cause or worsen insulin resistance and affect β-cell function, while insulin resistance and insufficient secretion can further aggravate lipid metabolism disorders. GDM women exhibit more significant insulin resistance or decreased sensitivity than normal pregnant women. Studies have shown significant associations between GDM and early-pregnancy hyperglycemia and hypertriglyceridemia. Meta-analyses demonstrate consistently elevated TG levels throughout pregnancy in GDM women. This study found higher dyslipidemia prevalence in early and mid-pregnancy among GDM women, with persistent hypertriglyceridemia and low HDL-C in later pregnancy, but paradoxically lower hypercholesterolemia and high LDL-C prevalence. Whether this reflects effective early risk screening and graded management requires further investigation.

Hyperlipidemia is a risk factor for preeclampsia, with abnormal lipid metabolism enhancing oxidative stress and inflammatory responses, causing vascular endothelial damage and dysfunction that participates in HDP pathophysiology. HDP women show elevated early-pregnancy lipid levels, and this study confirmed significantly higher dyslipidemia prevalence across all trimesters in HDP women.

Except for bile acid sequestrants, most lipid-lowering drugs are not approved for pregnancy. Therefore, early identification of high-risk pregnant women and timely lifestyle management are crucial for preventing pathological hyperlipidemia. Diet and exercise interventions during pregnancy can reduce adverse maternal-fetal outcomes, and animal studies show gestational dietary intervention can improve offspring lipid profiles and tolerance to high-fat diets. Early identification and intervention may improve outcomes in high-risk populations.

First-trimester lipid levels significantly correlate with later pregnancy levels. This study demonstrates that early lipid levels can predict second and third-trimester dyslipidemia with AUCs of 0.747-0.908, sensitivities of 0.567-0.835, and specificities of 0.701-0.872. Limited research exists on gestational lipid prediction, and the cutoff values identified here require validation in future studies.

In conclusion, TC, TG, and LDL-C levels increase progressively during pregnancy, while HDL-C rises from early to mid-pregnancy then declines slightly in the third trimester. Dyslipidemia prevalence does not increase during pregnancy, with lower rates in the second and third trimesters compared to the first. Significant differences exist based on pre-pregnancy BMI, GDM status, and HDP status. First-trimester lipid levels effectively predict dyslipidemia in later pregnancy. As a single-center retrospective study using hospital-specific reference ranges, multicenter large-scale epidemiological studies are needed to establish unified diagnostic criteria for gestational dyslipidemia.

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Note: Figure translations are in progress. See original paper for figures.