Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2026**; 53(11): 54469
https://doi.org/10.31083/CEOG54469

Original Research

First-Trimester Maternal Serum Lipid Profile in Missed Miscarriage: A Gestational Age Frequency-Matched Case-Control Study

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Academic Editor: Michael H. Dahan
Submitted: 2 June 2026 Revised: 12 August 2026 Accepted: 8 September 2026 Published: 13 November 2026

Abstract

Background: Maternal lipid metabolism undergoes physiological adaptations during early pregnancy. However, its potential association with missed miscarriage (MM) remains unclear. This study aimed to explore the relationship between maternal serum lipid levels during the first trimester and MM and to assess the discriminative performance of these lipid parameters. **Methods:** In this gestational age frequency-matched case-control study, lipid profiles were compared between 174 women, comprising 87 patients with MM and 87 healthy pregnant controls. Serum concentrations of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were measured. Multivariable binary logistic regression analysis was performed, adjusting for maternal age, history of miscarriage, gestational age, TG, LDL-C, and HDL-C. Lastly, exploratory receiver operating characteristic (ROC) curve analyses were conducted for individual lipid parameters and combined clinical-lipid models. **Results:** Women with MM demonstrated higher LDL-C levels and lower HDL-C levels than controls (both $p < 0.001$). Moreover, TG levels were lower in the MM group ($p = 0.027$). In the multivariable binary logistic regression model, a history of miscarriage (odds ratio [OR] = 54.208, 95% confidence interval [CI]: 17.369–169.181, $p < 0.001$), TG (OR = 0.987, 95% CI: 0.977–0.998, $p = 0.016$), LDL-C (OR = 1.054, 95% CI: 1.022–1.087, $p = 0.001$), and HDL-C (OR = 0.944, 95% CI: 0.903–0.986, $p = 0.009$) remained independently associated with MM. However, maternal age and gestational week were not significantly associated with MM in the model. Among the individual lipid parameters, LDL-C showed the highest discriminative ability (area under the curve [AUC] = 0.709), although its standalone performance remained modest. The combined clinical-lipid model demonstrated high apparent discrimination (AUC = 0.944); however, this finding remains exploratory and requires external validation. **Conclusions:** Alterations in maternal lipid parameters, particularly elevated LDL-C and reduced HDL-C levels, may be associated with MM during the first trimester, suggesting an unfavorable maternal metabolic profile.

Keywords: missed miscarriage; first trimester; maternal lipid profile; LDL-C; HDL-C; triglycerides; case-control study

1. Introduction

Missed miscarriage involves intrauterine embryonic or fetal demise without spontaneous expulsion of the products of conception and is typically diagnosed during routine ultrasonographic assessment in the first trimester [1,2]. Chromosomal abnormalities, uterine and endocrine disorders, immune mechanisms, and other maternal factors have been implicated in pregnancy loss; however, the underlying etiology remains incompletely understood [3,4,5]. Hence, additional maternal and placental mechanisms that may influence early pregnancy failure have been thoroughly explored.

Early pregnancy features coordinated hormonal, vascular, immunological, and metabolic adaptations that facilitate implantation, decidual remodeling, trophoblastic invasion, placental development, and embryonic growth [6]. Maternal lipid metabolism forms an essential component of this adaptive process. Circulating lipids foster steroid hormone synthesis, cell membrane formation, placental development, vascular homeostasis, and energy substrate availability at the maternal-fetal interface [6]. During normal pregnancy, serum concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) typically increase as gestational age advances, revealing physiological metabolic adaptation to pregnancy [6,7].

Abnormal maternal lipid profiles have been extensively examined concerning later pregnancy complications, including gestational diabetes mellitus, hypertensive disorders of pregnancy, preeclampsia, fetal growth restriction, macrosomia, and adverse perinatal outcomes [7,8,9,10,11,12]. Potential mechanisms include oxidative stress, endothelial dysfunction, altered inflammatory signaling, impaired vascular remodeling, and altered placental lipid transport. These processes may also be relevant during early gestation, when placental and vascular development are particularly active [13,14].

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The relationship between maternal lipid metabolism and early pregnancy loss has received less attention than pregnancy complications. Recent evidence posits that deviations from expected lipid adaptation in early pregnancy may be associated with early pregnancy loss; nonetheless, whether these alterations precede embryonic demise or represent metabolic consequences of a nonviable pregnancy remains inconclusive [2]. This distinction is particularly pivotal in missed miscarriage, where embryonic demise may occur before clinical diagnosis.

Therefore, this study aimed to assess whether first-trimester maternal serum lipid parameters are associated with missed miscarriage in a gestational age frequency-matched case-control cohort. Moreover, the secondary aim was to examine the discriminatory ability of individual lipid parameters and multivariable clinical-lipid models. Because the design is retrospective, the findings demonstrated associations rather than evidence of causality or of validated clinical prediction.

2. Materials and Methods

2.1 Study Design and Participants

The study was a retrospective gestational-age frequency-matched case-control study conducted at a tertiary obstetrics and gynecology center between January 2020 and December 2022. The study aligned with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies [15].

Women diagnosed with first-trimester missed miscarriage comprised the case group. Missed miscarriage was referred to as intrauterine embryonic or fetal demise without spontaneous expulsion of the products of conception and was verified by transvaginal ultrasonography. Ultrasonographic diagnostic criteria included the absence of fetal cardiac activity in embryos with a crown-rump length $\geq$7 mm or the absence of embryonic development in a gestational sac surpassing accepted diagnostic thresholds [16].

The control group comprised women with uncomplicated ongoing first-trimester pregnancies who attended the same obstetrics and gynecology outpatient clinic during the study period. Controls were used to ensure a gestational age distribution comparable to that of the missed miscarriage group.

Gestational age frequency matching was performed at the group level using one-week gestational-age strata from 6 to 13 weeks, without individual 1:1 matching. Gestational week was also included as a covariate in the multivariable model.

The excluded participants were women with multiple gestations, known chromosomal abnormalities, pre-existing metabolic or endocrine disorders including diabetes mellitus, thyroid disease, or known dyslipidemia, chronic inflammatory or autoimmune diseases, acute infections, or incomplete essential clinical or laboratory data.

The study was approved by the Tepecik Training and Research Hospital of the Ethics Committee (Approval number: 2023/11-11). The investigation was conducted in full compliance with the ethical mandates of the institutional review board and the fundamental principles delineated in the Declaration of Helsinki.

2.2 Data Collection and Laboratory Measurements

Maternal demographic characteristics, obstetric history, gestational week at clinical evaluation, and laboratory findings were retrospectively retrieved from medical records. Clinical data and fasting serum samples were obtained at the time of first-trimester clinical assessment. For all participants, gestational week at sampling was recorded and used both for group-level frequency matching and as a covariate in the revised multivariable model.

Fasting maternal serum lipid parameters, including total cholesterol, triglycerides, LDL-C, and HDL-C, were determined using an automated biochemical analyzer Beckman Coulter AU5800 (Beckman Coulter Inc, Brea, CA, USA) at the hospital central laboratory. For all measurements, routine internal laboratory quality-control procedures were used.

Because the study was retrospective, pre-pregnancy body mass index (BMI), BMI at clinical evaluation, fasting glucose, insulin resistance markers, and progesterone levels were not invariably available for all participants. Hence, incorporating these parameters into the main analysis without introducing substantial missing data and potential selection bias was not possible.

Upon diagnosis of a missed miscarriage, detecting the exact timing of embryonic demise is challenging. Therefore, the reliable determination of the exact temporal relationship between lipid measurement and embryonic demise was not possible in all cases. Hence, rather than being causal or temporal predictors of pregnancy loss, lipid parameters were interpreted as factors associated with missed miscarriage.

2.3 Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Because most continuous variables were not normally distributed, data were expressed as median and interquartile range and analyzed using the Mann-Whitney U test. Categorical variables were expressed as numbers and percentages and assessed using the chi-square test or Fisher's exact test, whichever was appropriate.

The multivariable binary logistic regression model included maternal age, gestational week, history of miscarriage, triglycerides, LDL-C, and HDL-C. Gravidity was excluded from the main model because of its structural relationship with parity and history of miscarriage. Similarly, the TC/HDL-C ratio was excluded from the main model

because it was derived from lipid components, which may introduce multicollinearity when included alongside LDL-C and HDL-C. History of miscarriage was entered as a binary variable, specified as no previous miscarriage versus at least one previous miscarriage. Multicollinearity was assessed using variance inflation factors (VIFs). Given the marked imbalance in previous miscarriage history between the groups and the potential for sparse-data bias, Firth penalized logistic regression was additionally performed as a sensitivity analysis using the same covariates as the primary model. Model calibration was determined using the Hosmer-Lemeshow goodness-of-fit test and the Brier score. Discriminative performance was assessed using receiver operating characteristic curve analysis and the area under the curve. Exploratory receiver operating characteristic (ROC) analyses were conducted for individual lipid parameters and for three multivariable models: a clinical model, a lipid model, and a combined clinical-lipid model. The clinical model parameters were maternal age, gestational week, and history of miscarriage, whereas the lipid model parameters were triglycerides, LDL-C, and HDL-C. The combined model comprised all clinical and lipid variables. Bootstrap resampling was used for internal validation of the combined model, and an optimism-corrected area under the curve (AUC) was calculated to account for potential model overfitting. ROC-derived cut-off values were determined using the Youden index and were inferred as exploratory thresholds rather than clinically validated diagnostic cut-offs. A two-sided p-value < 0.05 was considered significant.

3. Results

3.1 Baseline Characteristics

The study comprised 174 participants, of whom 87 were women with first-trimester missed miscarriage and 87 with uncomplicated ongoing first-trimester pregnancies. Table 1 depicts baseline demographic, obstetric, and biochemical characteristics. The missed miscarriage group had a higher median age than the control group ($p = 0.002$). Moreover, the number of pregnancies was higher in the missed miscarriage group ($p = 0.004$). History of miscarriage was more frequent among women with missed miscarriage ($p < 0.001$). No significant differences in parity or gestational week were observed between the groups.

3.2 Maternal Lipid Profile Comparisons

Assessment of maternal serum lipid profiles revealed group-level differences between women with missed miscarriage and controls. Even though LDL-C levels were higher in the missed miscarriage group, HDL-C levels were lower (both $p < 0.001$). Additionally, triglyceride levels were lower in the missed miscarriage group ($p = 0.027$). TG/HDL-C ratio did not differ between the groups, whereas the TC/HDL-C ratio was higher in the missed miscarriage group.

3.3 Multivariable Binary Logistic Regression Analysis

Maternal age, gestational week, history of miscarriage, triglycerides, LDL-C, and HDL-C were included in the multivariable binary logistic regression model. Gravidity and the TC/HDL-C ratio were excluded from the main model to reduce model instability and avoid multicollinearity stemming from structurally or mathematically related variables. History of miscarriage was entered as a binary variable.

History of miscarriage was strongly associated with missed miscarriage (odds ratio (OR) = 54.208, 95% confidence interval (CI): 17.369–169.181, $p < 0.001$). Among lipid parameters, higher LDL-C levels were independently associated with increased odds of missed miscarriage (OR = 1.054, 95% CI: 1.022–1.087, $p = 0.001$), whereas higher HDL-C levels were inversely associated with the outcome (OR = 0.944, 95% CI: 0.903–0.986, $p = 0.009$). Moreover, triglyceride levels were inversely associated with missed miscarriage (OR = 0.987, 95% CI: 0.977–0.998, $p = 0.016$). Maternal age and gestational week were not significantly associated with missed miscarriage in the adjusted model (Table 2). Firth penalized logistic regression yielded consistent results in the sensitivity analysis. The association with previous miscarriage history was attenuated but remained strong (OR = 40.328, 95% CI 15.049–128.138; $p < 0.001$), while the direction and statistical significance of the associations for TG, LDL-C, and HDL-C remained essentially unchanged (**Supplementary Table 1**).

3.4 Exploratory ROC Analysis

Exploratory ROC analyses were conducted to assess the discriminative ability of individual lipid parameters and multivariable models. Among individual lipid parameters, LDL-C had the highest AUC, even though its discriminative performance remained modest. LDL-C had an AUC of 0.709, followed by HDL-C with an AUC of 0.676 and triglycerides with an AUC of 0.597 (Figs. 1,2).

The clinical model, including maternal age, gestational week, and history of miscarriage, yielded an AUC of 0.912. Conversely, the lipid model, comprising triglycerides, LDL-C, and HDL-C, yielded an AUC of 0.818. The combined clinical and lipid model produced an apparent AUC of 0.944, with a bootstrap optimism-corrected AUC of 0.934 (Fig. 3). Addition of the lipid variables improved overall model fit compared with the clinical model (likelihood-ratio $\chi^2 = 24.90$, df = 3, $p < 0.001$), although the absolute increase in apparent AUC was modest (ΔAUC = 0.032). These results suggest that lipid parameters may provide complementary information when assessed alongside clinical variables. Nonetheless, because external validation was not conducted, these ROC findings should be interpreted as exploratory (Table 3).

Table 1. Comparison of demographic, obstetric, and biochemical characteristics between the groups.

Variable	Normal pregnancy (n = 87)	Missed miscarriage (n = 87)	*p*-value	Test statistic
Age (years)	27 (24–31)	31 (26–36)	0.002	Z = –3.163
Number of pregnancies	2 (1–3)	3 (2–4)	0.004	Z = –2.879
Parity	1 (0–2)	1 (1–2)	0.143	Z = –1.464
History of miscarriage, n (%)	13 (14.9%)	78 (89.7%)	<0.001	χ^2 = 97.332
Gestational age (weeks)	9 (7–11)	8 (7–10)	0.728	Z = 0.347
Total cholesterol (mg/dL)	162 (145–184)	171 (150–196)	0.095	Z = –1.668
Triglycerides (mg/dL)	102 (79–154)	87 (64–119)	0.027	Z = 2.205
LDL-C (mg/dL)	85 (71–97)	99 (84–122)	<0.001	Z = –4.757
HDL-C (mg/dL)	57 (50–68)	50 (44–60)	<0.001	Z = 4.002
TG/HDL-C ratio	2 (1–3)	2 (1–3)	0.938	Z = 0.078
TC/HDL-C ratio	3 (3–3)	3 (3–4)	<0.001	Z = –5.101

Data are presented as median (interquartile range) or n (%), whichever is appropriate. LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides. Continuous variables were compared using the Mann–Whitney U test, and standardized Z statistics are reported. History of miscarriage was compared using Pearson's chi-square test.

Table 2. Multivariable binary logistic regression analysis of factors associated with missed miscarriage.

Variable	B	SE	Wald χ^2	OR	95% CI for OR	*p*-value
Age	0.050	0.047	1.125	1.051	0.959–1.152	0.289
Gestational week	–0.097	0.111	0.757	0.908	0.730–1.129	0.384
History of miscarriage	3.993	0.581	47.279	54.208	17.369–169.181	<0.001
Triglycerides (mg/dL)	–0.013	0.005	5.854	0.987	0.977–0.998	0.016
LDL-C (mg/dL)	0.052	0.016	11.101	1.054	1.022–1.087	0.001
HDL-C (mg/dL)	–0.058	0.022	6.796	0.944	0.903–0.986	0.009

History of miscarriage was defined as at least one previous miscarriage before the index pregnancy and was entered into the model as a binary variable (no previous miscarriage vs. at least one previous miscarriage). The model was adjusted for maternal age, gestational week, history of miscarriage, triglycerides, LDL-C, and HDL-C. For triglycerides, LDL-C, and HDL-C, the ORs represent the change in odds associated with each 1 mg/dL increase in the respective parameter, holding other variables constant. VIFs ranged from 1.10 to 1.23, revealing the absence of serious multicollinearity. The Hosmer-Lemeshow test demonstrated acceptable calibration (chi-square = 9.353, df = 8, p = 0.313), and the Brier score was 0.082. The combined clinical and lipid model indicated high apparent discrimination (AUC = 0.944, 95% CI: 0.909–0.979), with a bootstrap optimism-corrected AUC of 0.934. Nevertheless, despite bootstrap internal validation, these findings should be regarded as exploratory pending external validation. OR, odds ratio; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; AUC, area under the curve.

Table 3. Exploratory ROC analysis of lipid parameters and multivariable models.

Parameter/Model	AUC	95% CI	Exploratory cut-off	Sensitivity (%)	Specificity (%)	*p*-value
LDL-C	0.709	0.633–0.785	≥92 mg/dL	64.4	69.0	<0.001
HDL-C	0.676	0.596–0.755	≤53 mg/dL	64.4	64.4	<0.001
Triglycerides	0.597	0.512–0.681	≤88 mg/dL	51.7	66.7	0.027
Clinical model	0.912	0.867–0.958	-	-	-	<0.001
Lipid model	0.818	0.757–0.880	-	-	-	<0.001
Combined clinical-lipid model	0.944	0.909–0.979	-	-	-	<0.001

The clinical model included maternal age, gestational week, and history of miscarriage. The lipid model comprised triglycerides, LDL-C, and HDL-C. The combined model included all clinical and lipid variables. Cut-off values for individual lipid parameters were derived from the Youden index and should be assessed as exploratory thresholds rather than clinically validated diagnostic cut-offs. ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

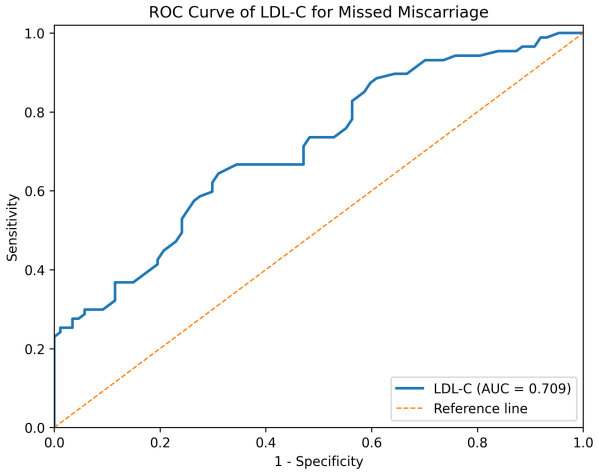


Fig. 1. ROC curve of LDL-C for missed miscarriage. ROC, Receiver operating characteristic.

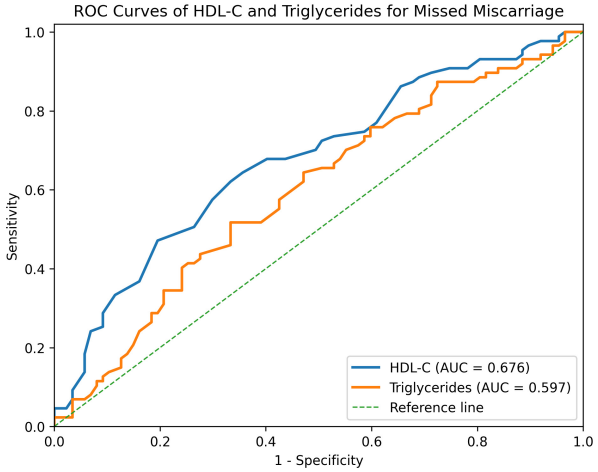


Fig. 2. ROC curves of HDL-C and triglycerides for missed miscarriage.

4. Discussion

This gestational age frequency-matched case-control study revealed that altered first-trimester maternal lipid parameters were associated with missed miscarriage. After adjusting for maternal age, gestational week, and history of miscarriage, higher LDL-C levels were positively associated with missed miscarriage. However, HDL-C and triglyceride levels demonstrated inverse associations. These findings suggest that lipid alterations may indicate an unfavorable maternal metabolic environment in early pregnancy. However, causality cannot be inferred from the present retrospective design [2,17].

Placental lipid metabolism is an active and dynamic process. Lipids are pivotal for placental development and embryonic organogenesis. In the later stages of pregnancy, they are vital for fetal growth and neurodevelopment [14]. Successful early pregnancy requires coordinated interactions among embryonic development, trophoblastic invasion, decidual remodeling, and maternal vascular adaptation. Moreover, maternal lipid metabolism is integral to this process, as lipids facilitate steroidogenesis, cellular membrane synthesis, placental development, and energy supply at the maternal-fetal interface [6,14]. During normal pregnancy, lipid concentrations gradually increase in response to hormonal and metabolic adaptations. Hence, deviations from gestational age-appropriate lipid changes may reveal an unfavorable maternal metabolic environment during the critical window of implantation and early placentation [2,18,19]. Previous prospective data have also demonstrated associations between maternal lipid concentrations in early pregnancy and embryonic size [17]. Nevertheless, in the context of missed miscarriage, the present retrospective design does not allow us to understand whether these alterations precede embryonic demise or occur secondary to a nonviable pregnancy.

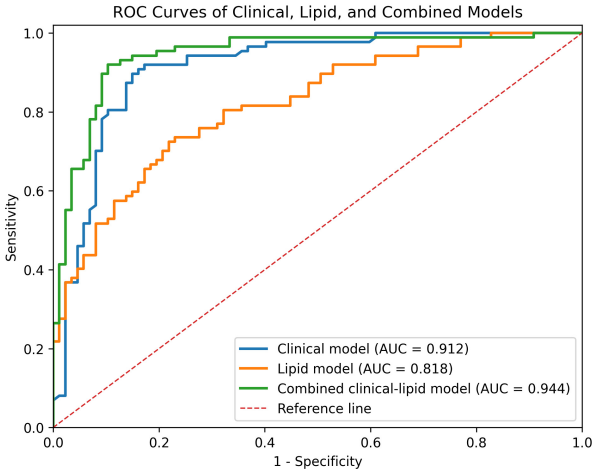


Fig. 3. ROC curves of clinical model (AUC = 0.912), lipid model (AUC = 0.818), and combined clinical–lipid model (AUC = 0.944). The AUC values displayed in the figure represent apparent (in-sample) estimates. The bootstrap optimism-corrected AUC for the combined model was 0.934.

The positive association between LDL-C and missed miscarriage is biologically plausible. LDL-C may foster oxidative lipid modification, endothelial dysfunction, and impaired vascular homeostasis. In early pregnancy, excessive oxidative stress and vascular dysfunction may interfere with trophoblastic invasion and spiral artery remodeling. These processes are essential for adequate uteroplacental perfusion [13]. Nevertheless, the present study determined LDL-C concentration rather than oxidized LDL or direct markers of oxidative stress. Thus, mechanistic interpretations remain speculative.

HDL-C levels and missed miscarriage were inversely associated. HDL particles are involved in reverse cholesterol transport, endothelial protection, antioxidant activity, anti-inflammatory signaling, and vascular homeostasis. These functions may have implications for implantation and early placental development [20]. Nonetheless, HDL-

C concentration does not fully demonstrate HDL functionality or remodeling during pregnancy. Future studies that incorporate HDL function, cholesterol efflux capacity, and inflammatory markers may reveal the biological vitality of this association.

The triglyceride findings should be interpreted cautiously. In normal pregnancies, triglyceride concentrations increase progressively, particularly as gestation advances, indicating enhanced hepatic lipogenesis, estrogen-mediated metabolic changes, and increased lipid availability for fetal growth [19]. Most studies exploring adverse pregnancy outcomes have focused on elevated triglyceride levels, particularly with respect to gestational diabetes mellitus, preeclampsia, pregnancy-induced hypertension, macrosomia, and preterm birth [7,8,9]. In the present study, the missed miscarriage group had lower triglyceride levels. This finding may reveal incomplete gestational metabolic adaptation. However, reverse causality cannot be excluded. In missed miscarriage, embryonic demise may occur before clinical diagnosis, and lipid values measured at clinical assessment may partly demonstrate metabolic consequences of a nonviable pregnancy rather than etiological factors.

Even though LDL-C had the highest AUC among individual lipid parameters, its discriminative performance was modest and does not justify its use as a standalone diagnostic marker. The exploratory combined clinical-lipid model demonstrated higher apparent discrimination than lipid markers alone. However, this apparent improvement should be interpreted cautiously, particularly because clinical history, especially history of miscarriage, contributed substantially to the observed discrimination. Therefore, these model findings should be regarded as hypothesis-generating and require external validation before any clinical application.

Altogether, our findings indicate the potential relevance of maternal lipid assessment as part of broader metabolic evaluation in early pregnancy research. Nevertheless, lipid parameters alone may not provide sufficient discriminative performance. Their potential clinical utility may be contingent upon integrating with maternal clinical history, BMI, glucose metabolism, inflammatory biomarkers, endocrine parameters, and ultrasonographic findings in prospective longitudinal cohorts [8,11,21].

Limitations

The gestational age–matched case–control design and the exclusion of women with known metabolic or endocrine disorders are the main strengths of this study. However, this study is not without limitations. First, its retrospective design and single-timepoint lipid measurement limit causal inference and preclude precise determination of the temporal relationship between lipid assessment and embryonic demise. Additionally, potential confounders including pre-pregnancy BMI, BMI at clinical evaluation, smoking status, dietary pattern, physical activity, insulin resistance markers, thyroid autoimmunity, inflammatory markers, progesterone treatment, assisted reproductive technology use, and embryonic chromosomal findings were not systematically available in the retrospective records. The absence of BMI data is pivotal because BMI may impact both lipid levels and early pregnancy outcomes. Furthermore, ROC-derived thresholds were obtained from the same dataset and were not externally validated. Even though bootstrap resampling was used to estimate optimism-corrected discrimination, the model should remain exploratory until it is validated in an independent cohort.

5. Conclusions

Altered maternal lipid parameters in the first trimester and missed miscarriage were associated in this gestational age frequency-matched case-control study. Moreover, LDL-C and HDL-C were independently associated with missed miscarriage in the adjusted model. Even though lower triglyceride levels were also associated with missed miscarriage, this finding requires careful consideration because reverse causality cannot be excluded.

Individual lipid parameters demonstrated only modest discriminative ability and should not be considered standalone diagnostic markers. Lipid parameters may provide complementary information when evaluated alongside clinical variables. Nevertheless, prospective longitudinal studies with standardized assessments of body mass index, glucose metabolism, endocrine, inflammatory, and chromosomal markers are essential for clarifying temporality, causality, and clinical utility.

Abbreviations

AUC, area under the curve; BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MM, missed miscarriage; OR, odds ratio; ROC, receiver operating characteristic; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; TC, total cholesterol; TG, triglycerides; VIF, variance inflation factor.

Availability of Data and Materials

The dataset is available from the corresponding author on reasonable request.

Author Contributions

IU: project administration, conceptualization, writing-review & editing, supervision. FT: conceptualization, data curation, writing – review & editing. KGO: data curation, investigation, writing – review & editing. MA: formal analysis, investigation, methodology, supervision, writing-review & editing. MBB: methodology, formal analysis, writing – review & editing. DK: investigation, data curation, writing-original draft. NK: conceptualization, investigation, methodology, supervision, writing – review & edit-

ing. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Local Ethics Committee of Training and Research Hospital, University of Health Sciences (Approval No. 2023/11-11) and was conducted in accordance with the Declaration of Helsinki. Due to the retrospective design of the study and the use of anonymized data, the requirement for obtaining informed consent was waived by the Tepecik Training and Research Hospital of the Ethics Committee.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG54469.

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