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ORIGINAL RESEARCH

Prediction of Pregnancy-Related Complications in Women of Advanced Maternal Age: A Nomogram Based on LASSO and Logistic Regression

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Background: The increasing prevalence of advanced maternal age (AMA) is significantly associated with a higher risk of diverse pregnancy-related complications, posing a challenge to maternal and fetal health. However, personalized risk assessment tools specifically designed for this high-risk population remain limited. This study aimed to develop and validate a multi-factor nomogram to predict composite pregnancy complications in AMA women, facilitating early clinical intervention.

Objective: To construct and validate a predictive nomogram integrating metabolic, immune-nutritional, and lifestyle indicators to quantify the risk of composite pregnancy complications in women of advanced maternal age (AMA).

Methods: A retrospective cohort study was conducted on 2212 AMA women. They were randomly divided into a training set (n = 1548) and a validation set (n = 664). The primary endpoint was the composite pregnancy complication. LASSO regression was used to screen candidate variables, followed by multivariate logistic regression to determine the independent predictors. A nomogram was then constructed to visualize the model. The performance was evaluated through the area under the receiver operating characteristic curve (AUC), calibration plot (Hosmer-Lemeshow test), and decision curve analysis (DCA).

Results: Seven independent predictors were identified. Risk factors included history of miscarriage, habitual high-salt/high-fat diet, elevated D-dimer, ALT/AST ratio, non-HDL-C, and importantly, the Triglyceride-Glucose (TyG) index (Calculated based on mmol/L) (OR = 5.817, 95% CI 3.893–8.693). Conversely, a higher CALLY index (OR = 0.754, 95% CI 0.675–0.842) served as a protective factor. The nomogram displayed favorable discrimination in both the training set (AUC = 0.733, 95% CI 0.707–0.758) and validation set (AUC = 0.754, 95% CI 0.709–0.786). Calibration curves demonstrated excellent agreement (P>0.05), and DCA confirmed significant net clinical benefit across threshold probabilities of 0.16–0.93.

Conclusion: This study developed a robust nomogram that effectively incorporates metabolic, immune-nutritional, and lifestyle profiles. It serves as a practical screening tool for early risk stratification in the AMA population, facilitating individualized clinical decision-making.

Keywords: advanced maternal age, pregnancy complications, nomogram, TyG index, cally index

Introduction

With the rapid economic development and recent adjustments in fertility policies in China, the prevalence of women of advanced maternal age (AMA) has escalated significantly. Specifically, the proportion of AMA in China rose from 8.5% prior to the universal two-child policy to 13.5% in the early phase of its implementation, and this trend continues to grow annually.[1] Consequently, the associated rise in pregnancy complications among AMA women has garnered widespread attention.

Previous studies have established that AMA is independently associated with a heightened risk of pregnancy complications, including hypertensive disorders of pregnancy (HDP), gestational diabetes mellitus (GDM), placental abnormalities, and disorders of amniotic fluid.[2,3] Epidemiological data indicate that the incidence rates of HDP and GDM in this population can reach as high as 15% and 18.2%, respectively.[4] These complications not only pose significant

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threats to maternal and fetal safety but also impose a substantial burden on public health systems. Therefore, early identification of high-risk individuals and the implementation of effective interventions are of great clinical importance.

However, most of the existing prediction models for pregnancy complications are targeted at pregnant women belonging to specific disease groups,[5–8] or at specific complication events.[9] There is a lack of objective and systematic quantitative tools and prediction models for assessing the comprehensive risk of pregnancy complications in the AMA-specific population. To fill this gap, this study aims to use LASSO-logistic regression to construct a prediction graph to improve the screening ability and risk stratification ability of pregnancy complications in AMA pregnant women. This tool is intended to identify candidates who require enhanced monitoring and achieve more efficient allocation of medical resources, thereby facilitating clinical decision-making.

Materials and Methods

Study Design and Population

This retrospective study was conducted at Cangzhou People's Hospital. A total of 2212 women of advanced maternal age (AMA, defined as age≥35 years) who underwent comprehensive prenatal care and delivery at our institution between January 2023 and July 2025 were enrolled as study participants.

The inclusion criteria were as follows: (1) singleton pregnancy; and (2) availability of complete clinical data.

The exclusion criteria included: (1) a history of pre-existing chronic diseases diagnosed prior to pregnancy, such as essential hypertension or diabetes mellitus (to distinguish from gestational complications); (2) presence of psychiatric disorders or cognitive impairment that might affect cooperation; (3) non-Chinese nationality (to ensure genetic homogeneity of the study population); and (4) history of chronic infectious diseases, such as hepatitis B virus infection.

Sample Size: According to the 10-event-per-variable (EPV) rule estimated by the logistic regression sample size, the minimum sample size should be at least 10 times the number of independent variables. This study ultimately included 7 independent variables. The total incidence rate of composite pregnancy complications was approximately 30%. Therefore, according to the formula N = (7×10) /30%, the required minimum sample size meets the requirements.

Data Collection and Measurements

Baseline Characteristics and Laboratory Assessment: Clinical data were retrospectively retrieved from electronic medical records. Demographic and obstetric characteristics included maternal age, body mass index (BMI), gravidity, parity, history of miscarriage, and dietary patterns. Dietary patterns were categorized based on self-reported habitual dietary habits recorded during the first prenatal visit via a standardized face-to-face interview.

Outcome Definition: The primary outcome was the occurrence of composite pregnancy complications. This included hypertensive disorders of pregnancy (HDP), gestational diabetes mellitus (GDM), intrahepatic cholestasis of pregnancy (ICP), placental abnormalities (eg, placenta previa/accreta), and amniotic fluid disorders. Rationale for Composite Outcome: Since women of AMA often exhibit a systemic decline in physiological adaptability, we utilized a composite endpoint to capture the overall "high-risk obstetrical state", rather than focusing on isolated disease phenotypes. This approach aims to maximize the sensitivity of early screening for generalized maternal-fetal vulnerability.

History of abortion: In this study, a history of abortion was defined as a binary variable (yes/no). It was recorded as "yes" if the patient self-reported any prior clinically confirmed termination of pregnancy, including both spontaneous and induced abortions. This definition did not distinguish the timing (eg, before or after marriage), specific circumstances, or partner relationship of the pregnancy loss.

Assessment of Dietary Habits: Dietary habits were assessed through a retrospective review of routine clinical consultation records, based on patients self-reported, long-term dietary patterns sustained for over six months. The identification of a habitual high-salt diet referred to the World Health Organization (WHO) recommendation of a daily intake of less than 5 grams (approximately 2000 mg of sodium). However, as precise individual measurement is challenging and dietary salt primarily originates from diverse sources such as processed foods and condiments,[10] this study employed qualitative behavioral indicators for identification. This was defined as a patient's self-description of having a "salty palate", accompanied by the habitual and frequent consumption of pickled foods, processed meats, or the

addition of extra salt or salty condiments during meals. The identification of a habitual high-fat diet was based on existing evidence: the intake of trans fats and saturated fats is associated with the risk of gestational diabetes mellitus,[11] and fried foods are a significant source of trans fatty acids.[12] Consequently, this study defined a high-fat diet tendency as the frequent consumption (≥3 times per week) of fried foods, fatty meats, animal organs, or a stated preference for oily cooking methods (eg, deep-frying, braising in oil). Based on the aforementioned evidence, patients identified with such habits are advised to reduce the intake of processed foods to control "hidden salt" and to modify cooking methods to improve the quality of fat intake.

Laboratory Parameters: Peripheral blood samples collected during the first prenatal visit (baseline) were analyzed for the following indicators: Fasting blood glucose (FBG), glycated hemoglobin (HbA1c), albumin (ALB), hemoglobin (HGB), platelet count (PLT), and absolute counts of neutrophils (NEUT#), absolute counts of lymphocytes (LYMPH#), and absolute counts of monocytes (MO#). Biochemical markers included creatinine (Cr), blood urea nitrogen (BUN), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), anti-thyroid peroxidase antibody (TPOAb), D-dimer, and C-reactive protein (CRP).

Calculation of Derived Indices: To comprehensively assess inflammatory and metabolic status, we calculated a panel of derived indices, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), triglyceride-glucose (TyG) index, neutrophil-to-albumin ratio (NAR), non-high-density lipoprotein cholesterol (non-HDL-C), albumin to non-HDL-C ratio (AAI), alanine aminotransferase to aspartate aminotransferase ratio (ALT/AST), and CALLY index. The detailed definitions and complete calculation formulas for all derived indices are provided in the Supplementary Material.

All the cases included in the analysis had complete records for the above-mentioned key variables, with no missing data.

Data Partitioning and Grouping

Grouping Criteria and Randomization Principle: We employed a stratified randomization approach. Using the key outcome of this study "occurrence of composite pregnancy complications"—as the stratification factor, all 2212 patients were first divided into two strata: the "complication group" (n = 751) and the "non-complication group" (n = 1461).

Random Sequence Generation and Grouping Method: Within each stratum, a random number between 0 and 1 was generated for each patient using the RAND() function in Microsoft Excel. Patients within each stratum were then sorted based on this random number and allocated in a 7:3 ratio: the top 70% of patients in each stratum were assigned to the training set, and the remaining 30% to the validation set.

Grouping Results: This method ensured that the incidence of composite complications in both the training and validation sets remained consistent with that of the overall population. Consequently, the training set included 1548 patients, and the validation set included 664 patients.

Evaluation Criteria for Training and Validation Sets: The training set was used to develop a machine learning model for predicting the risk of composite pregnancy complications. The validation set was used for internal validation of the trained model, with evaluation metrics focusing on: discrimination (assessed by the Area Under the Receiver Operating Characteristic Curve, AUC), calibration (assessed by calibration plots, the Hosmer-Lemeshow test, along with the Brier score and its 95% CI), and clinical utility (assessed by Decision Curve Analysis, DCA).

Statistical Analysis

All statistical analyses were performed using SPSS software (version 27.0; IBM Corp., Armonk, NY, USA) and R software (version 4.5.1; The R Foundation for Statistical Computing).

Descriptive Statistics: Continuous variables were first tested for normality. Those conforming to a normal distribution were expressed as mean ± standard deviation (mean ± SD) and compared between groups using the independent samples *t*-test. Non-normally distributed variables were presented as median and interquartile range [M (Q1, Q3)] and compared using the Mann–Whitney *U*-test. Categorical variables were expressed as frequencies and percentages (n (%)) and analyzed using the Chi-square (χ^2) test.

Model Development and Evaluation: To minimize multicollinearity and avoid overfitting, the Least Absolute Shrinkage and Selection Operator (LASSO) regression was employed to screen for optimal predictive features. Variables with non-zero coefficients were subsequently entered into a multivariate logistic regression analysis to identify independent risk factors. Based on the multivariate analysis results, a nomogram was constructed.

The performance of the nomogram was evaluated across three dimensions: Discrimination: Assessed by the Receiver Operating Characteristic (ROC) curve and the AUC; Calibration: Evaluated using calibration curves, the Hosmer-Lemeshow goodness-of-fit test, and the Brier score (with its 95% CI); Clinical Utility: Analyzed using DCA to determine the net benefit of the model at different threshold probabilities. A two-sided P-value<0.05 was considered statistically significant.

This study was conducted and reported in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) reporting guidelines.[13]

Results

Comparison of Baseline Characteristics

As presented in Table 1, significant differences were observed between the complication group and the non-complication group regarding clinical history and lifestyle. The complication group exhibited a significantly higher prevalence of history of miscarriage and a larger proportion of individuals adhering to a high-salt and high-fat diet compared to the non-complication group (all $P<0.05$). No statistically significant differences were found between the two groups regarding maternal age, BMI, gravidity, or parity (all $P>0.05$).

Regarding laboratory parameters (Table 2), the complication group demonstrated significantly elevated levels of HbA1c, HGB, CRP, Cr, ALT, ALT/AST ratio, TBIL, DBIL, D-dimer, TPOAb, LDL-C, TG, Non-HDL-C, AAI, and the TyG index (all $P<0.05$). Conversely, levels of HDL-C, ALB, and the CALLY index were significantly lower in the complication group (all $P<0.05$). No statistically significant differences were found between the two groups regarding FBG, PLT, BUN, AST, IBIL, TC, or immune cell counts and related indices (MO#, LYMPH#, NEUT#, NLR, PLR, SII, SIRI, and NAR) (all $P>0.05$).

Screening of Predictors via LASSO-Logistic Regression

To mitigate multicollinearity and ensure model robustness, a total of 13 candidate variables—selected based on clinical relevance and statistical correlation—were entered into the LASSO regression model. These included age, BMI, history of miscarriage, dietary patterns, TBIL, TPOAb, D-dimer, ALT/AST ratio, Non-HDL-C, TyG index, Cr, NLR, and CALLY index.

Table 1 Clinical Characteristics and Lifestyle Profiles of the Study Population

Variables	Complication Group (n=526)	Non-Complication Group (n=1022)	Z/χ^2	*P* value
Age [years, M(P_{25},P_{75})]	39.00(37.00,43.00)	39.00(36.00,44.00)	−0.406	0.685
BMI [kg/m^2, M(P_{25},P_{75})]	25.90(23.38,28.13)	25.59(22.50,28.60)	−1.452	0.147
Gravidity [times, M(P_{25},P_{75})]	4.00(3.00,5.00)	3.00(2.00,5.00)	−1.695	0.090
Parity [times, M(P_{25},P_{75})]	2.00(2.00,3.00)	2.00(2.00,3.00)	−0.781	0.435
History of miscarriage[cases, n(%)]			11.490	<0.001
Yes	370(70.34%)	630(61.64%)		
No	156(29.66%)	392(38.36%)		
Dietary Patterns [cases, n(%)]			7.590	0.006
Balanced diet	461(87.64%)	940(91.98%)		
High-salt and high-fat diet	65(12.36%)	82(8.02%)		

Table 2 Laboratory Parameters and Derived Biomarkers Categorized by Function

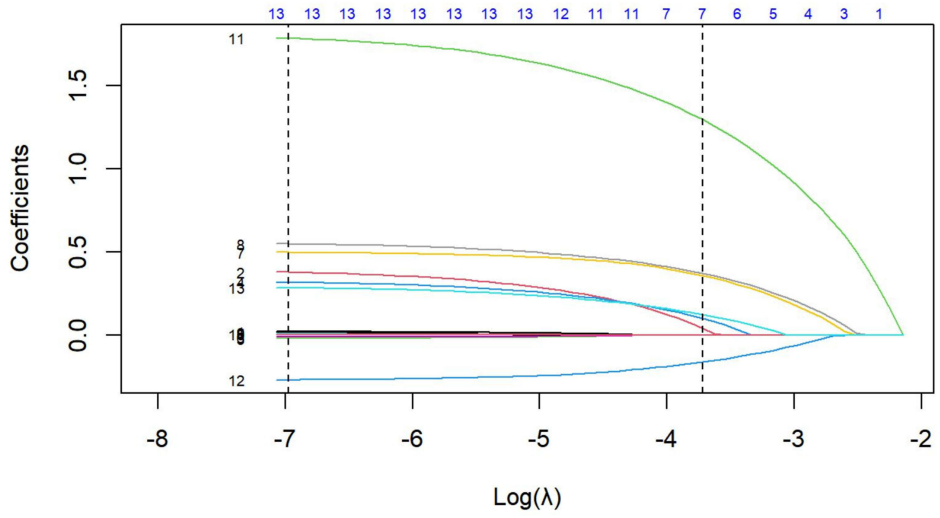
Variables	Complication Group (n=526)	Non-Complication Group (n=1022)	*t*/*Z*	*P* value
FBG [mmol/L, M(P_{25},P_{75})]	4.43(4.11,4.70)	4.35(4.08,4.65)	−1.962	0.050
HbA1c [%, M(P_{25},P_{75})]	5.40(5.10,5.60)	5.30(4.90,5.60)	−2.749	0.006
TC [mmol/L, M(P_{25},P_{75})]	6.13(5.38,6.36)	6.07(5.31,6.47)	−1.605	0.109
HDL-C [mmol/L, M(P_{25},P_{75})]	1.65(1.36,1.88)	1.73(1.43,2.05)	−4.060	<0.001
LDL-C [mmol/L, M(P_{25},P_{75})]	2.90(2.46,3.42)	2.89(2.25,3.46)	−2.753	0.006
AAI [M(P_{25},P_{75})]	0.12(0.11,0.14)	0.11(0.10,0.13)	−5.098	<0.001
TG [mmol/L, M(P_{25},P_{75})]	4.26(3.49,5.06)	3.60(3.16,4.45)	−9.148	<0.001
Non-HDL-C [mmol/L, $\bar{x} \pm s$]	4.36±0.74	4.17±0.94	−4.087	<0.001
TyG Index [M(P_{25},P_{75})]	2.24(2.04,2.40)	2.09(1.86,2.28)	−9.725	<0.001
CRP [mg/L, M(P_{25},P_{75})]	3.64(2.78,5.08)	3.57(2.17,5.33)	−3.014	0.003
ALB [g/L, M(P_{25},P_{75})]	36.30(34.35,38.10)	36.50(35.00,38.40)	−2.838	0.005
CALLY Index [M(P_{25},P_{75})]	1.42(0.95,2.10)	1.53(0.95,2.56)	−3.541	<0.001
TPOAb [IU/mL, M(P_{25},P_{75})]	12.73(10.37,15.76)	12.57(6.91,16.50)	−3.338	<0.001
NLR [M(P_{25},P_{75})]	4.38(3.53,5.29)	4.21(3.35,5.36)	−1.587	0.112
PLR [M(P_{25},P_{75})]	143.33(122.11,176.75)	145.64(114.56,180.50)	−0.542	0.588
SII [M(P_{25},P_{75})]	926.05(721.40,1181.57)	898.38(674.73,1191.35)	−1.561	0.119
SIRI [M(P_{25},P_{75})]	2.05(1.55,2.75)	1.96(1.43,2.69)	−1.828	0.067
MO# [10^9/L, M(P_{25},P_{75})]	0.47(0.39,0.57)	0.46(0.38,0.57)	−1.064	0.287
LYMPH# [10^9/L, M(P_{25},P_{75})]	1.48(1.23,1.72)	1.47(1.21,1.76)	−0.282	0.778
NEUT# [10^9/L, M(P_{25},P_{75})]	6.31(5.50,7.23)	6.28(5.30,7.28)	−1.123	0.340
ALT/AST Ratio [M(P_{25},P_{75})]	1.00(0.68,1.33)	0.73(0.57,1.00)	−8.851	<0.001
D-dimer [ng/mL, M(P_{25},P_{75})]	1.73(1.33,2.05)	1.42(0.90,1.83)	−8.426	<0.001
Cr [μmol/L, M(P_{25},P_{75})]	48.00(44.00,52.00)	46.00(39.00,53.00)	−4.159	<0.001
BUN [mmol/L, M(P_{25},P_{75})]	3.50(2.88,4.50)	3.50(2.80,4.60)	−0.279	0.780
ALT [U/L, M(P_{25},P_{75})]	16.00(11.00,22.00)	12.00(9.00,18.00)	−7.982	<0.001
AST [U/L, M(P_{25},P_{75})]	16.00(13.00,19.25)	16.00(13.00,20.00)	−1.281	0.200
TBIL [μmol/L, M(P_{25},P_{75})]	9.60(7.60,12.10)	9.20(7.00,12.00)	−2.025	0.043
DBIL [μmol/L, M(P_{25},P_{75})]	3.10(2.16,4.49)	2.53(1.74,4.26)	−4.780	<0.001
IBIL [μmol/L, M(P_{25},P_{75})]	6.30(4.53,8.41)	6.30(4.56,8.39)	−0.024	0.981
HGB [g/L, M(P_{25},P_{75})]	116.00(108.00,123.00)	117.00(109.00,125.00)	−2.124	0.034
PLT [10^9/L, M(P_{25},P_{75})]	209.50(176.75,250.00)	211.00(176.00,253.25)	−0.421	0.673

Notes: History of miscarriage: Defined as any previous pregnancy ending in spontaneous or induced abortion (including medical or surgical interventions) regardless of timing or intent. High-salt and high-fat diet: Refers to a self-reported long-term preference for foods with high sodium (>5g/day) and high lipid content, consistent with the Dietary Guidelines for Chinese Residents. #: Denotes absolute count (eg, MO# for monocyte absolute count; LYMPH# for lymphocyte absolute count; NEUT# for neutrophil absolute count). TyG Index: Calculated using units of mmol/L for both triglycerides and fasting blood glucose.

Abbreviations: AAI, Albumin to non-HDL cholesterol Ratio; ALB, Albumin; ALT, Alanine Transaminase; AST, Aspartate Transaminase; BMI, Body Mass Index; BUN, Blood Urea Nitrogen; CALLY, CRP-Albumin-Lymphocyte index; Cr, Creatinine; CRP, C-reactive Protein; DBIL, Direct Bilirubin; FBG, Fasting Blood Glucose; HbA1c, Glycated Hemoglobin; HDL-C, High-Density Lipoprotein Cholesterol; HGB, Hemoglobin; IBIL, Indirect Bilirubin; LDL-C, Low-Density Lipoprotein Cholesterol; LYMPH#, Lymphocyte count; MO#, Monocyte count; NEUT#, Neutrophil count; NLR, Neutrophil-to-Lymphocyte Ratio; Non-HDL-C, Non-High-Density Lipoprotein Cholesterol; PLR, Platelet-to-Lymphocyte Ratio; PLT, Platelet count; SII, Systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index; TBIL, Total Bilirubin; TC, Total Cholesterol; TG, Triglycerides; TPOAb, Anti-thyroid Peroxidase Antibody; TyG, Triglyceride-Glucose index.

Ten-fold cross-validation was utilized to determine the optimal penalty parameter (λ). Based on the 1-standard-error criterion ($\lambda_{1se} = 0.024$), the LASSO algorithm identified seven features with non-zero coefficients: history of miscarriage, dietary patterns, TyG index, D-dimer, ALT/AST ratio, Non-HDL-C, and CALLY index (Figures 1 and 2).

These seven selected variables were subsequently analyzed using multivariate binary logistic regression, with the occurrence of pregnancy complications as the dependent variable. The results demonstrated that history of miscarriage (OR = 1.388, 95% CI 1.089–1.770), adherence to a high-salt and high-fat diet (OR = 1.494, 95% CI 1.028–2.173), elevated TyG index (OR = 5.817, 95% CI 3.893–8.693), elevated D-dimer (OR = 1.742, 95% CI 1.471–2.063), elevated



To facilitate the identification of variables in the profile, the mapping of the curve numbers to the candidate variables is provided below:

Curve No.	Predictor Variable	Status in Final Model
11	Triglyceride – Glucose (TyG) index	Retained (B = 1.761)
8	D – dimer	Retained (B = 0.555)
7	ALT/AST ratio	Retained (B = 0.546)
2	Dietary Patterns	Retained (B = 0.402)
4	History of miscarriage	Retained (B = 0.328)
13	Non – HDL – C	Retained (B = 0.279)
12	CALLY index	Retained (B = – 0.282)
1, 3,5, 6,9,10	Other candidates (e.g., Age, BMI, NLR)	Excluded(Coefficient shrunken to 0)

Figure 1 The LASSO coefficient curves of these 13 candidate variables. The vertical axis represents the coefficient, and the horizontal axis represents the logarithm (λ). Each colored curve represents the path of the coefficient of a certain variable changing as the λ value increases, and its value gradually converges to zero. The two vertical dashed lines represent the λ values selected through 10-fold cross-validation: the left line corresponds to the λ value that minimizes the bias (lambda.min), and the right line corresponds to the λ value selected following the 1 standard error rule (lambda.1se). The 1 standard error criterion was adopted to obtain a more concise model. The embedded table shows the correspondence between the curve numbers and the predictor variables and their states in the final model (the retained variables and their coefficients, as well as the coefficients of the excluded variables are set to zero).

ALT/AST ratio (OR = 1.727, 95% CI 1.414–2.110), and elevated Non-HDL-C levels (OR = 1.321, 95% CI 1.157–1.510) were independent risk factors for pregnancy complications in AMA. Conversely, a higher CALLY index (OR = 0.754, 95% CI 0.675–0.842) was identified as an independent protective factor (Table 3).

Construction of the Predictive Nomogram

Based on the coefficients derived from the multivariate logistic regression analysis, the final predictive equation for assessing the risk of pregnancy complications in AMA women was established as follows:

$$\begin{aligned}\text{Logit}(P) &= -6.787 + 0.402 \times \text{Dietary} + 0.328 \times \text{Miscarriage} + 0.546 \times \text{ALT/AST Ratio} + 0.555 \times \text{D} - \text{dimer} \\ &\quad + 0.279 \times \text{Non} - \text{HDL} - \text{C} + 1.761 \times \text{TyG} - 0.282 \times \text{CALLY}\end{aligned}$$

(Note: Dietary Patterns: 0 = Balanced, 1 = High-salt/high-fat; History of Miscarriage: 0 = No, 1 = Yes; The ALT/AST ratio, D-dimer, non-HDL-C, TyG index, and CALLY index are all measured continuous values and should be directly substituted into the formula).

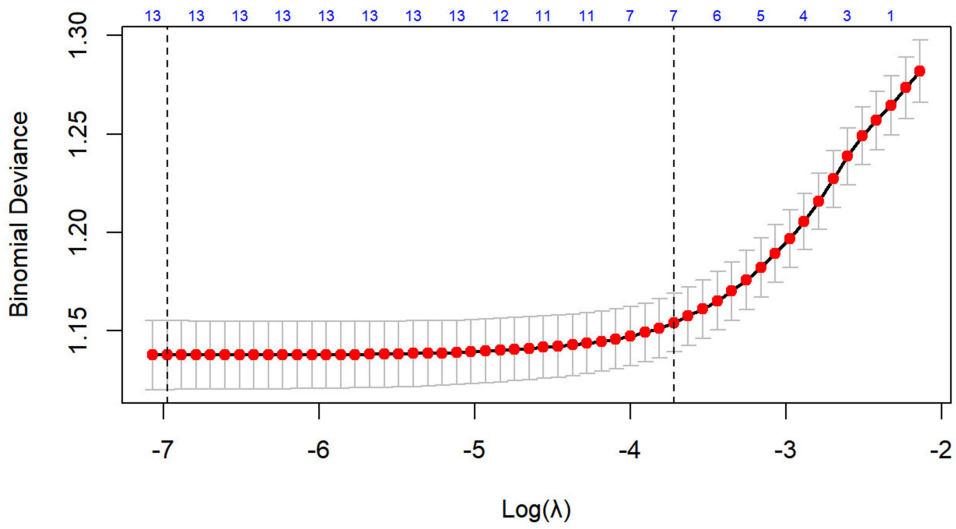


Figure 2 Using ten-fold cross-validation to select the optimal tuning parameters (λ) for the LASSO model. The binomial loss points were plotted against the logarithm of (λ). Two vertical dashed lines represent the λ value that minimizes the cross-validation loss points (lambda.min) and the λ value selected based on the 1 standard error rule (lambda.1se). The 1 standard error criterion is used to select the optimal λ value for a simpler model.

Based on this predictive model, a quantitative nomogram was constructed to visualize the risk assessment and facilitate clinical application (Figure 3).

Internal Validation of the Prediction Model

The predictive performance of the nomogram was comprehensively evaluated and validated in both the training and validation cohorts (Figure 4).

Discrimination: The model exhibited favorable discrimination performance. The AUC was 0.733 (95% CI 0.707–0.758) in the training set and 0.754 (95% CI 0.709–0.786) in the validation set, demonstrating the model's robust ability to distinguish between individuals with and without pregnancy-related complications (Figure 4A and D).

Calibration: The model demonstrated adequate calibration in both the training and validation sets. The Hosmer-Lemeshow goodness-of-fit test showed no statistically significant departure from perfect fit (training set: $\chi^2 = 4.879$, $P = 0.770$; validation set: $\chi^2 = 8.651$, $P = 0.373$). The overall prediction accuracy, as measured by the Brier score, was 0.191 (95% CI 0.181–0.201) in the training set and 0.186 (95% CI 0.173–0.200) in the validation set, indicating an acceptable level of prediction error. Visual inspection of the calibration curves (Figure 4B and E) confirmed that the predicted probabilities generally aligned well with the observed outcomes across the risk spectrum. Taken together, these results suggest that the model is not significantly miscalibrated and provides reliable probability estimates.

Table 3 Results of LASSO-Logistic Regression Analysis for Risk Factors of Pregnancy Complications in AMA Women

Variable	*B*	*SE*	*Wald*χ^2	*P* value	*OR* (95% CI)
History of miscarriage	0.328	0.124	7.003	0.008	1.388(1.089–1.770)
Dietary Patterns	0.402	0.191	4.427	0.035	1.494(1.028–2.173)
ALT/AST Ratio	0.546	0.102	28.660	<0.001	1.727(1.414–2.110)
Non-HDL-C	0.279	0.068	16.836	<0.001	1.321(1.157–1.510)
CALLY	−0.282	0.056	25.220	<0.001	0.754(0.675–0.842)
D-dimer	0.555	0.086	41.381	<0.001	1.742(1.471–2.063)
TyG Index	1.761	0.205	73.797	<0.001	5.817(3.893–8.693)
Intercept	−6.787	0.583	135.348	<0.001	0.001(NA)

Abbreviations: Non-HDL-C, Non-High-Density Lipoprotein Cholesterol; CALLY, CRP-Albumin-Lymphocyte index; TyG, Triglyceride-Glucose index.

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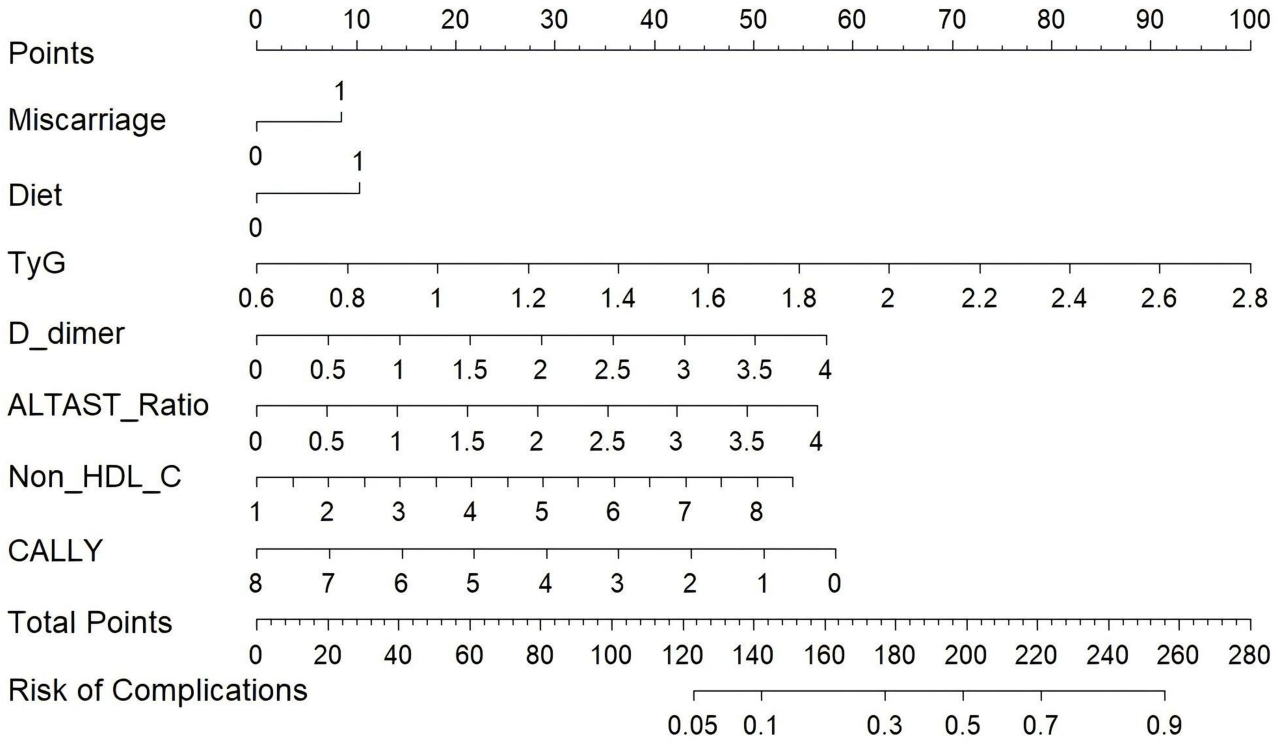

Figure 3 Predictive nomogram for pregnancy complications in AMA women. Predictive nomogram for individualized risk assessment of composite pregnancy outcomes in women of advanced maternal age. To use the nomogram, find the position of each predictor on the corresponding axis, draw a vertical line up to the "Points" axis to get the score, and sum the points for all variables. The total points are then located on the "Total Points" axis to determine the predicted probability of complications. (Dietary Patterns: 0=Balanced diet, 1=High-salt/high-fat; History of miscarriage: 0=No, 1=Yes).

Clinical Utility: DCA was performed to determine the clinical net benefit of the model. As illustrated in Figure 4C and F, the nomogram provided a significant net clinical benefit over the "treat-all" or "treat-none" strategies across a wide range of threshold probabilities (0.19–0.83 in the training set and 0.16–0.93 in the validation set), confirming its potential as an effective tool for clinical decision-making.

Discussion

The pathogenesis of pregnancy complications in women of advanced maternal age (AMA) is complex, resulting from the synergistic interplay of physiological aging, lifestyle factors, and pathological alterations. Despite this, there is a paucity of integrated predictive models specifically tailored for this high-risk population. One study indicated that among primiparous women, compared to non-AMA, AMA is associated with a higher rate of cesarean delivery, an increased risk of intrauterine fetal death, and lower 5-minute Apgar scores in newborns. However, the risks of postpartum hemorrhage, third-or fourth-degree perineal tears, and neonatal ICU admission are not elevated.[14] Therefore, the management of pregnancy outcomes in advanced maternal age primiparas should be based on a comprehensive consideration of multiple factors rather than age alone. To address this gap, our study employed LASSO-logistic regression to identify seven key predictors spanning multiple pathophysiological dimensions. These indicators can be systematically categorized as follows: (i) Metabolic function (TyG index and non-HDL-C),[15,16] (ii) Coagulation and vascular function (D-dimer),[17] (iii) Nutrition-inflammation-immune homeostasis (CALLY index),[18] (iv) Subclinical hepatic stress (ALT/AST ratio),[19] and (v) Clinical history and lifestyle (history of miscarriage and high-salt/high-fat diet).

Notably, although hypertensive disorders of pregnancy (HDP), gestational diabetes mellitus (GDM), and placental disorders present as distinct clinical entities, they are thought to share a "common pathological soil" in AMA women, primarily characterized by vascular endothelial dysfunction and chronic systemic inflammation.[20–22] The predictors in our model collectively quantify this underlying burden. For instance, insulin resistance (TyG index) and dyslipidemia (non-

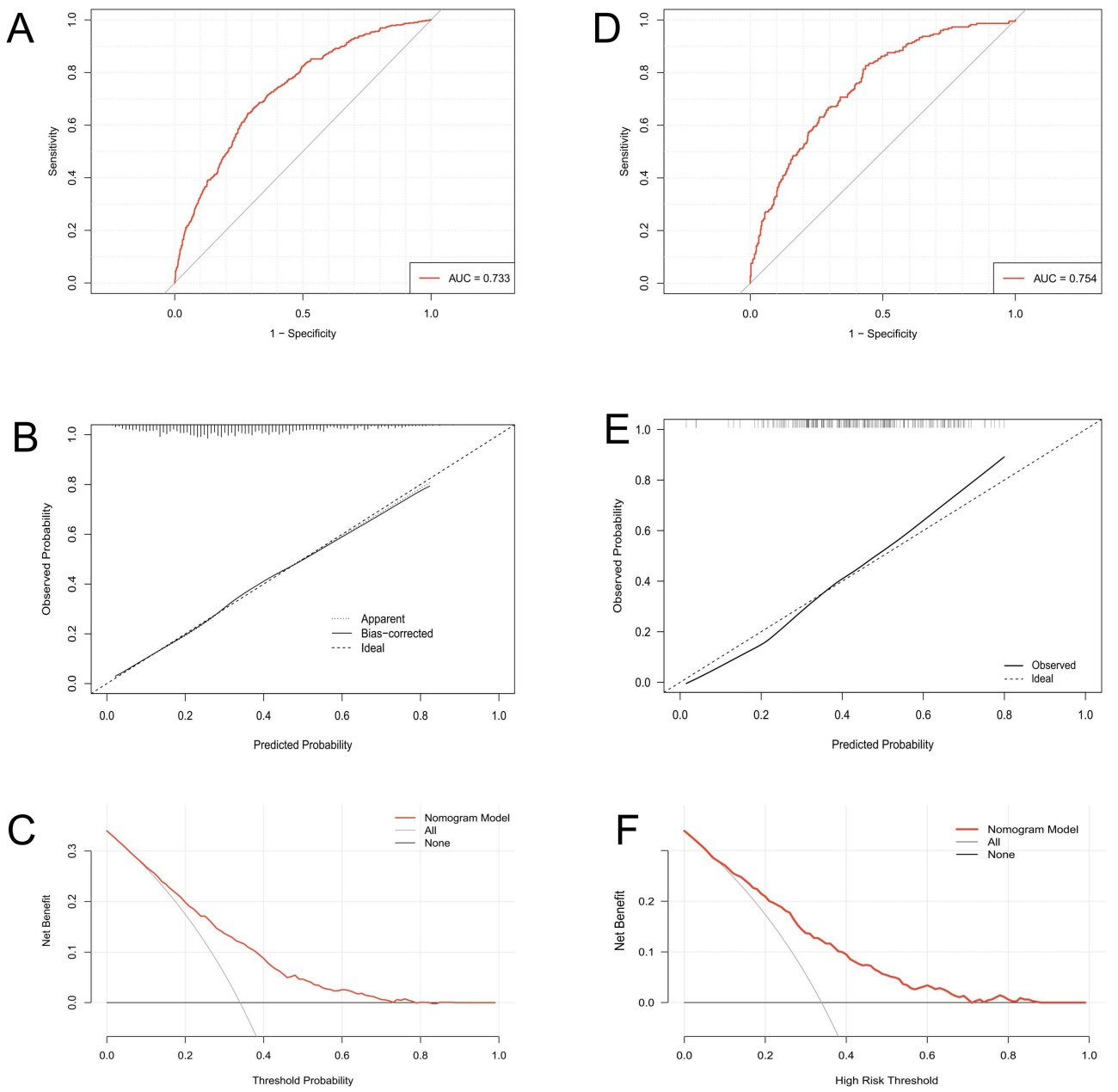

Figure 4 Performance and clinical utility evaluation of the nomogram in the training and validation cohorts. (**A** and **D**) Receiver operating characteristic (ROC) curves demonstrating the discrimination ability in the training set (**A**) and validation set (**D**). (**B** and **E**) Calibration plots showing the consistency between predicted and observed probabilities in the training set (**B**) and validation set (**E**). (**C** and **F**) Decision curve analysis (DCA) curves illustrating the clinical net benefit of the model across different threshold probabilities in the training set (**C**) and validation set (**F**).

HDL-C) directly promote endothelial injury and a pro-inflammatory state.[23–25] Concurrently, a low CALLY index reflects compounded nutritional deficiency and inflammatory activation,[18] while elevated D-dimer marks consequent hypercoagulability.[26] This integrative approach explains the model's capacity to predict a broad spectrum of complications, as it captures the severity of the shared vascular-metabolic-inflammatory derangement rather than a single disease pathway.

The TyG index is a sensitive surrogate for insulin resistance. Previous studies[27] have shown that elevated TyG increases the risk of preeclampsia even in the absence of hyperglycemia, particularly in women over 35. Similarly, combining baseline TyG with BMI in early pregnancy has been shown to reliably predict GDM in a dose-dependent manner.[28] Gurza et al[29] further identified a TyG threshold >8.6 in the first trimester as significantly associated with

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adverse perinatal outcomes. Note: While the standard TyG index calculation often uses mg/dL, our study utilized mmol/L directly from laboratory reports. This results in a lower numerical range (typically ~1.5–3.0) compared to the mg/dL-based index (~8.0–10.0). However, since the transformation is logarithmic, the correlation with insulin resistance remains mathematically equivalent, though the absolute values and cut-offs differ. This discrepancy may be attributed to the exacerbated state of insulin resistance and metabolic dysregulation inherent to the AMA phenotype,[30–32] thereby underscoring the central role of glucolipid metabolism in driving complications in this specific cohort.

Beyond the composite TyG index, core lipid parameters are also closely linked to pregnancy complications. Research indicates that women with pregnancy complications exhibit significantly higher TC and TG levels, and lower HDL-C levels, compared to healthy controls.[33] Spracklen et al[34] associated elevated TC, non-HDL-C, and TG with preeclampsia, while Xiang et al[35] highlighted non-HDL-C as the most potent predictor of GDM among non-traditional lipid profiles in early pregnancy. Consistent with these findings, our study identified non-HDL-C as an independent risk factor, validating the utility of non-traditional lipid parameters in the risk assessment of AMA pregnancies.

Abnormalities in coagulation, specifically fibrinolysis, constitute another critical pathological basis. D-dimer, a marker of fibrin degradation, is well-documented to correlate with thrombotic risk. Wang et al[36] reported that D-dimer is an independent risk factor for gestational hypertension (OR = 2.67; 95% CI 1.56–4.56). Similarly, Chen et al[37] suggested that D-dimer might be the optimal predictor for hypertensive disorders, and Rodriguez-Pena et al[38] found a strong correlation between elevated D-dimer and severe preeclampsia. Our results corroborate these findings, confirming that heightened coagulation and impaired fibrinolysis are pivotal mechanisms in the development of AMA-related complications.

The nutritional-inflammatory-immune status of AMA women also warrants attention. The CALLY index serves as a comprehensive quantitative tool for evaluating this status. Niu et al[39] demonstrated that the CALLY index is negatively correlated with the severity of preeclampsia. The AUC value for predicting preeclampsia was 0.941 (95% CI 0.900–0.981), suggesting its protective role. Our study also found that the CALLY index in the complication group was significantly lower than that in the non-complication group. A high CALLY index was an independent protective factor for AMA composite pregnancy complications (OR = 0.754), highlighting the regulatory role of the "nutrition-inflammation-immune" network in the progression of composite pregnancy complications.

Liver function markers also played a significant role in our model. The ALT/AST ratio emerged as an independent risk factor for composite pregnancy complications (OR = 1.727). Traditionally, the AST/ALT ratio (De Ritis ratio) is used to differentiate liver etiologies. However, in our study population, the ALT/AST ratio was a more prominent predictor, reflecting the relative dominance of ALT elevation in the complication group. Since ALT is a more specific marker of hepatocellular injury, an elevated ALT/AST ratio suggests active liver stress or subclinical hepatic dysfunction. This aligns with findings by Yılmaz et al[40] who highlighted the diagnostic value of aminotransferase ratios in ICP, suggesting that imbalances in these enzymes are sensitive indicators of pregnancy-related hepatic burden.

Clinical history, specifically a history of miscarriage, remains a non-negligible risk factor. Previous evidence[41] links prior miscarriage—especially recurrent loss-to an increased risk of placental abnormalities (eg, placenta previa, accreta). Linehan et al[42] proposed that recurrent miscarriage serves as a "sentinel risk marker" for future complications, and Ge et al[43] associated it with preeclampsia and GDM. Our data supports these observations, showing that a history of miscarriage is an independent predictor, likely reflecting underlying endometrial damage or chronic inflammatory states.[44]

Currently, research linking a high-salt and high-fat diet directly to composite pregnancy complications is limited. Our study bridges this gap, identifying it as an independent risk factor (OR = 1.494). Two plausible mechanisms may underpin this association: First, high salt intake activates the renin-angiotensin-aldosterone system (RAAS), leading to sodium retention and vasoconstriction, thereby increasing the risk of HDP.[45] Second, high fat intake induces lipid metabolic disorders and atherosclerosis, potentially exacerbating placental vascular pathology and increasing the risk of placental and amniotic fluid abnormalities.[46]

It is important to recognize that these seven predictors are not isolated; rather, they form an interconnected risk network. For instance, a high-salt/high-fat diet may trigger metabolic disturbances (elevating TyG and non-HDL-C) while simultaneously activating inflammation (lowering CALLY). Similarly, a history of miscarriage may predispose patients to chronic inflammation and endothelial damage, further elevating D-dimer levels. This multidimensional synergy validates the complexity of the AMA condition and demonstrates the robust predictive efficacy of our integrated model.

The predictive model and nomogram developed in this study offer value beyond serving as a ready-to-use risk assessment tool; they provide a foundational framework for future advanced risk prediction schemes. First, the multi-dimensional, interpretable key predictors integrated into our model (eg, the TyG index, CALLY index) offer a clinically validated feature set for developing machine learning (particularly deep learning) models, ensuring the biological and pathophysiological relevance of inputs for complex algorithms. Second, the nomogram itself, as a well-performing baseline model, can serve as a benchmark for evaluating the incremental predictive value of future novel AI models. In the context of the rapid evolution of artificial intelligence-supported clinical decision support systems, the core logic of this study—quantifying the "vascular-metabolic-inflammatory" common pathological soil to predict multiple complications—can be translated into an intelligent module embeddable within electronic health records. Building upon this framework, future work can develop dynamic, personalized risk assessment tools that automate data extraction and real-time risk calculation. This would enable a full spectrum of decision support for AMA, ranging from early risk warning to the formulation of individualized intervention strategies, ultimately propelling obstetric care toward precision prevention and intelligent management.

Limitations

Our study is subject to several limitations inherent to its retrospective design. Primarily, as a single-center study, potential selection bias related to regional demographics exists, and the external validity of the model remains to be verified in broader populations. Consequently, certain confounders, such as precise physical activity levels and medication history during pregnancy, were not fully captured, which might influence the model's precision.

A methodological note concerns the TyG index, which was calculated using mmol/L rather than the conventional mg/dL. While this difference does not impact the model's discriminatory power (AUC), the specific cut-off values and the magnitude of the Odds Ratios are not directly comparable to studies utilizing the mg/dL-based formula. Future meta-analyses should account for this unit variation.

Regarding the outcome definition, we utilized a composite endpoint. We acknowledge that this approach may mask the pathophysiological heterogeneity between distinct complications (eg, placenta previa vs. GDM). However, from a pragmatic clinical standpoint, this nomogram is designed as a high-sensitivity surveillance tool to identify "at-risk" AMA women requiring intensive monitoring, rather than to serve as a diagnostic instrument for specific pathologies.

Due to the retrospective nature of this study, the assessment of dietary habits relied on qualitative clinical descriptions from medical records rather than quantitative dietary surveys. The dietary data were based on self-reports, which inevitably introduces recall bias. Although we could not quantify caloric or sodium intake, this variable effectively captures the patient's dominant lifestyle pattern and serves as a pragmatic risk indicator in a clinical setting. Future prospective studies utilizing validated Food Frequency Questionnaires (FFQ) are warranted to improve data granularity and accuracy.

Conclusion

In this study, we developed and validated a nomogram for predicting the risk of composite pregnancy complications in women of advanced maternal age (AMA) using the LASSO-logistic regression approach. The model integrates seven key predictors spanning multiple dimensions: clinical history (history of miscarriage), lifestyle (high-salt and high-fat diet), metabolic indicators (TyG index, non-HDL-C), coagulation function (D-dimer), liver function (ALT/AST ratio), and nutritional-inflammatory-immune status (CALLY index). Internal validation demonstrated that the model possesses good discrimination, calibration, and clinical utility. This nomogram serves as an intuitive and quantitative tool to assist clinicians in the early identification of high-risk individuals and may inform targeted prenatal monitoring and management. It is important to emphasize that this is a retrospective predictive modeling study aimed at providing a risk stratification instrument rather than establishing causality. In particular, it must be noted that the performance of the current model requires further validation through external, multicenter, prospective studies. Future research should focus on evaluating the generalizability of the model across diverse populations and healthcare settings, as well as exploring its real-world impact on improving pregnancy outcomes when integrated into the clinical decision-making pathway for AMA women.

Ethical Approval

This study was approved by the Medical Ethics Committee of Cangzhou People's Hospital (Approval No. K2025-128-01). All patients provided written informed consent to review their medical records and participate in the study, and all personal clinical data were strictly anonymized and kept confidential in accordance with the ethical guidelines of clinical research. The study was conducted in accordance with the Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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