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Research Article

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Development and Validation of an Early Prediction Model for Neonatal Hypoglycemia in Full-Term Appropriate-for-Gestational-Age Newborns within 24 Hours of Birth

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Abstract

Background: Standardized screening for neonatal hypoglycemia (NH) in full-term, appropriate-for-gestational-age (AGA) newborns is lacking. We aimed to develop a bedside prediction model for early NH (≤24 hours) in this population.

Methods: This retrospective study included 1,543 full-term AGA newborns, randomly split them into training and testing sets at a ratio of 7:3. From 51 candidate variables, LASSO and multivariate logistic regression were used to select predictors and construct a nomogram. Model performance was evaluated via area under the curve (AUC), calibration, and decision curve analysis (DCA).

Results: NH occurred in 15.4% (237/1,543) of the cohort. LASSO regression identified nine core predictive variables: maternal factors (gestational diabetes mellitus, gestational hypertension, mode of delivery, 1-hour glucose level on the oral glucose tolerance test, total bile acids, and hemoglobin) and neonatal factors (sex, gestational age, and feeding method). It demonstrated good discrimination, yielding an AUC of 0.943 (95% CI: 0.919–0.967) in the training set and 0.934 (95% CI: 0.896–0.971) in the testing set. Calibration curves and DCA confirmed robust predictive accuracy and high clinical net benefit.

Conclusion: This bedside nomogram enables accurate, early risk stratification of NH in full-term AGA newborns, optimizing targeted screening in a frequently overlooked population.

Keywords: neonatal hypoglycemia; full-term appropriate-for-gestational-age newborns; prediction model; nomogram; risk factors

1 Introduction

Neonatal hypoglycemia (NH) is one of the most prevalent metabolic abnormalities in the early postnatal period. Its incidence in healthy, full-term newborns is approximately 5%–15% but rises to 50% when high-risk factors, such as preterm birth, maternal gestational diabetes mellitus (GDM), small-for-gestational-age (SGA) or large-for-gestational-age (LGA) newborns, are concurrently present[1-3]. Glucose is the primary energy source for the neonatal brain. Recurrent or persistent NH can impair cerebral energy metabolism and is closely associated with later neurodevelopmental abnormalities, including cognitive impairment, learning disabilities, visual-motor integration deficits, and cerebral palsy[4]. Furthermore, NH imposes substantial burdens on healthcare resources and long-term socioeconomic costs, including those related to hospitalization, neurological rehabilitation, and reduced quality of life[5]. Therefore, early identification and timely intervention are significant for improving neurodevelopmental outcomes and optimizing perinatal care.

In clinical practice, full-term appropriate-for-gestational-age (AGA) newborns are typically considered a low-risk population because they lack traditional risk factors and are therefore not included in routine intensive blood glucose monitoring protocols[6]. However, a retrospective cohort study reported that approximately 26.3% of healthy newborns met the screening criteria for NH[3], suggesting that the NH risk in this population may be underestimated. Currently published prediction models for NH primarily focus on preterm newborns, newborns born to GDM mothers, or those with established risk factors such as respiratory distress[7-10]. Specialized prediction tools for full-term AGA newborns remain lacking. Therefore, it is vital to discern risk factors for NH in this population and develop effective predictive tools.

Current screening strategies for NH primarily depend on predefined risk factors; however, they may not adequately account for the cumulative effects of various maternal and neonatal variables. Consequently, individualized prediction models that incorporate clinical factors could enhance early risk stratification and facilitate targeted glucose monitoring. In this single-center retrospective study, we developed and validated a prediction model for NH in full-term AGA newborns within 24 hours after birth, aiming to provide a practical tool for individualized risk assessment and optimized neonatal glucose management.

2 Methods

2.1 Study Design and Study Population

This retrospective cohort study included full-term AGA newborns delivered at our hospital between January 2020 and December 2025. The NH group consisted of infants born in the obstetric department who were diagnosed with NH within 24 hours after birth through postnatal glucose screening and subsequently transferred to the neonatal department. The non-NH group comprised contemporaneous full-term AGA infants born in the neonatal department without NH within 24 hours after birth. All data were extracted from the hospital's electronic

medical record system, covering obstetric inpatient records, delivery records, neonatal inpatient records, laboratory test results, and neonatal bedside blood glucose monitoring records. After standardized processing, a mother-infant paired database was established. This study protocol was reviewed and approved by the hospital's Medical Ethics Committee (Approval No.: XMFHIIT-2026SL 187-01), and informed consent was waived.

Inclusion criteria included: neonatal gestational age of 37^{+0} to 41^{+6} weeks; AGA defined as a birth weight falling between the 10th and 90th percentiles on the growth standard curve for the same gestational age and sex[11]; newborns delivered at this hospital who had undergone at least one blood glucose measurement within 24 hours of birth; complete clinical and laboratory data from the mother during pregnancy and delivery, as well as from the early neonatal period, allowing for the extraction of all candidate variables and outcome measures. Exclusion criteria included: the presence of major congenital malformations, chromosomal abnormalities, or confirmed congenital metabolic disorders; postnatal asphyxia, defined as a 1-minute Apgar score ≤ 7; confirmed neonatal infection, sepsis, or a severe medical condition requiring emergency resuscitation; death, voluntary discharge, or transfer to another hospital within 24 hours of birth, which precluded outcome assessment.

2.2 Data Collection and Candidate Predictors

Before data collection, a standardized checklist was developed. Two investigators independently extracted the data and cross-checked their findings. Disagreements were reviewed and settled by a third researcher. Based on a literature review, clinical consensus, and data availability, 51 candidate predictors were included, all of which were baseline variables available before or during delivery.

Maternal factors covered age, pre-pregnancy body mass index (BMI), intrapartum BMI, weight gain during pregnancy, height, educational level, GDM, insulin use, dietary control, gestational hypertension (GH), hypothyroidism, days of prenatal hospitalization, Group B

Streptococcus (GBS) infection, intrapartum fever, number of pregnancies, parity, and twin pregnancies.

For laboratory tests, at 24–28 weeks of gestation, the 75-gram oral glucose tolerance test (OGTT) was performed to measure fasting plasma glucose (0 h), 1-hour post-load glucose (1 h), and 2-hour post-load glucose (2 h). Maternal venous blood was collected during early pregnancy to measure thyroid-stimulating hormone (TSH) and Treponema pallidum antibodies. Within 72 hours before delivery, complete blood count was performed, including white blood cell count (WBC), neutrophil count (NEU), red blood cell count, hemoglobin (Hb), and platelet count. Liver function, including total bile acids (TBA), total protein (TP), and albumin (ALB), was examined. Kidney function, including blood urea nitrogen, creatinine, and uric acid, was examined. Lipid profiles, including total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C), were examined.

Delivery-related factors covered mode of delivery, type of anesthesia, premature rupture of membranes, and meconium-stained amniotic fluid.

Neonatal factors covered sex, gestational age, birth weight, body length, Apgar score, and feeding method. The feeding method referred to early feeding within 1 hour of birth. This variable was recorded before or at the time of the first glucose measurement.

2.3 Outcome Variable

The outcome was NH within 24 hours of birth, defined as any bedside glucose measurement < 47 mg/dL （2.6 mmol/L)[12]. Blood samples were collected from the heel by trained personnel to examine blood glucose using a Roche AccuChek-V003 blood glucose meter and corresponding test strips (Switzerland) in the neonatal intensive care unit or the mother-baby room. Blood glucose values recorded within 24 hours were used as the basis for analysis.

2.4 Statistical Methods

2.4.1 Sample Size Estimation

Sample size was estimated based on the Events Per Variable (EPV) principle, with a minimum threshold of EPV ≥ 15. Typically, the final number of variables included in a model ranged from 5 to 10. Assuming we ultimately included 10 variables, the training set must contain at least 150 cases of NH. Previous studies showed that the incidence of NH in healthy full-term newborns was approximately 5%–15%. Assuming an incidence of 15% for this study, the training set would ultimately require 1,000 cases. Using a 7:3 split between the training and test sets, a minimum of 1,429 newborns would be required.

2.4.2 Management of Missing Values

This study strictly adhered to data quality control protocols, verifying the clinical data of mothers and newborns item by item. When a predictor variable had a missing proportion of 20% or higher, that variable was excluded; when the missing proportion was below 20%, multiple imputation methods were applied. Cases with missing outcome variables were eliminated. In the final dataset included in the analysis, all candidate predictors and outcome variables were free of missing values. Therefore, multiple imputations were not performed. Data entry errors, outliers, and logically inconsistent data were all cross-checked against the original medical records and corrected or excluded based on the review results to ensure data quality.

2.4.3 Descriptive Statistics and Intergroup Comparisons

For continuous variables, the Shapiro-Wilk test was first utilized to determine normality. Variables with a normal distribution were depicted as mean ± standard deviation ($x \pm s$), and two-group comparisons were made via the independent samples t-test. Variables with a non-normal distribution were depicted as median and interquartile range [M (Q1, Q3)] and were compared via the Mann-Whitney U test. Categorical variables were depicted as frequency and percentage and were compared via the chi-square test or Fisher's exact test.

2.4.4 Data Splitting and Validation Strategy

A stratified random sampling method based on outcome (whether NH occurred within 24 hours of birth) was used to split the overall cohort into a training set and a test set in a 7:3 ratio. The training set was applied for selecting variables and building a model, while the test set was used for internal validation and performance evaluation of the model.

2.4.5 Variable Selection Strategy

Intergroup comparisons were performed on all candidate predictors in the training set. Variables with $P < 0.1$ were incorporated into the multivariate logistic regression model, and forward stepwise regression was used for variable selection.

LASSO (Least Absolute Shrinkage and Selection Operator) logistic regression was applied for penalized regression screening of candidate variables. Through 10-fold cross-validation, binomial deviance was used as the metric for evaluating model error, and the optimal penalty parameter λ (i.e., λ_min) was selected based on the minimum error criterion. Finally, the intersection of the variables selected by both methods was adopted as the final predictor variables.

2.4.6 Model Development and Evaluation

NH within 24 hours of birth was used as the dependent variable. The final set of predictor variables was incorporated into a multivariate logistic regression model to develop a prediction model for NH. Model discriminatory power was examined via the receiver operating characteristic (ROC) curve, and the area under the curve (AUC), optimal cutoff value, and corresponding sensitivity, specificity, and precision were calculated. Model calibration was assessed using calibration curves. Additionally, the model's clinical utility was tested via decision curve analysis (DCA). Through comparison of the net benefit at different threshold probabilities, the model's clinical utility was further evaluated.

2.4.7 Statistical Analysis

All data cleaning, variable selection, model construction, and validation were performed in R (version 4.5.2) mainly using glmnet (LASSO regression), MASS (stepwise regression), pROC (ROC analysis), rms (calibration curves), ggDCA (decision curves), and ggplot2 (plotting) packages. Two-sided tests were performed. $P < 0.05$ was considered statistically significant. Detailed code is available in the Supplementary Materials.

3 Results

3.1 Baseline Features

3.1.1 Baseline Features of the Overall Population

Between January 2020 and December 2025, 10,725 newborns were delivered at our hospital, including 672 cases of NH. This study enrolled 1,543 full-term AGA newborns, including 237 (15.4%) in the NH group and 1,306 (84.6%) in the non-NH group. Baseline features of the NH and non-NH groups are outlined in Table 1.

Compared with non-NH newborns, the NH group had a markedly higher prevalence of GDM (71.7% vs. 15.2%) and GH (17.3% vs. 4.3%), higher rates of insulin use (8.9% vs. 1.0%) and dietary control (62.9% vs. 14.5%), and a higher proportion of twin pregnancies (10.5% vs. 3.5%) (all $P < 0.001$). Maternal age, pre-pregnancy BMI, intrapartum BMI, OGTT glucose levels at 0 h, 1 h, and 2 h, and TBA levels were also substantially higher (all $P < 0.001$).

For delivery factors, the cesarean section rate (67.1% vs. 35.8%) and the scheduled cesarean section rate (64.1% vs. 34.5%) were both substantially higher in the NH group (both $P < 0.001$). Regarding neonatal factors, the proportions of female newborns (54.4% vs. 41.3%) and newborns who had not been fed (58.2% vs. 1.6%) were both markedly higher in the NH group (both $P < 0.001$). Gestational age and birth weight were notably lower in the NH group (both $P < 0.001$). No statistical differences were identified between the two groups regarding hypothyroidism, days of prenatal hospitalization, GBS infection, intrapartum fever, type of analgesia, premature rupture of membranes, or lipid profiles (all $P > 0.05$).

3.1.2 Baseline Features of the Training and Test Sets

Baseline features of the training set (n = 1,079) and the test set (n = 464) are outlined in Table 2. There was no marked difference in NH incidence between the two sets (15.3% vs. 15.5%, P = 0.972), and most clinical variables were well-balanced and comparable between the two sets (all P > 0.05). Statistical differences were present only for days of prenatal hospitalization (10.1% vs. 5.0%, P = 0.001), NEU (median 6.59 vs. 6.32, P = 0.033), and LDL-C (median 2.97 vs. 2.80, P = 0.004).

3.2 Selection of Predictor Variables

3.2.1 Between-Group Comparisons and Stepwise Logistic Regression

To identify potential predictor variables for NH in full-term AGA newborns, we conducted between-group comparisons of all candidate variables in the training set (n = 1,079) (Table 3). Among the 51 candidate variables, 31 were significantly associated with NH (P < 0.05), including maternal factors [educational level, GDM, insulin use, dietary control, GH, mode of delivery (cesarean section), scheduled cesarean section, spinal anesthesia, meconium-stained amniotic fluid, maternal age, number of deliveries, parity, pre-pregnancy BMI, weight gain during pregnancy, intrapartum BMI, height, OGTT glucose levels at 0h/1h/2h, twin pregnancies, prenatal WBC, NEU, Hb, TBA, ALB, and TSH] and neonatal factors (newborn sex, feeding method, gestational age, birth weight, body length).

Variables that showed statistical significance in the between-group comparisons were included in a forward stepwise logistic regression model for further screening. The final model retained 10 variables for multivariate regression analysis (Table 4), including maternal factors [GDM, mode of delivery (cesarean section), scheduled cesarean section, TBA, 1-hour OGTT, Hb, and GH] and neonatal factors [sex (male), feeding mode (breastfeeding, formula feeding), and gestational age].

Compared with no feeding, both breastfeeding ([OR, 95% CI]: 0.17, 0.05–0.56, P = 0.004) and formula feeding (0.01, 0.00–0.01, P < 0.001) notably reduced the NH risk. In addition, male newborns (0.56, 0.32–0.99, P = 0.047) and scheduled cesarean sections (0.19, 0.04–0.85, P = 0.030) also demonstrated a protective effect against NH.

GDM (6.40, 3.01–13.61, P < 0.001), cesarean section (13.43, 3.06–59.04, P < 0.001), TBA (1.11, 1.03–1.19, P = 0.005), 1-hour OGTT (1.23, 1.00–1.50, P = 0.047), and GH (2.43, 1.00–5.91, P = 0.049) were all related to an increased NH risk. Although Hb (0.98, 0.96–1.00, P = 0.086) and gestational age (0.79, 0.59–1.06, P = 0.111) were retained in the multivariable model, they did not reach statistical significance.

3.2.2 LASSO Regression Screening

This study employed LASSO regression to screen 51 candidate predictors to mitigate model overfitting and identify features with reliable predictive performance. The results identified that the optimal penalty parameter was λ_min = 0.008 (Figure 1A), with 18 variables having non-zero coefficients retained in the model. Additionally, λ_1se = 0.037 was selected based on the 1 SE criterion to evaluate the model's simplicity and robustness. The coefficient path plot (Figure 1B) further illustrates how the coefficients of each variable converge to zero as the penalty strength increases.

3.2.3 Final Predictor Variables

To enhance the robustness of the variable selection results, this study combined the results from stepwise logistic regression and LASSO regression, selecting the variables retained by both methods as the final predictor variables (Figure 2). Nine variables were ultimately included: at the maternal level—GDM, mode of delivery, TBA, OGTT 1h, GH, and Hb; and at the neonatal level—neonatal sex, feeding method, and gestational age. A multivariate logistic regression predictive model was constructed based on these variables.

3.3 Model Construction and Nomogram

3.3.1 Multivariate Logistic Regression Model

Based on the variables identified through the intersection of LASSO regression and stepwise regression, the final multivariate logistic regression model included nine predictor variables (Table 5). Compared with non-feeding, formula feeding ([OR, 95% CI]: 0.006, 0.003–0.014, P < 0.001) and breastfeeding (0.168, 0.050–0.544, P = 0.003) both substantially reduced NH risk. GDM (6.297, 2.998–13.467, P < 0.001) and cesarean delivery (2.884, 1.607–5.292, P < 0.001) were strongly associated with NH risk. For every 1 μmol/L increase in maternal TBA, the NH risk rose by 10.8% (1.108, 1.037–1.190, P = 0.005). Male newborns had a lower risk (0.560, 0.317–0.978, P = 0.043). Although GH (OR = 2.367, P = 0.056), OGTT 1h (OR = 1.214, P = 0.058), Hb (OR = 0.981, P = 0.073), and gestational age (OR = 0.832, P = 0.207) did not reach statistical significance, they were retained by both screening methods and were therefore included in the final prediction model.

3.3.2 Construction of the Nomogram

Based on the variables selected above, a visual nomogram was developed (Figure 3) to provide a bedside, individualized prediction of NH within 24 hours of birth in full-term AGA newborns. The scores corresponding to each indicator were added together to obtain a total score. This total score was then plotted on the risk probability axis, yielding the individualized predicted probability of NH for that newborn.

3.4 Model Evaluation

Model discriminative power was evaluated using AUC. The prediction model performed well on the training set (Figure 4A) (AUC = 0.943; 95% CI: 0.919–0.967), with an optimal cutoff value of 0.103 (sensitivity: 0.891, specificity: 0.882, precision: 0.883). It also maintained favorable performance on the test set (Figure 4B) (AUC = 0.934; 95% CI: 0.896–0.971), with a cutoff value of 0.103 (sensitivity: 0.889, specificity: 0.865, precision: 0.869). Overall, the

model had sound discriminatory power for identifying the risk of NH in full-term AGA newborns within 24 hours of birth.

The DCA results (Figure 5) demonstrated that, across a wide range of risk thresholds, from 0.05 to 0.95 for the training set and from 0.05 to 0.9 for the test set, the net benefits for this prediction model were consistently higher than those for the two extreme strategies, full intervention and no intervention. This observation indicated that deploying the model for risk stratification and delivering targeted interventions within this threshold range may translate into greater net clinical benefit.

Regarding model calibration, the calibration curve for the training set (Figure 6A) closely followed the ideal diagonal line, indicating high consistency between predicted probabilities and actual incidence. The calibration curve for the test set (Figure 6B) exhibited a mild S-shaped deviation overall. While slight deviations from the ideal reference line were observed in the extremely low and extremely high predicted probability ranges, there was high consistency between predicted probabilities and actual incidence in the clinically critical low-to-medium risk range (0.1–0.6). This indicated that the model exhibited sound overall calibration performance.

4 Discussion

This study developed and internally validated a prediction model for NH within 24 hours of birth in full-term AGA newborns. The model was based on routinely accessible maternal and neonatal indicators. The model incorporated nine predictors, all of which could be rapidly obtained at birth or shortly thereafter. The constructed model demonstrated relatively good accuracy and did not require additional invasive procedures or complex laboratory tests. It can assist healthcare providers in the early identification of high-risk newborns and guide timely feeding interventions and blood glucose monitoring.

4.1 Clinical Significance and Mechanisms of Key Predictors

4.1.1 Feeding and Postnatal Metabolic Adaptation in Newborns

Feeding method was identified as a significant predictor in the prediction model of this study and showed a strong association with NH risk. Multivariate analysis indicated that, compared with delayed feeding, early feeding—whether with breast milk or formula—notably reduced the NH risk within the first 24 hours of life. Current findings regarding the effects of different feeding methods on neonatal blood glucose levels remain inconsistent.

Previous studies indicated no significant difference between breastfeeding and formula feeding in their effects on neonatal blood glucose levels in the early postnatal period[13]. Evidence also suggested that early, proper breastfeeding helped maintain blood glucose levels and effectively reduced the NH incidence[14]. Although blood glucose levels in breastfed newborns were relatively low, they could provide an alternative energy source for the brain by increasing ketone bodies. This physiological metabolic adaptation explains why some breastfed newborns can tolerate lower blood glucose levels without developing significant neurological damage[15]. Such findings suggest that traditional thresholds for blood glucose intervention may not be entirely applicable to breastfed newborns. Furthermore, our findings aligned with previous literature, which identified delayed feeding as an independent risk factor for NH[16]. This conclusion echoes guidelines from the World Health Organization and the American Academy of Pediatrics[17, 18], which emphasize initiating breastfeeding within 1 hour of birth for healthy newborns and within 30 minutes of birth for newborns of mothers with diabetes. This study further underscores the critical role of early feeding in stabilizing blood glucose levels.

Notably, there was a certain proportion of newborns who experienced delayed feeding, insufficient maternal milk production in the early postpartum period, separation from mothers following cesarean section, and hospitalization that prevented timely breastfeeding. These practical circumstances limited the proportion of exclusively breastfed infants in this study.

Therefore, the cohort may not fully reflect the true metabolic characteristics of breastfed newborns. Furthermore, although early formula feeding can rapidly raise blood glucose levels, it may have potential implications for the colonization of the neonatal gut microbiota and the success rate of exclusive breastfeeding. Therefore, prospective studies are needed to further evaluate the long-term effects of different feeding patterns on neonatal glucose homeostasis and metabolic health[19]. Overall, this study suggests that initiating feeding as early as possible after birth may have positive implications for reducing the NH risk in full-term AGA newborns. For high-risk newborns who are temporarily unable to receive adequate breastfeeding, appropriate amounts of formula or oral glucose gel should be administered promptly to rapidly stabilize blood glucose levels, while minimizing the impact on subsequent breastfeeding[13, 20, 21].

4.1.2 Maternal Metabolic Status and Intrauterine Environment

GDM was identified in the prediction model as a significant factor raising the NH risk (OR = 6.297, 95% CI: 2.998–13.467). Maternal hyperglycemia can chronically stimulate excessive proliferation of fetal pancreatic β-cells via the placenta, inducing fetal hyperinsulinemia. After delivery, the maternal glucose supply is abruptly interrupted, but the state of hyperinsulinemia persists, leading to a rapid drop in blood glucose levels and substantially raising NH risk[16]. The present findings align with conclusions from existing literature[22, 23]. Furthermore, even in cases of GDM managed by dietary control or insulin therapy, the risk of NH remains markedly higher than in the general pregnant population[24]. This study further suggests that full-term AGA newborns delivered by GDM women should receive early routine blood glucose monitoring.

Maternal TBA was identified as a risk factor for NH. For every 1 μmol/L increase in TBA, the NH risk was elevated by 10.8%. Clinically, mild elevations in TBA are often overlooked, but they may indicate intrahepatic cholestasis and placental dysfunction in the mother. Bile

acids, as signaling molecules in energy metabolism, participate in glucose and lipid metabolism by modulating relevant receptors, thereby directly affecting neonatal glucose homeostasis. Moreover, abnormal bile acid levels may be involved in the onset and progression of gestational glucose metabolism disorders[25, 26]. Currently, research on the link between maternal TBA levels and NH remains limited. Our findings suggest that clinicians should pay close attention to pregnant women with elevated TBA levels during pregnancy and strengthen early blood glucose screening and dynamic monitoring for their newborns to facilitate the early identification and intervention of NH.

The 1-hour OGTT glucose level was included in the prediction model, and elevated 1-hour OGTT levels showed a certain association with an elevated risk of NH. Maternal 1-hour OGTT glucose levels effectively reflect impaired pancreatic β-cell function and insulin resistance[27]. Previous studies indicated that newborns born to mothers with impaired glucose tolerance faced markedly increased risks of NH[28]. Even below the diagnostic threshold for GDM, elevated 1-hour OGTT glucose levels were linked to a greater risk of NH in LGA newborns[29]. This study further found that among full-term AGA newborns, elevated 1-hour OGTT glucose levels were similarly related to an enhanced risk of NH. Such findings suggest that clinicians should place greater emphasis on women with abnormal 1-hour OGTT glucose levels during pregnancy and strengthen early postnatal glucose monitoring and assessment for their offspring.

Maternal Hb was included in the prediction model, suggesting that it may be associated with the risk of NH. However, its specific role requires further empirical validation. Pal et al.[30] demonstrated a positive link between maternal Hb and neonatal blood glucose levels. Maternal anemia can reduce oxygen supply to the placenta and the transport of nutrients, decrease fetal glycogen reserves, and impair postnatal gluconeogenesis, thereby heightening the risk of NH.

4.1.3 Pregnancy Complications and Mode of Delivery

As one of the variables in the prediction model, GH showed a positive association with NH risk. GH can cause systemic arteriolar spasm, reduce placental blood flow, and result in chronic intrauterine fetal hypoxia. As a perinatal stressor, GH can elevate fetal catecholamine release, leading to hyperresponsive secretion by pancreatic β-cells after birth[31]. Meanwhile, ischemia and hypoxia can suppress glycogen synthase activity, impeding glycogen synthesis, and thereby elevating the risk of NH[32]. Furthermore, GH coupled with insulin resistance can disrupt fetal pancreatic endocrine homeostasis[33]. One study revealed that commonly used clinical beta-blockers, such as labetalol, could cross the placenta and inhibit neonatal glycogenolysis and gluconeogenesis, thereby raising the risk of NH by 68% (OR = 1.68)[34]. However, this study did not distinguish between GH subtypes or collect data on antihypertensive medication use, which may have influenced the assessment of the association between GH and NH.

Cesarean section was a risk factor for NH (OR = 2.884, 95% CI: 1.607–5.292). During vaginal delivery, the fetus is exposed to the stress of labor, which stimulates the release of catecholamines and cortisol, thereby facilitating postnatal endogenous glucose production and adaptation of glucose metabolism. In contrast, neonates delivered by cesarean section lack this physiological stress stimulus, which may lead to delayed adaptation of glucose metabolism and increased susceptibility to NH[35]. Furthermore, routine preoperative fasting, postoperative separation of mother and infant, and delayed initiation of breastfeeding in women who undergo cesarean section further heighten the risk of NH[36]. Therefore, our findings suggest that for full-term AGA newborns delivered via cesarean section, early postnatal blood glucose monitoring and timely feeding interventions should be prioritized, even in the absence of other traditional risk factors.

4.1.4 Neonatal Characteristics

Among full-term AGA newborns, male sex showed a negative association with NH risk in the prediction model (OR = 0.560, 95% CI: 0.317–0.978). Consistently, Tessema et al.[37] in their Ethiopian NICU cohort suggested that male newborns faced a lower risk of NH. However, the existing literature remains controversial on this issue. Some studies suggest that male newborns have a higher risk of NH[38, 39]. The discrepancies among study results may be related to differences in ethnic backgrounds, inclusion criteria for study participants, and their baseline characteristics. As this study included only full-term AGA newborns, it suggested that the effect of sex on the risk of NH may exhibit significant population-specific heterogeneity. Further multicenter, large-sample studies are needed to corroborate these findings.

This study indicated that gestational age might be negatively correlated with the risk of NH. Li et al.[40] found in a cohort of preterm newborns that a smaller gestational age was linked to increased susceptibility to NH. DePuy et al.[41] reported in full-term, non-diabetic pregnancies that for every additional week of gestational age, the risk of NH dropped by 34% (OR = 0.66). Taken together, gestational age, as a continuous variable, exerts a protective effect from preterm birth through late term. This study implied that even within the term range, differences in gestational age might still influence a newborn's ability to adapt to glucose metabolism after birth.

4.2 Clinical Value of the Model

Unlike previous NH prediction models that focused on preterm newborns, newborns born to mothers with diabetes, or other high-risk newborns[9, 10, 40], this study targeted the low-risk population of full-term AGA newborns. Previous models predominantly included well-defined high-risk factors, such as preterm birth, SGA newborns, LGA newborns, and newborns born to mothers with diabetes[23, 29, 42, 43], with limited application to the population in this study. This may lead to inadequate identification of NH and an enhanced risk of missed diagnoses in this group. In contrast, this study constructed a prediction model based on

routinely available maternal and neonatal indicators, with no need for additional specialized tests. Compared with single-factor assessment strategies, the nomogram we developed showed superior discrimination and clinical applicability by incorporating multiple risk factors. DCA further indicated that the model may provide greater clinical benefit by supporting individualized monitoring decisions, rather than relying on routine monitoring based solely on isolated risk factors.

4.3 Limitations and Future Directions

This study has certain limitations. First, as a single-center retrospective study, it had inherent selection bias and information bias arising from the single-center diagnostic and treatment protocols, baseline features of the study population, and the retrospective data. Consequently, the model's generalizability to broader settings was limited. External validation using a multicenter, prospective, large-sample cohort is therefore necessary to adapt the model to clinical scenarios in different regions. Second, given limitations in data sources, this study failed to include certain potential risk factors previously reported in the literature that were closely associated with NH. These factors included prenatal maternal use of beta-blockers[34], monitoring of apolipoproteins and glycated hemoglobin during pregnancy[44], umbilical cord blood biomarkers[45], and postnatal mother-infant skin contact[46]. Future research should integrate additional perinatal and metabolic indicators to optimize the model's predictive accuracy. Furthermore, this study focused solely on NH within the first 24 hours after birth and did not assess delayed NH or long-term neurodevelopmental outcomes through follow-up. Future long-term longitudinal follow-up studies could be conducted to further refine the risk prediction and prognostic assessment system.

5. Conclusion

This study develops and internally validates a model for predicting the risk of NH within 24 hours of birth in full-term AGA newborns. Based on routinely accessible clinical indicators,

the model demonstrates sound discriminatory power, calibration performance, and clinical utility. It can serve as a bedside tool for individualized risk assessment to support precise screening and early intervention. This model may reduce unnecessary blood glucose testing and related procedures, lower healthcare resource consumption, and alleviate parental anxiety, thereby providing an evidence-based foundation for optimizing NH management strategies in full-term AGA newborns.

Declaration

Ethics approval and consent to participate

This study protocol was reviewed and approved by the hospital's Medical Ethics Committee (Approval No.: XMFHIIT-2026SL 187-01), and informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding authors.

Competing interests

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Author contributions

All authors contributed to the study conception and design. Writing - original draft preparation: [Tong Liu]; Writing - review and editing: [Tong Liu, Shaoqing Guo]; Conceptualization: [Tong Liu]; Methodology: [Tong Liu]; Formal analysis and investigation: [Tong Liu, Fei Wu];

Resources: [Shaoqing Guo]; Supervision: [Shaoqing Guo], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figure legends:

Figure 1. Variable selection results from LASSO regression. (A) Cross-validation curve: The x-axis represents log(λ), and the y-axis represents the binomial bias. The numbers at the top indicate the number of non-zero coefficients in the model at the corresponding λ value. The dashed line on the left represents log(λ) corresponding to the minimum deviance, and the dashed line on the right represents log(λ) corresponding to the 1 SE criterion. (B) Coefficient path diagram: The x-axis represents log(λ), and the y-axis represents the standardized coefficients of each variable. Each curve represents a variable; as λ increases, the coefficients converge to zero.

Figure 2. The Venn diagram illustrates the screening of candidate variables in the training set using stepwise regression (based on the AIC criterion) and LASSO regression (10-fold cross-validation, 1 SE criterion).

Figure 3. Nomogram for predicting the risk of neonatal hypoglycemia in full-term appropriate-for-gestational-age newborns. Each predictor is assigned a specific score. The total score is calculated by summing the scores of all predictors, and the total score corresponds to the predicted probability shown below.

Figure 4. Area under the ROC curve (AUC) for the prediction model on the (A) training set and (B) test set. The x-axis represents 1-specificity, and the y-axis represents sensitivity.

Figure 5. Decision curve analysis. The x-axis represents the threshold probability, and the y-axis represents the net benefit. Black horizontal line: no intervention; gray diagonal line: full intervention; red curve: training set; blue curve: test set.

Figure 6. Calibration curves of the prediction model. (A) Logistic calibration curve for the training set. The x-axis represents the model's predicted probability of neonatal hypoglycemia, and the y-axis represents the observed probability. (B) Logistic calibration curve for the test set. The x-axis represents the model's predicted probability of neonatal hypoglycemia, and the y-axis represents the observed probability.

Table 1 Comparison of baseline characteristics between the neonatal hypoglycemia group and the non-hypoglycemia group in the overall population

Variable	Level	Overall (n=1543)	Non-hypoglycemia Group (n=1306)	Hypoglycemia Group (n=237)	p
MATERNAL					
Education (%)	Primary or below/Junior high/Senior high	291 (18.9)	229 (17.5)	62 (26.2)	0.003
	Technical school	441 (28.6)	369 (28.3)	72 (30.4)	
	College	702 (45.5)	617 (47.2)	85 (35.9)	
	Bachelor or above	109 (7.1)	91 (7.0)	18 (7.6)	
Gestational Diabetes Mellitus (%)	No	1174 (76.1)	1107 (84.8)	67 (28.3)	<0.001
	Yes	369 (23.9)	199 (15.2)	170 (71.7)	
Insulin Use (%)	No	1509 (97.8)	1293 (99.0)	216 (91.1)	<0.001
	Yes	34 (2.2)	13 (1.0)	21 (8.9)	
Diet Control (%)	No	1205 (78.1)	1117 (85.5)	88 (37.1)	<0.001
	Yes	338 (21.9)	189 (14.5)	149 (62.9)	
Gestational Hypertension (%)	No	1446 (93.7)	1250 (95.7)	196 (82.7)	<0.001
	Yes	97 (6.3)	56 (4.3)	41 (17.3)	
Hypothyroidism (%)	No	1405 (91.1)	1190 (91.1)	215 (90.7)	0.94
	Yes	138 (8.9)	116 (8.9)	22 (9.3)	
Antenatal Length of Stay (%)	No	1411 (91.4)	1197 (91.7)	214 (90.3)	0.574
	Yes	132 (8.6)	109 (8.3)	23 (9.7)	
Group B Streptococcus Colonization (%)	No	1415 (91.7)	1201 (92.0)	214 (90.3)	0.467
	Yes	128 (8.3)	105 (8.0)	23 (9.7)	
Intrapartum Fever (%)	No	1512 (98.0)	1278 (97.9)	234 (98.7)	0.612
	Yes	31 (2.0)	28 (2.1)	3 (1.3)	
Treponema Pallidum Antibody (%)	No	1505 (97.5)	1269 (97.2)	236 (99.6)	0.022
	Yes	38 (2.5)	37 (2.8)	1 (0.4)	
Mode of Delivery (%)	Vaginal delivery	916 (59.4)	838 (64.2)	78 (32.9)	<0.001
	Cesarean section	627 (40.6)	468 (35.8)	159 (67.1)	

Elective Cesarean Section (%)	No	940 (60.9)	855 (65.5)	85 (35.9)	<0.001
	Yes	603 (39.1)	451 (34.5)	152 (64.1)	
Emergency Cesarean Section (%)	No	1519 (98.4)	1289 (98.7)	230 (97.0)	0.108
	Yes	24 (1.6)	17 (1.3)	7 (3.0)	
Spinal Anesthesia (%)	No	957 (62.0)	871 (66.7)	86 (36.3)	<0.001
	Yes	586 (38.0)	435 (33.3)	151 (63.7)	
General Anesthesia (%)	No	1502 (97.3)	1273 (97.5)	229 (96.6)	0.598
	Yes	41 (2.7)	33 (2.5)	8 (3.4)	
Premature Rupture of Membranes (%)	No	1378 (89.3)	1172 (89.7)	206 (86.9)	0.239
	Yes	165 (10.7)	134 (10.3)	31 (13.1)	
Meconium-stained Amniotic Fluid (%)	No	1426 (92.4)	1196 (91.6)	230 (97.0)	0.005
	Yes	117 (7.6)	110 (8.4)	7 (3.0)	
Neonatal Sex (%)	Female	668 (43.3)	539 (41.3)	129 (54.4)	<0.001
	Male	875 (56.7)	767 (58.7)	108 (45.6)	
Gravida (%)	1	625 (40.5)	554 (42.4)	71 (30.0)	<0.001
	2	439 (28.5)	376 (28.8)	63 (26.6)	
	3	249 (16.1)	196 (15.0)	53 (22.4)	
	4 or above	230 (14.9)	180 (13.8)	50 (21.1)	
Parity (median [IQR])		1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 2.00]	<0.001
Twin Pregnancy (%)	No	1472 (95.4)	1260 (96.5)	212 (89.5)	<0.001
	Yes	71 (4.6)	46 (3.5)	25 (10.5)	
Feeding Mode (%)	None	159 (10.3)	21 (1.6)	138 (58.2)	<0.001
	Breastfeeding	42 (2.7)	18 (1.4)	24 (10.1)	
	Formula feeding	1342 (87.0)	1267 (97.0)	75 (31.6)	
Maternal Age (median [IQR])		32.00 [29.00, 35.00]	31.00 [29.00, 34.00]	33.00 [30.00, 37.00]	<0.001
Pre-pregnancy Body Mass Index (median [IQR])		21.10 [19.36, 23.54]	20.94 [19.23, 23.31]	22.32 [20.43, 24.89]	<0.001
Gestational Weight Gain (median [IQR])		12.00 [10.00, 15.00]	12.20 [10.00, 15.00]	11.00 [9.20, 14.50]	0.002
Delivery Body Mass Index (median [IQR])		26.17 [24.19, 28.60]	26.05 [24.04, 28.44]	26.83 [24.78, 30.00]	<0.001

Maternal Height (median [IQR])	160.00 [157.00, 163.00]	160.00 [157.00, 163.00]	159.00 [156.00, 163.00]	0.004
Oral Glucose Tolerance Test, 0 hour (median [IQR])	4.35 [4.12, 4.63]	4.33 [4.11, 4.58]	4.58 [4.28, 4.94]	<0.001
Oral Glucose Tolerance Test, 1 hour (median [IQR])	8.07 [6.87, 9.26]	7.82 [6.68, 8.92]	9.72 [8.45, 10.67]	<0.001
Oral Glucose Tolerance Test, 2 hours (median [IQR])	6.68 [5.76, 7.81]	6.51 [5.68, 7.50]	8.17 [6.88, 9.21]	<0.001
Pre-delivery WBC (median [IQR])	8.91 [7.51, 10.80]	9.04 [7.59, 10.86]	8.34 [7.13, 10.12]	0.001
NEU (median [IQR])	6.51 [5.28, 8.22]	6.61 [5.35, 8.27]	5.98 [4.98, 7.94]	0.002
RBC (median [IQR])	4.04 [3.79, 4.32]	4.05 [3.80, 4.32]	4.00 [3.75, 4.32]	0.414
Hb (median [IQR])	125.00 [116.00, 132.00]	125.00 [117.00, 132.00]	123.00 [115.00, 131.00]	0.088
PLT (median [IQR])	204.00 [170.00, 240.00]	205.00 [172.00, 240.00]	198.00 [164.00, 239.00]	0.272
TBA (median [IQR])	2.60 [1.90, 4.10]	2.60 [1.90, 4.00]	3.00 [2.00, 4.70]	0.011
TP (median [IQR])	63.80 [60.90, 67.00]	64.00 [61.10, 67.10]	63.00 [59.90, 66.50]	0.002
ALB (median [IQR])	35.60 [33.80, 37.30]	35.70 [33.92, 37.40]	34.90 [32.50, 37.00]	<0.001
BUN (median [IQR])	3.39 [2.82, 4.09]	3.36 [2.81, 4.05]	3.64 [2.85, 4.47]	0.003
Cr (median [IQR])	47.00 [41.00, 53.00]	47.00 [41.00, 52.00]	46.00 [41.00, 54.00]	0.755
UA (median [IQR])	316.00 [269.00, 370.00]	314.00 [268.00, 367.00]	331.00 [273.00, 382.00]	0.04
TC (median [IQR])	6.22 [5.32, 7.04]	6.26 [5.34, 7.09]	5.99 [5.20, 6.90]	0.07
TG (median [IQR])	2.94 [2.28, 3.91]	2.96 [2.28, 3.90]	2.86 [2.24, 3.96]	0.883
HDL-C (median [IQR])	2.00 [1.74, 2.28]	2.00 [1.75, 2.29]	1.97 [1.69, 2.23]	0.311
LDL-C (median [IQR])	2.91 [2.35, 3.56]	2.94 [2.35, 3.58]	2.74 [2.35, 3.45]	0.04
TSH (median [IQR])	1.55 [1.21, 2.20]	1.58 [1.23, 2.20]	1.38 [1.02, 2.19]	0.011
NEONATAL				
Gestational Age (median [IQR])	39.00 [38.00, 39.79]	39.00 [38.14, 39.86]	38.43 [37.57, 39.00]	<0.001
Birth Weight (median [IQR])	3180.00 [2970.00, 3400.00]	3200.00 [2990.00, 3400.00]	3095.00 [2900.00, 3345.00]	<0.001
Birth Length (median [IQR])	50.00 [49.00, 51.00]	50.00 [49.00, 51.00]	50.00 [48.00, 50.00]	<0.001
Apgar 1min (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.262
Apgar 5min (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.182

WBC, white blood cell count; NEU, neutrophil count; RBC, red blood cell count; Hb, hemoglobin; PLT, platelet count; TBA, total bile acid; TP, total protein; ALB, albumin; BUN, blood urea nitrogen; Cr, creatinine; UA, uric acid; TC, total cholesterol; TG, triglyceride; HDL C, high-density lipoprotein cholesterol; LDL C, low-density lipoprotein cholesterol; TSH, thyroid-stimulating hormone

Table 2 Comparison of baseline Characteristics between the training set and the test set

Variable	Level	Overall (n=1543)	Test (464)	Train (n=1079)	p
MATERNAL					
Hypoglycemia (%)	No	1306 (84.6)	392 (84.5)	914 (84.7)	0.972
	Yes	237 (15.4)	72 (15.5)	165 (15.3)	
Education (%)	Primary or below/Junior high/Senior high	291 (18.9)	102 (22.0)	189 (17.5)	0.213
	Technical school	441 (28.6)	131 (28.2)	310 (28.7)	
	College	702 (45.5)	201 (43.3)	501 (46.4)	
	Bachelor or above	109 (7.1)	30 (6.5)	79 (7.3)	
Gestational Diabetes Mellitus (%)	No	1174 (76.1)	356 (76.7)	818 (75.8)	0.749
	Yes	369 (23.9)	108 (23.3)	261 (24.2)	
Insulin Use (%)	No	1509 (97.8)	452 (97.4)	1057 (98.0)	0.629
	Yes	34 (2.2)	12 (2.6)	22 (2.0)	
Diet Control (%)	No	1205 (78.1)	367 (79.1)	838 (77.7)	0.578
	Yes	338 (21.9)	97 (20.9)	241 (22.3)	
Gestational Hypertension (%)	No	1446 (93.7)	432 (93.1)	1014 (94.0)	0.594
	Yes	97 (6.3)	32 (6.9)	65 (6.0)	
Hypothyroidism (%)	No	1405 (91.1)	429 (92.5)	976 (90.5)	0.243
	Yes	138 (8.9)	35 (7.5)	103 (9.5)	
Antenatal Length of Stay (%)	No	1411 (91.4)	441 (95.0)	970 (89.9)	0.001
	Yes	132 (8.6)	23 (5.0)	109 (10.1)	
Group B Streptococcus Colonization (%)	No	1415 (91.7)	427 (92.0)	988 (91.6)	0.842
	Yes	128 (8.3)	37 (8.0)	91 (8.4)	
Intrapartum Fever (%)	No	1512 (98.0)	453 (97.6)	1059 (98.1)	0.641
	Yes	31 (2.0)	11 (2.4)	20 (1.9)	
Treponema Pallidum Antibody (%)	No	1505 (97.5)	455 (98.1)	1050 (97.3)	0.49
	Yes	38 (2.5)	9 (1.9)	29 (2.7)	
Mode of Delivery (%)	Vaginal delivery	916 (59.4)	270 (58.2)	646 (59.9)	0.576

	Cesarean section	627 (40.6)	194 (41.8)	433 (40.1)	
Elective Cesarean Section (%)	No	940 (60.9)	276 (59.5)	664 (61.5)	0.483
	Yes	603 (39.1)	188 (40.5)	415 (38.5)	
Emergency Cesarean Section (%)	No	1519 (98.4)	458 (98.7)	1061 (98.3)	0.748
	Yes	24 (1.6)	6 (1.3)	18 (1.7)	
Spinal Anesthesia (%)	No	957 (62.0)	282 (60.8)	675 (62.6)	0.546
	Yes	586 (38.0)	182 (39.2)	404 (37.4)	
General Anesthesia (%)	No	1502 (97.3)	452 (97.4)	1050 (97.3)	>0.999
	Yes	41 (2.7)	12 (2.6)	29 (2.7)	
Premature Rupture of Membranes (%)	No	1378 (89.3)	407 (87.7)	971 (90.0)	0.216
	Yes	165 (10.7)	57 (12.3)	108 (10.0)	
Meconium-stained Amniotic Fluid (%)	No	1426 (92.4)	437 (94.2)	989 (91.7)	0.107
	Yes	117 (7.6)	27 (5.8)	90 (8.3)	
Neonatal Sex (%)	Female	668 (43.3)	192 (41.4)	476 (44.1)	0.348
	Male	875 (56.7)	272 (58.6)	603 (55.9)	
Gravida (%)	1	625 (40.5)	172 (37.1)	453 (42.0)	0.133
	2	439 (28.5)	129 (27.8)	310 (28.7)	
	3	249 (16.1)	85 (18.3)	164 (15.2)	
	4 or above	230 (14.9)	78 (16.8)	152 (14.1)	
Parity (median [IQR])		1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	0.11
Twin Pregnancy (%)	No	1472 (95.4)	445 (95.9)	1027 (95.2)	0.624
	Yes	71 (4.6)	19 (4.1)	52 (4.8)	
Feeding Mode (%)	None	159 (10.3)	50 (10.8)	109 (10.1)	0.819
	Breastfeeding	42 (2.7)	14 (3.0)	28 (2.6)	
	Formula feeding	1342 (87.0)	400 (86.2)	942 (87.3)	
Maternal Age (median [IQR])		32.00 [29.00, 35.00]	32.00 [29.00, 35.00]	32.00 [29.00, 35.00]	0.143
Pre-pregnancy Body Mass Index (median [IQR])		21.10 [19.36, 23.54]	21.01 [19.19, 23.33]	21.21 [19.44, 23.64]	0.236

Gestational Weight Gain (median [IQR])	12.00 [10.00, 15.00]	12.00 [10.00, 15.00]	12.00 [10.00, 15.00]	0.964
Delivery Body Mass Index (median [IQR])	26.17 [24.19, 28.60]	25.89 [23.98, 28.49]	26.26 [24.29, 28.60]	0.122
Maternal Height (median [IQR])	160.00 [157.00, 163.00]	160.00 [157.00, 163.00]	160.00 [157.00, 163.00]	0.201
Oral Glucose Tolerance Test, 0 hour (median [IQR])	4.35 [4.12, 4.63]	4.36 [4.13, 4.65]	4.35 [4.12, 4.62]	0.482
Oral Glucose Tolerance Test, 1 hour (median [IQR])	8.07 [6.87, 9.26]	7.98 [6.85, 9.13]	8.11 [6.90, 9.29]	0.553
Oral Glucose Tolerance Test, 2 hours (median [IQR])	6.68 [5.76, 7.81]	6.68 [5.82, 7.77]	6.68 [5.75, 7.82]	0.92
Pre-delivery WBC (median [IQR])	8.91 [7.51, 10.80]	8.71 [7.34, 10.58]	9.03 [7.58, 10.88]	0.053
NEU (median [IQR])	6.51 [5.28, 8.22]	6.32 [5.19, 7.99]	6.59 [5.36, 8.30]	0.033
RBC (median [IQR])	4.04 [3.79, 4.32]	4.02 [3.77, 4.29]	4.05 [3.80, 4.33]	0.345
Hb (median [IQR])	125.00 [116.00, 132.00]	125.00 [116.00, 131.00]	124.00 [117.00, 132.00]	0.68
PLT (median [IQR])	204.00 [170.00, 240.00]	200.50 [166.00, 237.00]	205.00 [173.00, 242.00]	0.087
TBA (median [IQR])	2.60 [1.90, 4.10]	2.80 [2.00, 4.23]	2.60 [1.90, 4.00]	0.085
TP (median [IQR])	63.80 [60.90, 67.00]	63.75 [60.60, 66.93]	63.90 [61.00, 67.00]	0.469
ALB (median [IQR])	35.60 [33.80, 37.30]	35.60 [33.77, 37.32]	35.60 [33.80, 37.30]	0.893
BUN (median [IQR])	3.39 [2.82, 4.09]	3.49 [2.86, 4.16]	3.36 [2.80, 4.07]	0.165
Cr (median [IQR])	47.00 [41.00, 53.00]	47.00 [41.00, 53.00]	47.00 [42.00, 53.00]	0.594
UA (median [IQR])	316.00 [269.00, 370.00]	313.00 [270.75, 364.00]	318.00 [267.00, 375.00]	0.807
TC (median [IQR])	6.22 [5.32, 7.04]	6.00 [5.23, 7.00]	6.30 [5.36, 7.06]	0.073
TG (median [IQR])	2.94 [2.28, 3.91]	2.98 [2.28, 3.96]	2.93 [2.28, 3.88]	0.571
HDL_C (median [IQR])	2.00 [1.74, 2.28]	2.00 [1.73, 2.26]	2.00 [1.74, 2.29]	0.425
LDL_C (median [IQR])	2.91 [2.35, 3.56]	2.80 [2.25, 3.50]	2.97 [2.40, 3.60]	0.004
TSH (median [IQR])	1.55 [1.21, 2.20]	1.52 [1.21, 2.14]	1.56 [1.21, 2.22]	0.57
NEONATAL				
Gestational Age (median [IQR])	39.00 [38.00, 39.79]	39.00 [38.00, 39.86]	39.00 [38.00, 39.71]	0.912
Birth Weight (median [IQR])	3180.00 [2970.00, 3400.00]	3180.00 [2970.00, 3392.50]	3185.00 [2975.00, 3400.00]	0.906
Birth Length (median [IQR])	50.00 [49.00, 51.00]	50.00 [49.00, 51.00]	50.00 [49.00, 51.00]	0.832
Apgar 1min (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.834
Apgar 5min (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.643

Table 3 Comparison of baseline characteristics between the neonatal hypoglycemia group and the non-hypoglycemia group in the training set

Variable	Level	Overall (n=1079)	Non-hypoglycemia Group(n=914)	Hypoglycemia Group(n=165)	p
MATERNAL					
Education (%)	Primary or below/Junior high/Senior high	189 (17.5)	151 (16.5)	38 (23.0)	0.014
	Technical school	310 (28.7)	256 (28.0)	54 (32.7)	
	College	501 (46.4)	443 (48.5)	58 (35.2)	
	Bachelor or above	79 (7.3)	64 (7.0)	15 (9.1)	
Gestational Diabetes Mellitus (%)	No	818 (75.8)	771 (84.4)	47 (28.5)	<0.001
	Yes	261 (24.2)	143 (15.6)	118 (71.5)	
Insulin Use (%)	No	1057 (98.0)	905 (99.0)	152 (92.1)	<0.001
	Yes	22 (2.0)	9 (1.0)	13 (7.9)	
Diet Control (%)	No	838 (77.7)	778 (85.1)	60 (36.4)	<0.001
	Yes	241 (22.3)	136 (14.9)	105 (63.6)	
Gestational Hypertension (%)	No	1014 (94.0)	875 (95.7)	139 (84.2)	<0.001
	Yes	65 (6.0)	39 (4.3)	26 (15.8)	
Hypothyroidism (%)	No	976 (90.5)	826 (90.4)	150 (90.9)	0.942
	Yes	103 (9.5)	88 (9.6)	15 (9.1)	
Antenatal Length of Stay (%)	No	970 (89.9)	825 (90.3)	145 (87.9)	0.427
	Yes	109 (10.1)	89 (9.7)	20 (12.1)	
Group B Streptococcus Colonization (%)	No	988 (91.6)	840 (91.9)	148 (89.7)	0.432
	Yes	91 (8.4)	74 (8.1)	17 (10.3)	
Intrapartum Fever (%)	No	1059 (98.1)	895 (97.9)	164 (99.4)	0.343
	Yes	20 (1.9)	19 (2.1)	1 (0.6)	
Treponema Pallidum Antibody (%)	No	1050 (97.3)	886 (96.9)	164 (99.4)	0.11
	Yes	29 (2.7)	28 (3.1)	1 (0.6)	
Mode of Delivery (%)	Vaginal delivery	646 (59.9)	592 (64.8)	54 (32.7)	<0.001
	Cesarean section	433 (40.1)	322 (35.2)	111 (67.3)	
Elective Cesarean Section (%)	No	664 (61.5)	606 (66.3)	58 (35.2)	<0.001

	Yes	415 (38.5)	308 (33.7)	107 (64.8)	
Emergency Cesarean Section (%)	No	1061 (98.3)	900 (98.5)	161 (97.6)	0.503
	Yes	18 (1.7)	14 (1.5)	4 (2.4)	
Spinal Anesthesia (%)	No	675 (62.6)	615 (67.3)	60 (36.4)	<0.001
	Yes	404 (37.4)	299 (32.7)	105 (63.6)	
General Anesthesia (%)	No	1050 (97.3)	891 (97.5)	159 (96.4)	0.577
	Yes	29 (2.7)	23 (2.5)	6 (3.6)	
Premature Rupture of Membranes (%)	No	971 (90.0)	826 (90.4)	145 (87.9)	0.4
	Yes	108 (10.0)	88 (9.6)	20 (12.1)	
Meconium-stained Amniotic Fluid (%)	No	989 (91.7)	829 (90.7)	160 (97.0)	0.011
	Yes	90 (8.3)	85 (9.3)	5 (3.0)	
Neonatal Sex (%)	Female	476 (44.1)	390 (42.7)	86 (52.1)	0.03
	Male	603 (55.9)	524 (57.3)	79 (47.9)	
Gravida (%)	1	453 (42.0)	401 (43.9)	52 (31.5)	0.003
	2	310 (28.7)	264 (28.9)	46 (27.9)	
	3	164 (15.2)	128 (14.0)	36 (21.8)	
	4 or above	152 (14.1)	121 (13.2)	31 (18.8)	
Parity (median [IQR])		1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	2.00 [1.00, 2.00]	<0.001
Twin Pregnancy (%)	No	1027 (95.2)	880 (96.3)	147 (89.1)	<0.001
	Yes	52 (4.8)	34 (3.7)	18 (10.9)	
Feeding Mode (%)	None	109 (10.1)	10 (1.1)	99 (60.0)	<0.001
	Breastfeeding	28 (2.6)	13 (1.4)	15 (9.1)	
	Formula feeding	942 (87.3)	891 (97.5)	51 (30.9)	
Maternal Age (median [IQR])		32.00 [29.00, 35.00]	31.00 [29.00, 34.00]	33.00 [31.00, 36.00]	<0.001
Pre-pregnancy Body Mass Index (median [IQR])		21.21 [19.44, 23.64]	21.08 [19.35, 23.43]	22.07 [20.31, 24.43]	<0.001
Gestational Weight Gain (median [IQR])		12.00 [10.00, 15.00]	12.10 [10.00, 15.00]	11.00 [10.00, 14.00]	0.007
Delivery Body Mass Index (median [IQR])		26.26 [24.29, 28.60]	26.20 [24.24, 28.52]	26.72 [24.63, 29.73]	0.025
Delivery Body Mass Index (median [IQR])		160.00 [157.00, 163.00]	160.00 [157.00, 164.00]	160.00 [157.00, 162.00]	0.025

Oral Glucose Tolerance Test, 0 hour (median [IQR])	4.35 [4.12, 4.62]	4.31 [4.11, 4.56]	4.59 [4.28, 4.84]	<0.001
Oral Glucose Tolerance Test, 1 hour (median [IQR])	8.11 [6.90, 9.29]	7.84 [6.69, 8.96]	9.69 [8.51, 10.60]	<0.001
Oral Glucose Tolerance Test, 2 hours (median [IQR])	6.68 [5.75, 7.82]	6.50 [5.66, 7.51]	8.19 [7.00, 9.13]	<0.001
Pre-delivery WBC (median [IQR])	9.03 [7.58, 10.88]	9.18 [7.65, 10.93]	8.40 [7.13, 10.11]	0.003
NEU (median [IQR])	6.59 [5.36, 8.30]	6.70 [5.42, 8.35]	6.07 [5.00, 8.00]	0.014
RBC (median [IQR])	4.05 [3.80, 4.33]	4.07 [3.81, 4.33]	3.99 [3.65, 4.32]	0.133
Hb (median [IQR])	124.00 [117.00, 132.00]	125.00 [117.00, 132.00]	123.00 [113.00, 130.00]	0.035
PLT (median [IQR])	205.00 [173.00, 242.00]	206.00 [174.00, 242.00]	199.00 [164.00, 242.00]	0.366
TBA (median [IQR])	2.60 [1.90, 4.00]	2.50 [1.90, 3.98]	3.00 [2.00, 4.30]	0.049
TP (median [IQR])	63.90 [61.00, 67.00]	64.00 [61.20, 67.00]	63.20 [60.00, 66.90]	0.064
ALB (median [IQR])	35.60 [33.80, 37.30]	35.70 [33.90, 37.40]	35.20 [33.00, 37.00]	0.011
BUN (median [IQR])	3.36 [2.80, 4.07]	3.35 [2.81, 4.05]	3.48 [2.72, 4.26]	0.294
Cr (median [IQR])	47.00 [42.00, 53.00]	47.00 [42.00, 53.00]	46.00 [41.00, 53.00]	0.379
UA (median [IQR])	318.00 [267.00, 375.00]	317.00 [268.00, 373.00]	329.00 [265.00, 381.00]	0.461
TC (median [IQR])	6.30 [5.36, 7.06]	6.30 [5.38, 7.09]	6.18 [5.21, 6.97]	0.325
TG (median [IQR])	2.93 [2.28, 3.88]	2.95 [2.27, 3.87]	2.84 [2.29, 3.91]	0.927
HDL_C (median [IQR])	2.00 [1.74, 2.29]	2.01 [1.75, 2.30]	1.94 [1.67, 2.22]	0.096
LDL_C (median [IQR])	2.97 [2.40, 3.60]	2.99 [2.41, 3.60]	2.81 [2.38, 3.56]	0.216
TSH (median [IQR])	1.56 [1.21, 2.22]	1.58 [1.23, 2.22]	1.36 [1.02, 2.19]	0.035
NEONATAL				
Gestational Age (median [IQR])	39.00 [38.00, 39.71]	39.00 [38.14, 39.86]	38.43 [37.57, 39.00]	<0.001
Birth Weight (median [IQR])	3185.00 [2975.00, 3400.00]	3200.00 [2980.00, 3400.00]	3120.00 [2900.00, 3370.00]	0.01
Birth Length (median [IQR])	50.00 [49.00, 51.00]	50.00 [49.00, 51.00]	50.00 [48.00, 50.00]	<0.001
Apgar 1min (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.162
Apgar 5min (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.074

Table 4 Results of univariate and multivariate logistic regression analysis of the training set

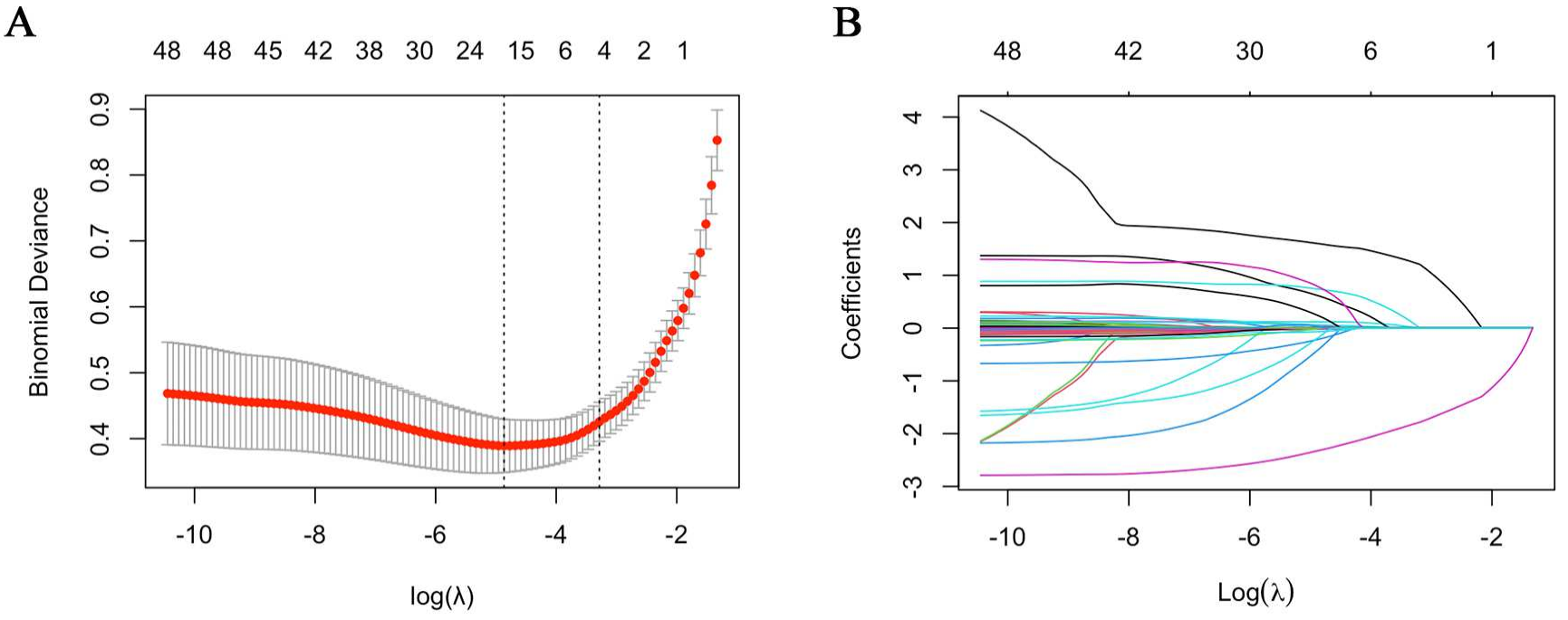
Dependent: hypoglycemia		Non-hypoglycemia Group (n=914)	Hypoglycemia Group (n=165)	OR (univariable)	OR (multivariable)
Feeding_Mode	None	10 (1.1%)	99 (60%)	-	-
	Breastfeeding	13 (1.4%)	15 (9.1%)	0.12 (0.04-0.31, p<.001)	0.17 (0.05-0.56, p=.004)
	Formula feeding	891 (97.5%)	51 (30.9%)	0.01 (0.00-0.01, p<.001)	0.01 (0.00-0.01, p<.001)
Gestational Diabetes Mellitus	No	771 (84.4%)	47 (28.5%)	-	-
	Yes	143 (15.6%)	118 (71.5%)	13.54 (9.24-19.84, p<.001)	6.40 (3.01-13.61, p<.001)
Mode of Delivery	Vaginal delivery	592 (64.8%)	54 (32.7%)	-	-
	Cesarean section	322 (35.2%)	111 (67.3%)	3.78 (2.66-5.38, p<.001)	13.43 (3.06-59.04, p<.001)
TBA	Mean ± SD	3.4 ± 2.8	4.7 ± 8.0	1.06 (1.02-1.10, p=.002)	1.11 (1.03-1.19, p=.005)
Oral Glucose Tolerance Test, 1 hour	Mean ± SD	7.9 ± 1.6	9.6 ± 1.7	1.84 (1.64-2.06, p<.001)	1.23 (1.00-1.50, p=.047)
Gestational Hypertension	No	875 (95.7%)	139 (84.2%)	-	-
	Yes	39 (4.3%)	26 (15.8%)	4.20 (2.48-7.11, p<.001)	2.43 (1.00-5.91, p=.049)
Neonatal_Sex	Female	390 (42.7%)	86 (52.1%)	-	-
	Male	524 (57.3%)	79 (47.9%)	0.68 (0.49-0.95, p=.025)	0.56 (0.32-0.99, p=.047)
Hb	Mean ± SD	124.2 ± 12.4	122.2 ± 12.5	0.99 (0.97-1.00, p=.056)	0.98 (0.96-1.00, p=.086)
Elective Cesarean Section	No	606 (66.3%)	58 (35.2%)	-	-
	Yes	308 (33.7%)	107 (64.8%)	3.63 (2.56-5.14, p<.001)	0.19 (0.04-0.85, p=.030)
Gestational Age	Mean ± SD	39.0 ± 1.1	38.4 ± 0.9	0.57 (0.49-0.68, p<.001)	0.79 (0.59-1.06, p=.111)

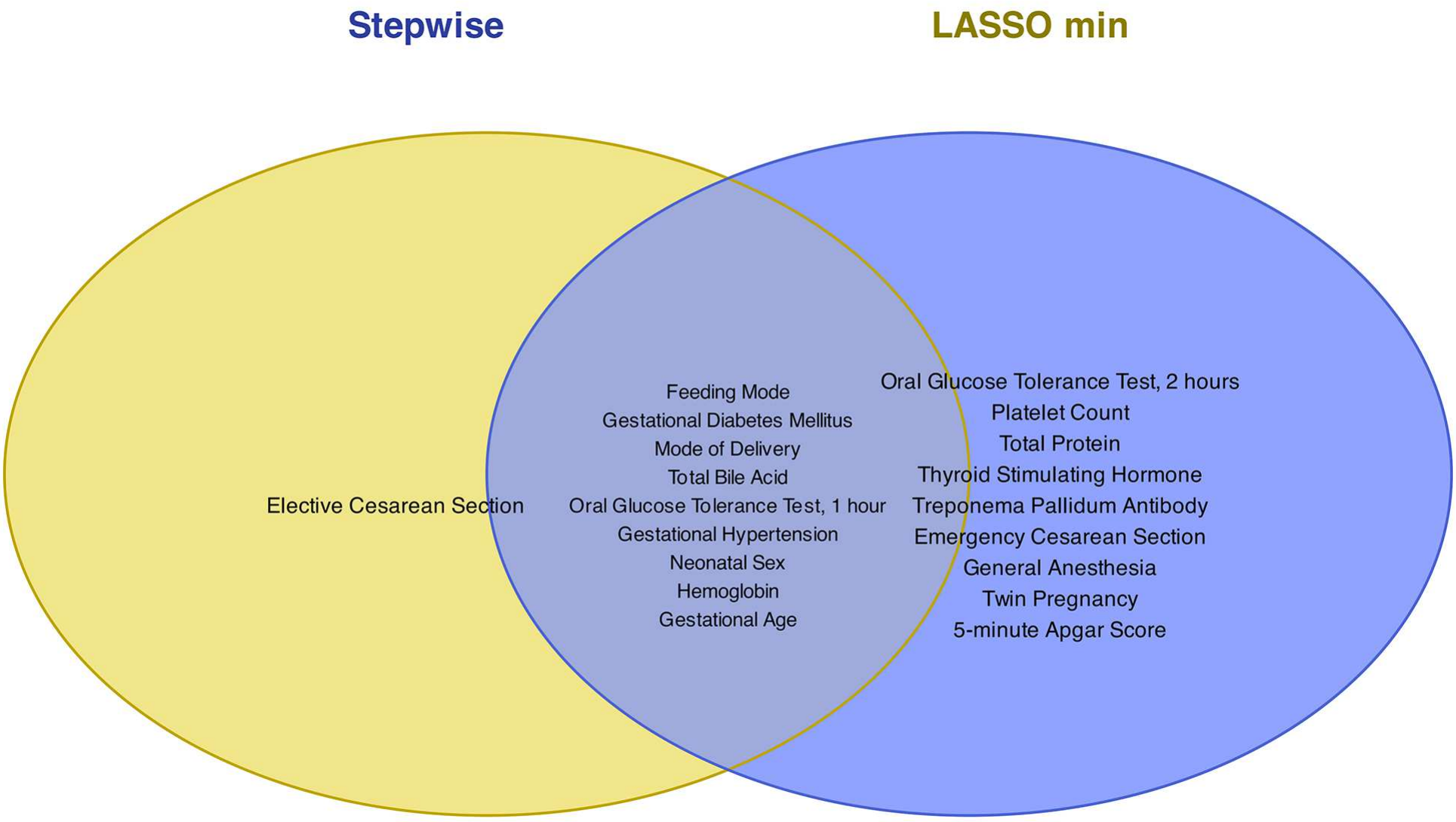
TBA, total bile acid; Hb, hemoglobin

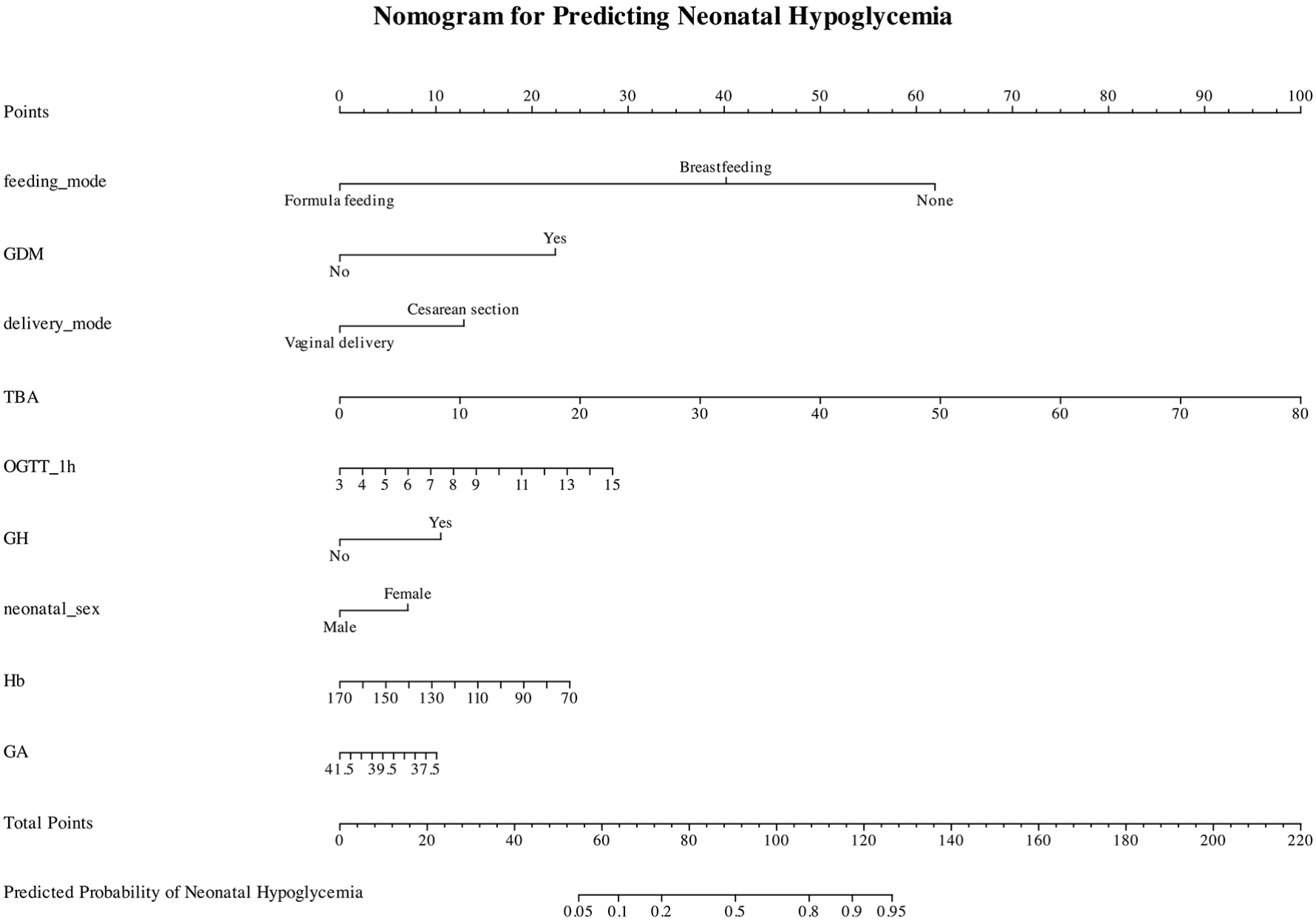
Table 5 Multivariate logistic regression model

Variable	OR	LCL	UCL	P_value
(Intercept)	5465.410	0.064	613676572.748	0.141
Feeding_Mode (Breastfeeding)	0.168	0.050	0.544	0.003
Feeding_Mode (Formula feeding)	0.006	0.003	0.014	<0.001
Gestational Diabetes Mellitus (Yes)	6.297	2.998	13.467	<0.001
Mode of Delivery (Cesarean section)	2.884	1.607	5.292	<0.001
TBA	1.108	1.037	1.190	0.005
Oral Glucose Tolerance Test, 1 hour	1.214	0.996	1.490	0.058
Gestational Hypertension (Yes)	2.367	0.954	5.611	0.056
Neonatal_Sex (Male)	0.560	0.317	0.978	0.043
Hb	0.981	0.960	1.002	0.073
Gestational Age	0.832	0.623	1.105	0.207

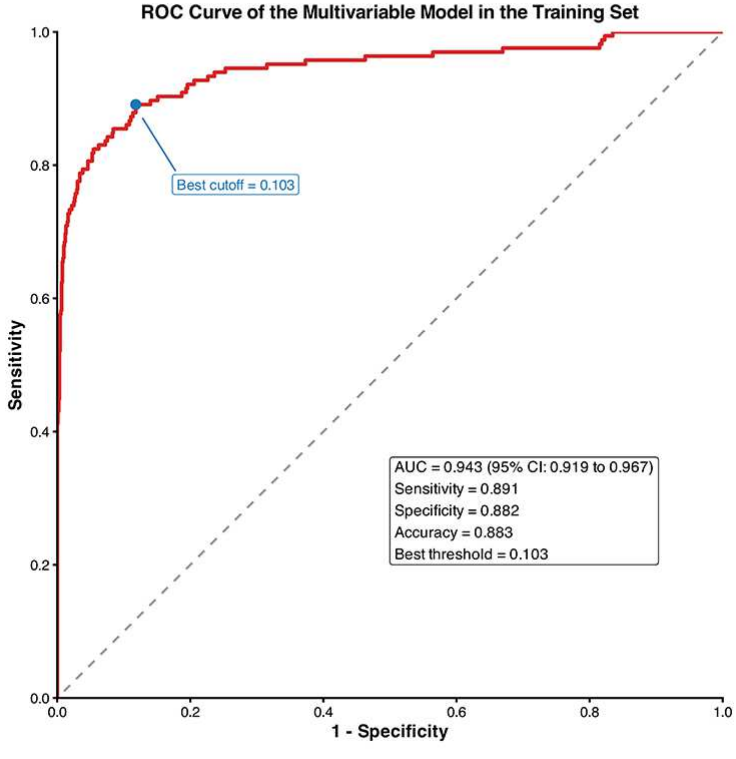
TBA, total bile acid; Hb, hemoglobin


A
48 48 45 42 38 30 24 15 6 4 2 1
Binomial Deviance
0.4 0.5 0.6 0.7 0.8 0.9
-10 -8 -6 -4 -2
log(λ)
B
48 42 30 6 1
Coefficients
-3 -2 -1 0 1 2 3 4
-10 -8 -6 -4 -2
Log(λ)

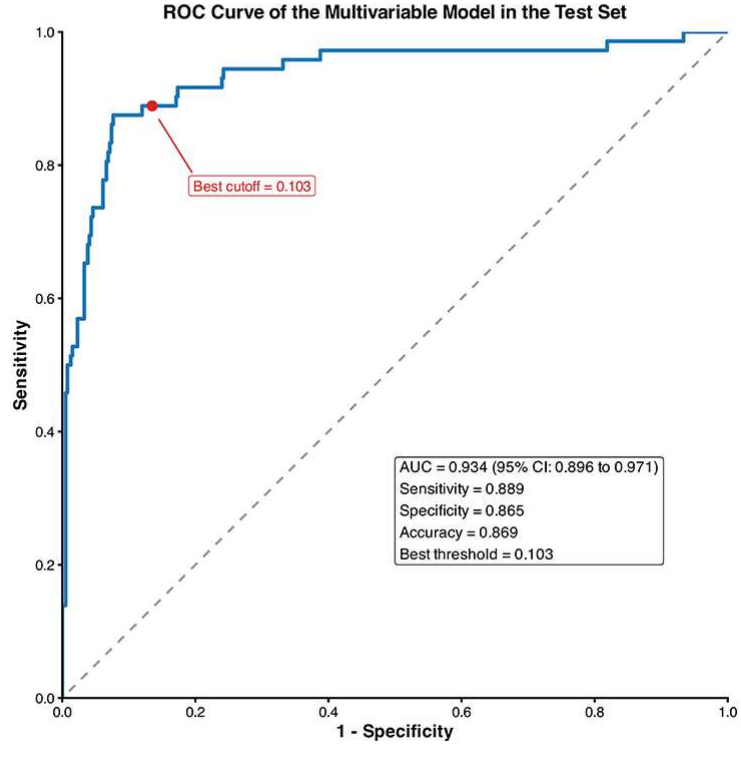

Stepwise
LASSO min
Elective Cesarean Section
Feeding Mode
Gestational Diabetes Mellitus
Mode of Delivery
Total Bile Acid
Oral Glucose Tolerance Test, 1 hour
Gestational Hypertension
Neonatal Sex
Hemoglobin
Gestational Age
Oral Glucose Tolerance Test, 2 hours
Platelet Count
Total Protein
Thyroid Stimulating Hormone
Treponema Pallidum Antibody
Emergency Cesarean Section
General Anesthesia
Twin Pregnancy
5-minute Apgar Score

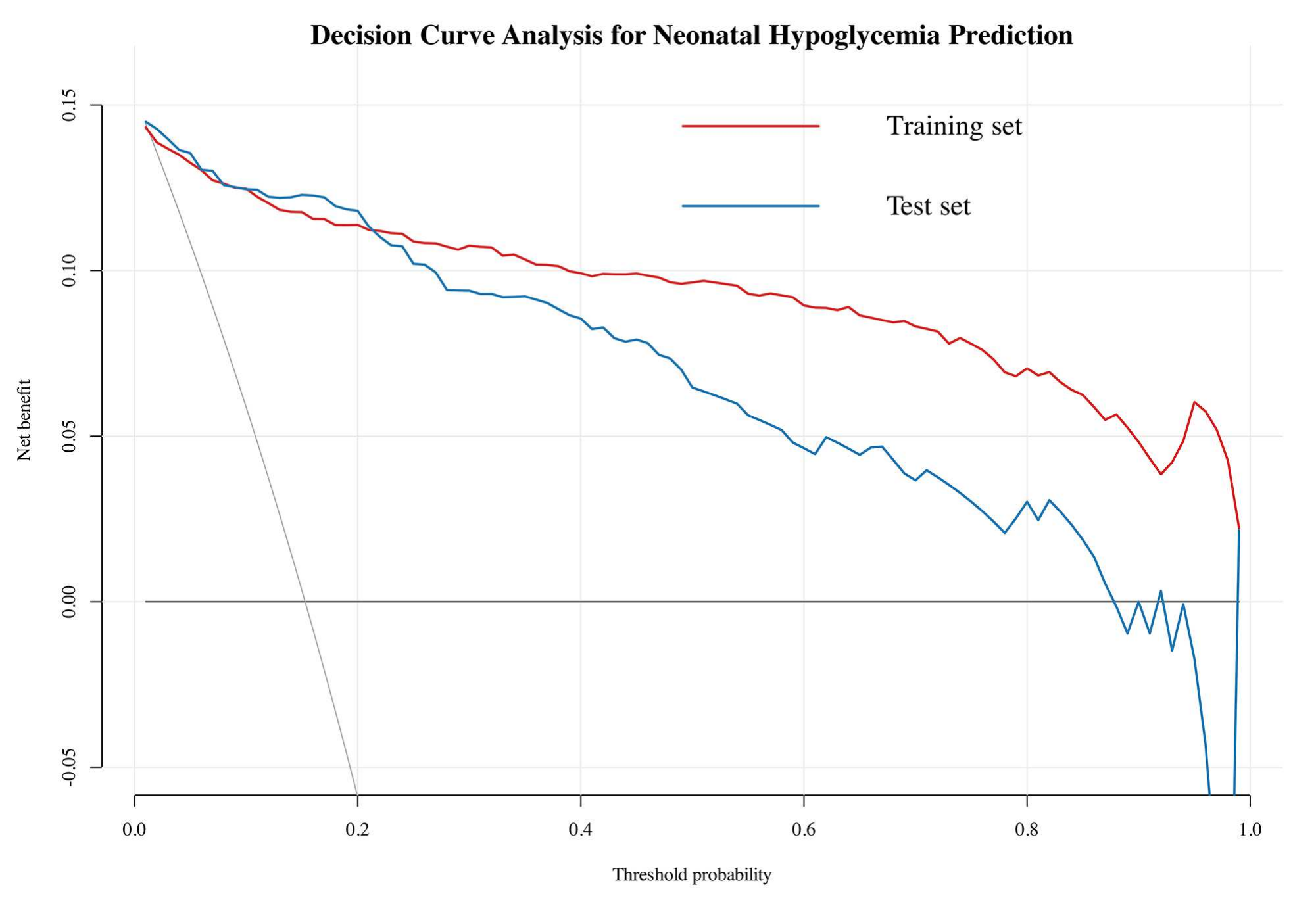

Nomogram for Predicting Neonatal Hypoglycemia
Points
0 10 20 30 40 50 60 70 80 90 100
feeding_mode
Breastfeeding
Formula feeding
None
GDM
Yes
No
delivery_mode
Cesarean section
Vaginal delivery
TBA
0 10 20 30 40 50 60 70 80
OGTT_1h
3 4 5 6 7 8 9 11 13 15
GH
Yes
No
neonatal_sex
Female
Male
Hb
170 150 130 110 90 70
GA
41.5 39.5 37.5
Total Points
0 20 40 60 80 100 120 140 160 180 200 220
Predicted Probability of Neonatal Hypoglycemia
0.05 0.1 0.2 0.5 0.8 0.9 0.95

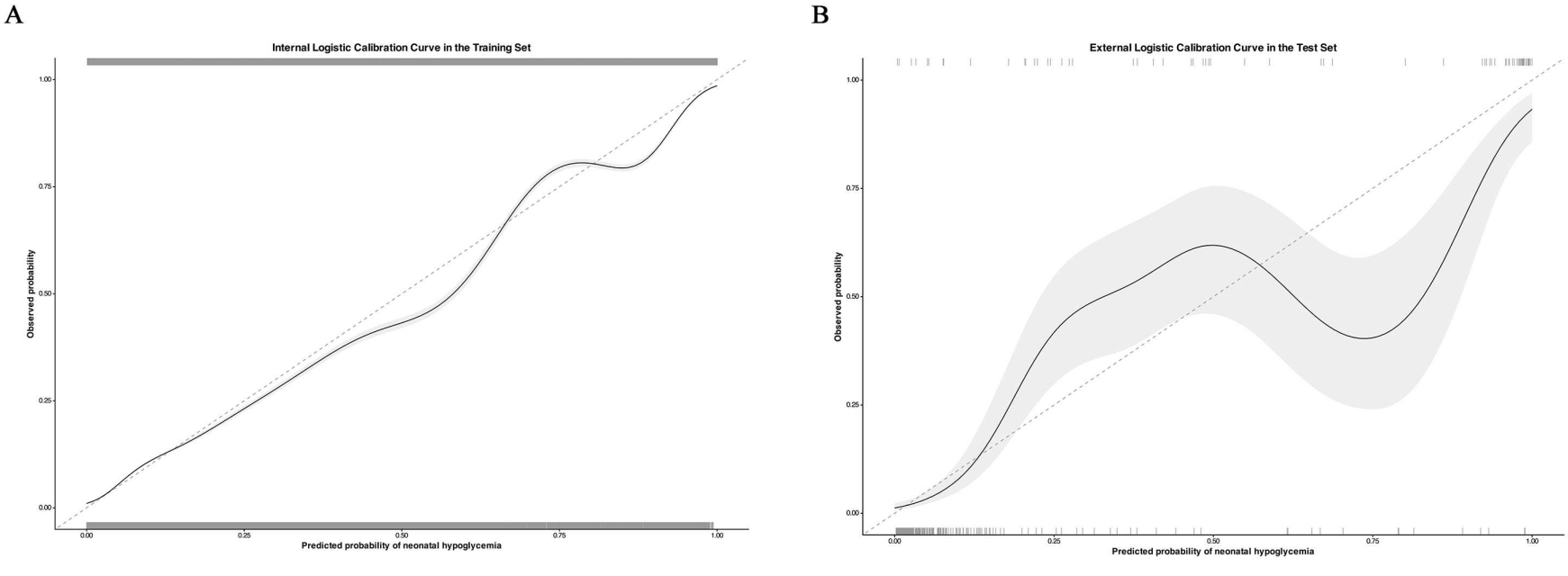
A


ROC Curve of the Multivariable Model in the Training Set
Best cutoff = 0.103
AUC = 0.943 (95% CI: 0.919 to 0.967)
Sensitivity = 0.891
Specificity = 0.882
Accuracy = 0.883
Best threshold = 0.103
Sensitivity
1 - Specificity
0.0
0.2
0.4
0.6
0.8
1.0

B


ROC Curve of the Multivariable Model in the Test Set
Best cutoff = 0.103
AUC = 0.934 (95% CI: 0.896 to 0.971)
Sensitivity = 0.889
Specificity = 0.865
Accuracy = 0.869
Best threshold = 0.103
Sensitivity
1 - Specificity
0.0
0.2
0.4
0.6
0.8
1.0


Decision Curve Analysis for Neonatal Hypoglycemia Prediction
Training set
Test set
Net benefit
0.15
0.10
0.05
0.00
-0.05
0.0
0.2
0.4
0.6
0.8
1.0
Threshold probability


A
Internal Logistic Calibration Curve in the Training Set
Observed probability
1.00
0.75
0.50
0.25
0.00
0.00
0.25
0.50
0.75
1.00
Predicted probability of neonatal hypoglycemia
B
External Logistic Calibration Curve in the Test Set
Observed probability
1.00
0.75
0.50
0.25
0.00
0.00
0.25
0.50
0.75
1.00
Predicted probability of neonatal hypoglycemia