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ORIGINAL RESEARCH

Factors related to the occurrence of fetal birth defects and the construction of a Nomogram model

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Objective: To explore the influencing factors of fetal birth defects (BD) and construct a nomogram model.

Methods: A total of 341 newborns admitted to Meizhou people's hospital from September 2021 to September 2023 were randomly grouped into a modeling group (239 cases) and a validation group (102 cases). The modeling group fetuses were separated into BD and non-BD groups. Multivariate logistic regression analyzed risk factors for BD; R software constructed a nomogram model; Receiver operating characteristic (ROC) curve evaluated the model's discrimination for BD.

Results: The top 5 types of BD were congenital heart disease, polydactyly/syndactyly, cleft lip/palate, ear malformation, and foot malformation, with incidence rates of 23.81%, 20.63%, 12.70%, 11.11%, and 7.94%, respectively. BD incidence was 26.36% (63/239). Significant differences between BD and non-BD groups were found in maternal age, gestational age, history of adverse pregnancy/childbirth, gestational hypertension, adverse emotions during pregnancy, and folic acid intake duration ($P<0.05$). Logistic regression showed maternal age (OR: 4.125), gestational age (OR: 3.066), adverse pregnancy history (OR: 10.628), gestational hypertension (OR: 5.658), adverse emotions (OR: 5.467), and folic acid intake duration (OR: 4.586) were risk factors for BD ($P<0.05$). The modeling group's ROC AUC was 0.938, calibration curve slope close to 1, H-L test =8.342, P=0.692; external validation AUC was 0.961, calibration slope close to 1, H-L test =7.634, P=0.635.

Conclusion: Identified risk factors include maternal age, gestational age, adverse pregnancy history, gestational hypertension, adverse emotions, and folic acid intake duration. The nomogram model shows good discrimination and consistency for evaluating neonatal BD risk.

Keywords: fetus, birth defects, influencing factors, nomogram

Introduction

Birth defects (BD), also known as congenital anomalies, are abnormal phenomena that occur in embryos or fetuses during development, including physical, physiological, and metabolic aspects. Specifically, they manifest as various congenital disabilities such as congenital malformations and metabolic defects. However, BD can lead to early miscarriage and fetal malformation.[1,2] The etiology of BD in newborns is not yet clear, and the causes are complex. Most scholars believe that it may be related to genetics and the environment, or possibly a combination of multiple factors.[3,4] The study found that over 7.9 million newborns worldwide are born with BD each year. The likelihood of BD occurrence is 6.42% in low-income countries, 5.57% in middle-income countries, and 4.72% in high-income countries, accounting for nearly 3% of all newborns. In China, there are 900,000 new cases of BD each year.[5] The occurrence of BD not only affects the health of newborns but also severely impacts their quality of life due to treatment and brings economic burdens to families. Therefore, identifying factors influencing neonatal BD in clinical settings, and implementing prevention and treatment can effectively reduce the risk of its occurrence. The nomogram, as a risk assessment

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model, can integrate various influencing factors and intuitively present the risk values of assessment results.[6] Currently, there are few reports on the risk research of BD in newborns. Therefore, this study aims to explore the construction of a nomogram model and the factors influencing the occurrence of fetal BD.

Data and Methods

General Data

From September 2021 to September 2023, 341 newborns treated in Meizhou people's hospital were selected and randomly divided into a modeling group (239 cases) and a validation group (102 cases) in a 7:3 ratio (using a random number table method). The case collection flow chart is shown in Figure 1. Based on fetal outcomes, the modeling group was divided into a BD group and a non-BD group. Inclusion criteria: (1) Meeting the diagnostic criteria for fetal BD;[7] (2) Complete data; (3) Consent form signed by family members. Exclusion criteria: (1) Parents with birth defects; (2) Pregnant women with cognitive impairments; (3) Patients with malignant tumors; (4) Pregnant women unwilling to participate in this study. See Figure 1.This study was approved by the ethics committee of our hospital.

Clinical Data Collection

Prenatal examination and delivery data of pregnant women in the modeling group and validation group were collected, mainly including maternal age, fetal gender, gestational age, history of adverse pregnancy outcomes, gestational hypertension, alcohol consumption, smoking, history of colds, educational level, place of residence, whether it was the first pregnancy, history of antibiotic use during pregnancy, adverse emotions during pregnancy, timing of folic acid intake, whether it was a multiple pregnancy, and eugenic screening.

Data Collection Method

Data collectors with over five years of work experience and strong research capabilities were responsible for verifying and entering the data to ensure its validity and authenticity.

Observational Indicators

Clinical data was collected to: (1) Analyze the distribution of types of neonatal BD (Birth Defects); (2) Compare the clinical data between the modeling group and the validation group; (3) Compare the clinical data between the BD group

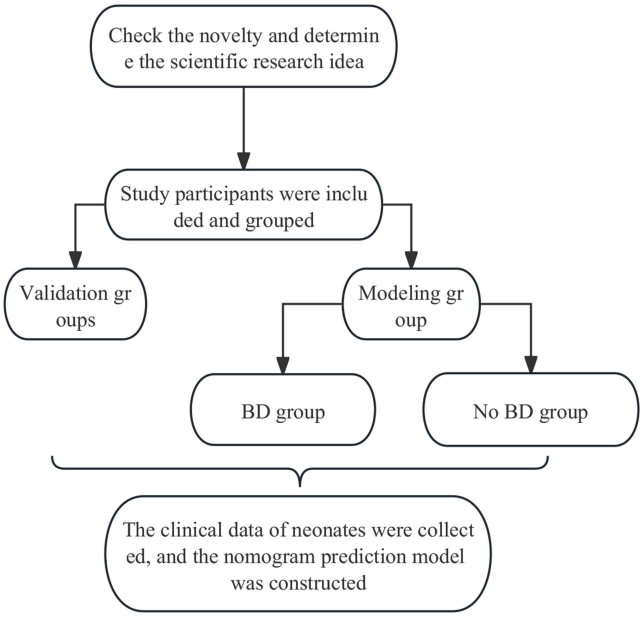

Figure 1 Flow chart of case collection.

and the non-BD group; (4) Develop a nomogram model for fetal BD, and draw an ROC curve to evaluate the discrimination and consistency of the BD nomogram model in assessing fetuses.

Statistical Processing

Data was analyzed using SPSS 25.0. Count data were tested with X^2 test and expressed as cases (%). Multifactorial logistic regression analysis was used to analyze the risk factors for BD in fetuses; R3.6.3 software was used to construct the Nomogram model for assessing BD in fetuses. ROC curves were drawn to evaluate the discrimination of the Nomogram model for BD in fetuses; calibration curves were drawn to assess consistency. A P-value of <0.05 was considered statistically significant.

Results

Distribution of Neonatal BD Types

As shown in Table 1, the top five BDs were congenital heart disease, polydactyly and syndactyly, cleft lip and palate, ear deformities, and foot deformities, with incidence rates of 23.81%, 20.63%, 12.70%, 11.11%, and 7.94%, respectively.

Comparison of Clinical Data Between Modeling and Validation Groups

Table 2 shows that there was no significant difference in clinical data between the modeling and validation groups ($P > 0.05$).

Comparison of Clinical Data Between BD and Non-BD Groups

In this study, 63 out of 239 newborns had BD, with an incidence rate of 26.36%. There were significant differences between the BD and non-BD groups in terms of maternal age, gestational weeks, history of adverse pregnancy outcomes, gestational hypertension, adverse emotions during pregnancy, and timing of folic acid intake ($P < 0.05$). There were no significant differences in other clinical data between the two groups ($P > 0.05$). See Table 3.

Multifactorial Logistic Regression Analysis of Neonatal BD Occurrence

Taking whether neonates had BD as the dependent variable (yes=1, no=0), and maternal age, gestational weeks, history of adverse pregnancy outcomes, gestational hypertension, adverse emotions during pregnancy, and timing of folic acid intake as independent variables, with variable assignment methods shown in Table 4. The results of the multifactorial logistic regression analysis indicated that maternal age (OR: 4.125, 95% *CI*: 1.475–11.537), gestational weeks (OR: 3.066, 95% *CI*: 1.143–8.224), history of adverse pregnancy outcomes (OR: 10.628, 95% *CI*: 3.725–30.318), gestational hypertension (OR: 5.658, 95% *CI*: 1.878–17.043), adverse emotions during pregnancy (OR: 5.467, 95% *CI*: 2.032–14.705), and timing of folic acid intake (OR: 4.586, 95% *CI*: 1.603–13.120) were risk factors for neonatal BD ($P < 0.05$). See Table 5.

Table 1 Distribution of Neonatal Defects

The type of Defect	n	Incidence (%)
Congenital heart disease	15	23.81
Polydactyly and syndactyly	13	20.63
Cleft lip and palate	8	12.70
Ear deformities	7	11.11
Foot deformity	5	7.94
Foetal chromosome abnormality	4	6.35
Congenital hydrocephalus	4	6.35
Hypospadias	3	4.76
Abnormalities of the digestive system	2	3.17
other	2	3.17
total	63	100.00

Table 2 Comparison of Clinical Data Between the Modeling Group and the Validation Group

Factor	Modeling Group (n=239)	Validation Groups (n=102)	X^2	*P*
Maternal age (year old)			1.251	0.263
≥35	95 (39.75)	34 (33.33)		
<35	144 (60.25)	68 (66.67)		
Fetal sex			0.062	0.803
man	123 (51.46)	54 (52.94)		
woman	116 (48.54)	48 (47.06)		
Gestational weeks (week)			0.067	0.795
≥37	182 (76.15)	79 (77.45)		
<37	57 (23.85)	23 (22.55)		
History of adverse maternal and maternal conditions			0.031	0.860
yes	56 (23.43)	23 (22.55)		
no	183 (76.57)	79 (77.45)		
High blood pressure during pregnancy			0.046	0.830
yes	56 (23.43)	25 (24.51)		
no	183 (76.57)	77 (75.49)		
History of alcohol use during pregnancy			0.336	0.562
yes	21 (8.79)	11 (10.78)		
no	218 (91.21)	91 (89.22)		
History of smoking during pregnancy			1.248	0.264
yes	21 (8.79)	13 (12.75)		
no	218 (91.21)	89 (87.25)		
History of colds during pregnancy			0.012	0.912
yes	107 (44.77)	45 (44.12)		
no	132 (55.23)	57 (55.88)		
Education			0.030	0.862
Junior high school and below	82 (34.31)	34 (33.33)		
High school and above	157 (65.69)	68 (66.67)		
Place of residence			0.062	0.803
town	123 (51.46)	54 (52.94)		
countryside	116 (48.54)	48 (47.06)		
First-time mothers			0.194	0.659
yes	114 (47.70)	46 (45.10)		
no	125 (52.30)	56 (54.90)		
History of taking antibiotic medications during pregnancy			0.019	0.890
yes	20 (8.37)	9 (8.82)		
no	219 (91.63)	93 (91.18)		
Bad mood during pregnancy			2.407	0.121
yes	58 (24.27)	17 (16.67)		
no	181 (75.73)	85 (83.33)		
Folic acid taking time (month)			0.035	0.851
≥3	190 (79.50)	82 (80.39)		
<3	49 (20.50)	20 (19.61)		
Multiple pregnancies			0.019	0.890
yes	224 (93.72)	96 (94.12)		
no	15 (5.88)	6 (6.28)		
Eugenics screening			0.048	0.827
yes	206 (86.19)	87 (85.29)		
no	33 (13.81)	15 (14.71)		

Table 3 Comparison of Clinical Data Between BD Group and BD Group

Factor	BD Group (n=63)	No BD Group (n=176)	X^2	*P*
Maternal age (year old)			25.883	<0.001
≥35	42 (66.67)	53 (30.11)		
<35	21 (33.33)	123 (69.89)		
Fetal sex			0.215	0.643
man	34 (53.97)	89 (50.57)		
woman	29 (46.03)	87 (49.43)		
Gestational weeks (week)			42.732	<0.001
≥37	29 (46.03)	153 (86.93)		
<37	34 (53.97)	23 (13.07)		
History of adverse maternal and maternal conditions			54.194	<0.001
yes	36 (57.14)	20 (11.36)		
no	27 (42.86)	156 (88.64)		
High blood pressure during pregnancy			49.210	<0.001
yes	35 (55.56)	21 (11.93)		
no	28 (44.44)	155 (88.07)		
History of alcohol use during pregnancy			1.633	0.201
yes	8 (12.70)	13 (7.39)		
no	55 (87.30)	163 (92.61)		
History of smoking during pregnancy			0.577	0.448
yes	7 (11.11)	14 (7.95)		
no	56 (88.89)	162 (92.05)		
History of colds during pregnancy			0.895	0.344
yes	25 (39.68)	82 (46.59)		
no	38 (60.32)	94 (53.41)		
Education			0.249	0.617
Junior high school and below	20 (31.75)	62 (35.23)		
High school and above	43 (68.25)	114 (64.77)		
Place of residence			0.029	0.865
town	33 (47.62)	90 (48.86)		
countryside	30 (52.38)	86 (51.14)		
First-time mothers			0.078	0.780
yes	31 (49.21)	83 (50.79)		
no	32 (50.78)	93 (52.84)		
History of taking antibiotic medications during pregnancy			0.149	0.699
yes	6 (9.52)	14 (7.95)		
no	57 (90.48)	162 (92.05)		
Bad mood during pregnancy			36.790	<0.001
yes	33 (52.38)	25 (14.20)		
no	30 (47.62)	151 (85.80)		
Folic acid taking time (month)			64.496	<0.001
≥3	28 (44.44)	162 (92.05)		
<3	35 (55.56)	14 (7.95)		
Multiple pregnancies			0.109	0.741
yes	58 (92.06)	166 (94.32)		
no	5 (7.94)	10 (5.68)		
Eugenics screening			0.307	0.580
yes	53 (84.13)	153 (86.93)		
no	10 (15.87)	23 (13.07)		

Table 4 Methods for Assigning Values to Independent Variables

Variable	Assignment Method
Maternal age	<35 year old=0, ≥35 year old=1
Gestational weeks	≥37 weeks =0, <37 weeks=1
History of adverse maternal and maternal conditions	no=0, yes=1
High blood pressure during pregnancy	no=0, yes=1
Bad mood during pregnancy	no=0, yes=1
Folic acid taking time	≥3 months=0, <3 months=1

Table 5 Results of Multivariate Logistic Regression Analysis of Fetal BD

Variable	B Value	SE Value	Wald X^2 Value	*P* Value	OR Value	95% CI
Maternal age	1.417	0.525	7.294	0.007	4.125	1.475~11.537
Gestational weeks	1.120	0.503	4.951	0.026	3.066	1.143~8.224
History of adverse maternal and maternal conditions	2.363	0.535	19.527	<0.001	10.628	3.725~30.318
High blood pressure during pregnancy	1.733	0.563	9.489	0.002	5.658	1.878~17.043
Bad mood during pregnancy	1.699	0.505	11.322	0.001	5.467	2.032~14.705
Folic acid taking time	1.523	0.536	8.068	0.005	4.586	1.603~13.120
constant	−4.899	0.656	55.779	<0.001	0.007	–

Construction of the Nomogram Model for Neonatal BD Occurrence

The identified risk factors were introduced into R software to construct the Nomogram model for assessing the risk of neonatal BD occurrence. By summing the scores of each variable, a total score is calculated to assess the risk of neonatal BD occurrence. It can be seen that in this model, the most important factor affecting the score was the history of adverse pregnancy outcomes, followed by gestational hypertension, adverse emotions during pregnancy, timing of folic acid intake, maternal age, and gestational weeks. See Figure 2.

Internal Validation of the Nomogram Model for Neonatal BD

The area under the ROC curve (AUC) of the modeling group was 0.938 (95% CI: 0.892–0.984) (see Figure 3A), and the slope of the calibration curve was close to 1 (see Figure 3B), with an H-L test result of $X^2 = 8.342$, P = 0.692, indicating good consistency.

External Validation of the Nomogram Model for Neonatal BD

The AUC of the external validation was 0.961 (95% CI: 0.938–0.984) (Figure 4A); the slope of the calibration curve was close to 1 (Figure 4B), with an H-L test result of $X^2 = 7.634$, P = 0.635, indicating good consistency.

Discussion

BD is a global public health issue, with high disability and mortality rates in newborns. Furthermore, the pathogenesis of BD is complex, likely caused by a combination of various factors.[8,9] Studies report that the incidence of BD in newborns in China is about 5%, with nearly one-third of pediatric hospitalizations due to BD. Additionally, BD accounts for approximately 20% of total deaths (infants and young children), significantly impacting families and society.[10] This study shows that out of 239 newborns, 63 had BD, with an incidence rate of 26.36%, indicating a higher incidence and underscoring the need to strengthen the prevention and control of BD. Therefore, constructing a Nomogram model for the occurrence of BD in newborns is particularly important.

This study, after analyzing neonatal BD types, found that congenital heart disease, polydactyly and syndactyly, etc., had higher incidence rates, severely affecting the health of newborns, although some conditions can be corrected with treatment.[11] Multifactor logistic regression analysis in this study showed that maternal age, gestational weeks, history of adverse pregnancy outcomes, gestational hypertension, adverse emotions during pregnancy, and timing of folic acid

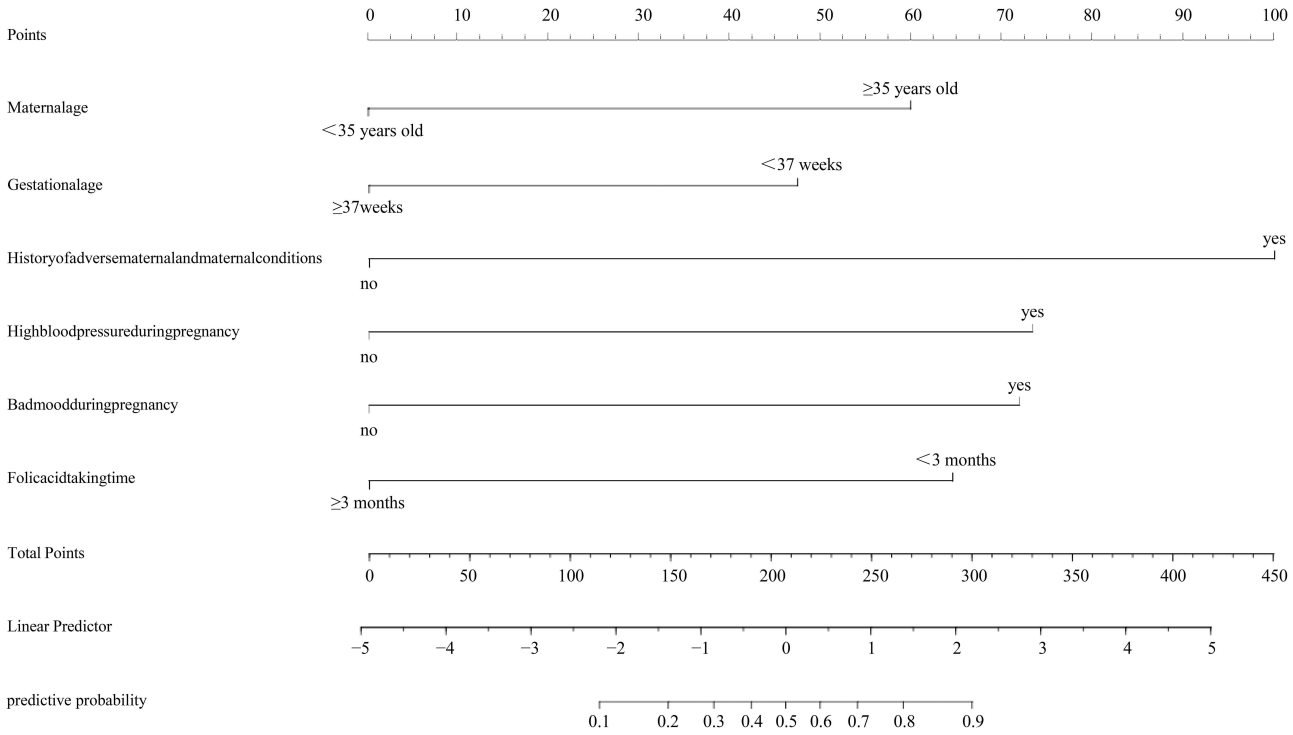

Figure 2 Nomogram model of BD in the fetus.

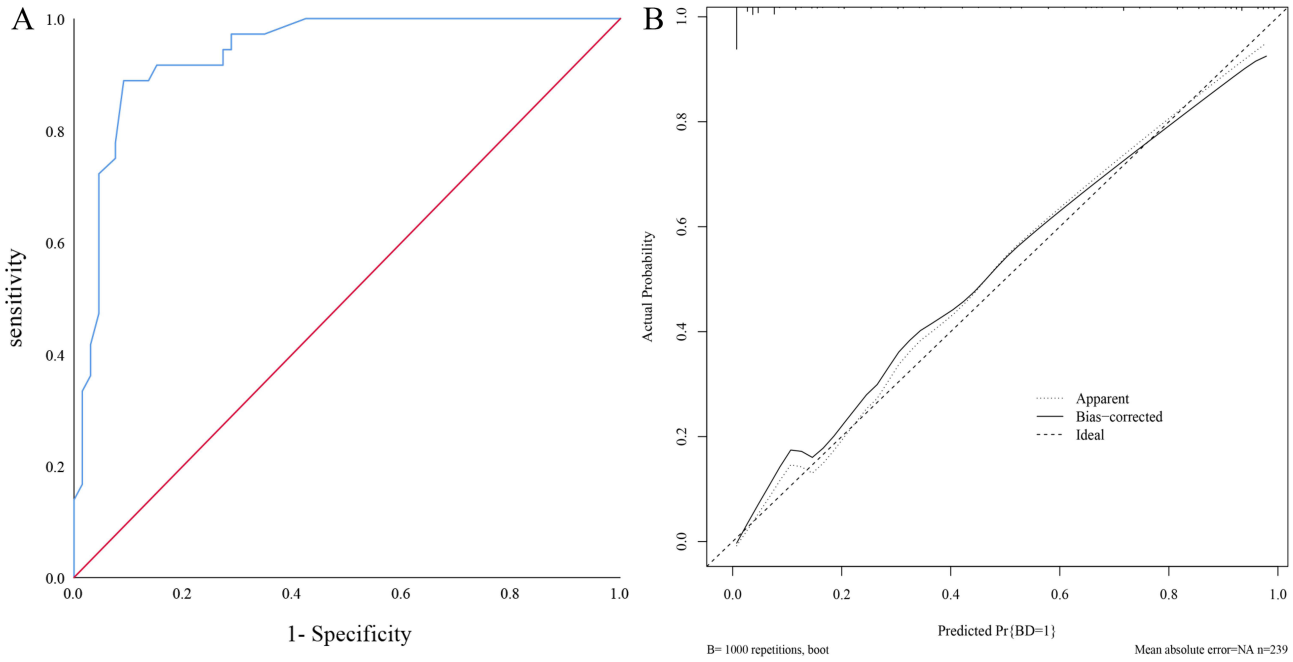

Figure 3 Internal validation of a Nomogram model of neonatal BD. (**A**) ROC **curves of** the modeling group; (**B**) Calibration curves of the modeling group.

intake are risk factors for neonatal BD. Among these, (1) maternal age >35 years increases the risk of BD due to reduced vitality of body functions, endocrine disorders, declining fertility, decreased ovarian function, insufficient nutrient supply to the fetus, placental disorders, and increased risk of chromosomal abnormalities in the fetus. With the implementation of the two-child policy, the number of older mothers is increasing, thus raising the risk of BD. Therefore, it is necessary to intensify publicity, encourage childbirth at the optimal age, and conduct thorough examinations.[12,13] (2) Neonates born

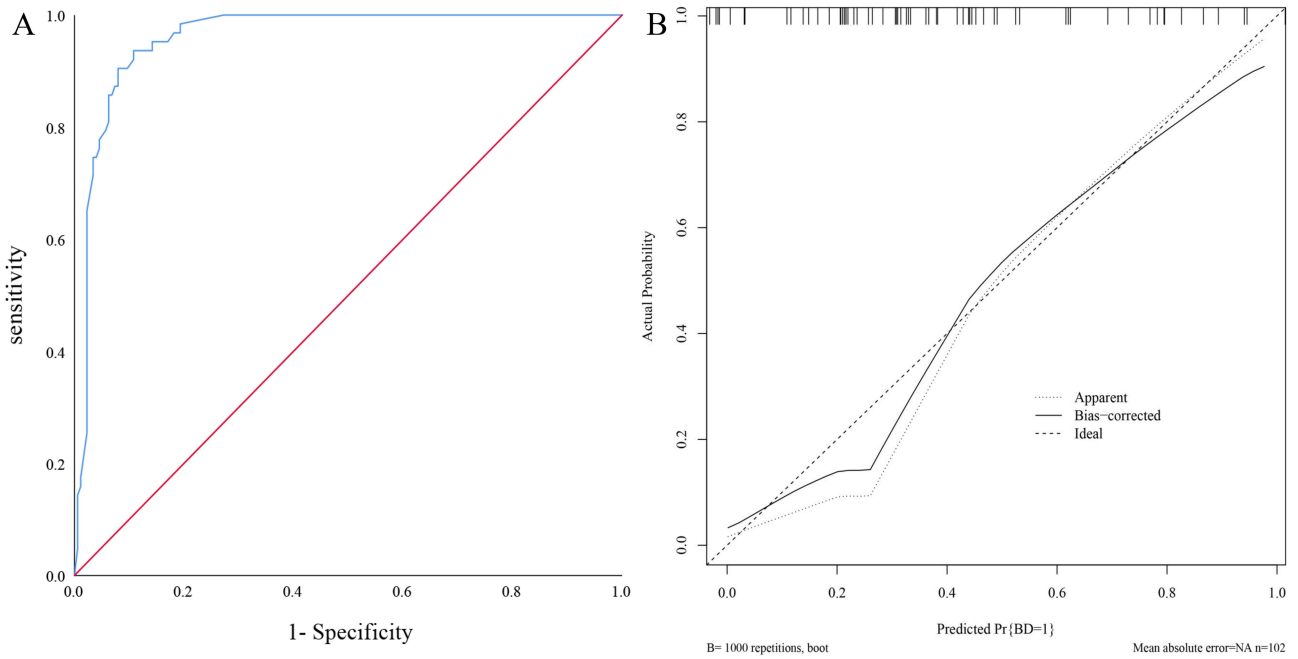

Figure 4 External validation of a Nomogram model of neonatal BD. (**A**):Verify the group ROC curves; (**B**)Calibration curve of the verification group.

before 37 weeks of gestation have a higher risk of BD, possibly related to various maternal diseases and potentially influencing BD. Pregnant women should focus on nutritional intake to ensure sufficient nutrition for fetal development and reduce the occurrence of BD.[14,15] (3) Couples with a history of adverse pregnancy outcomes have a higher likelihood of chromosomal abnormalities, which may also be associated with chromosomal abnormalities in the mother.[16,17] (4) Hypertension during pregnancy can lead to various diseases in the fetus, including cardiovascular diseases, increasing the risk of BD.[18] (5) Adverse emotions during pregnancy can increase the secretion of thyroid hormones and adrenocortical hormones, which are transmitted to the embryo through the placenta and other pathways, hindering fetal development and affecting the formation of fetal organs, thereby leading to BD. Hence, pregnant women should regulate their emotions, participate in psychological counseling, ensure emotional stability, and avoid adverse emotions.[19,20] (6) Folic acid is essential in embryonic development and can prevent congenital heart diseases and other BDs. Taking folic acid for less than three months increases the risk of BD.[21,22] In light of these risk factors, it is important to emphasize the popularization of eugenics knowledge, strengthen propaganda and education, ensure proper prenatal care, timely supplement folic acid, maintain a balanced diet, exercise regularly, ease the tension of pregnant women, and advise them to avoid harmful substances to possibly prevent the occurrence of BD.

In this study, a Nomogram model for the occurrence of BD in newborns was constructed based on the above-mentioned influencing factors. The Nomogram can effectively assess risks, thereby enabling effective prevention in clinical practice. In our study, the AUCs for the modeling and validation groups were 0.938 and 0.961, respectively, indicating high discrimination. Furthermore, the slope of the calibration curve was close to 1, suggesting that the model's assessment of the risk of BD in newborns is consistent with the actual risk. Clinical medical staff can use the risk factors to assess the risk of BD in newborns and intervene early. This study has limitations, such as a small sample size. Future work will aim to validate the findings with a larger sample size.

Conclusion

In summary, maternal age, gestational weeks, history of adverse pregnancy outcomes, gestational hypertension, adverse emotions during pregnancy, and timing of folic acid intake are risk factors for the occurrence of BD in newborns. The Nomogram model constructed based on these factors demonstrates good discrimination and consistency and can assess the risk of BD in newborns.

Research Involving Human Participants

The study was approved by Meizhou People's Hospital ethics review board (2023-091-09) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Data Sharing Statement

The original contributions presented in the study are included in the article.

Consent for Publication

All authors give consent for publication.

Disclosure

The authors declare no conflicts of interest in this work.

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