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ORIGINAL RESEARCH

Construction and Validation of a Nomogram Model for Predicting the Risk of Neonatal Sepsis Complicated by Purulent Meningitis

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Background: Neonatal purulent meningitis (NPM) is a severe infection with high morbidity and mortality. NPM is a common complication in cases of neonatal sepsis (NS). This study aims to develop and validate a risk prediction model for NS complicated by NPM.

Methods: A retrospective study of 535 neonates diagnosed with sepsis at the Affiliated Children's Hospital of Zhengzhou University between January 2016 and October 2024 was conducted. The primary outcome was the presence of NPM. Multivariate logistic regression was used to identify predictive factors, and a nomogram model was created using R software.

Results: Multivariate analysis identified fever, seizures, tachycardia, and decreased levels of alkaline phosphatase (ALP) and total bilirubin (TBIL) as independent risk factors for NS complicated by NPM ($P < 0.05$). The area under the receiver operating characteristic curve (ROC) for the training set was 0.765 (95% CI: 0.711–0.819), and 0.713 (95% CI: 0.625–0.800) for the validation set. The Hosmer-Lemeshow test confirmed good model fit ($\chi^2 = 8.963$, $P = 0.345$). Calibration and decision curve analysis showed high predictive performance and clinical applicability.

Conclusion: The nomogram developed in this study demonstrates promising predictive ability and clinical value for NS complicated by NPM.

Keywords: neonatal purulent meningitis, NPM, neonatal sepsis, NS, prediction model, nomogram

Introduction

Neonatal sepsis (NS) and neonatal purulent meningitis (NPM) are common and highly fatal infectious diseases in neonates.[1,2] NPM is a common complication in cases of NS.[3–5] NPM carries a high mortality rate, with 20% to 50% of surviving neonates experiencing varying degrees of neurological sequelae.[6] Lumbar puncture (LP) to obtain cerebrospinal fluid (CSF) for analysis is the most reliable method for diagnosing NPM. However, in clinical practice, approximately 30% to 70% of septic neonates do not undergo LP due to the absence of meningitis symptoms and concerns about the risks of the procedure.[7] Furthermore, the early clinical manifestations of NS and NPM are similar, making it challenging to predict NPM in neonates with sepsis. Although predictive models for purulent meningitis have been established in adults and children, there are fewer studies on related models for septic neonates, and these studies have limitations. It remains unclear whether perinatal indicators and clinical symptoms influence the prediction models.[8–10] Therefore, there is a clinical need for a predictive model that can assess whether NS is complicated by NPM before cerebrospinal fluid testing. This study aims to construct and validate a clinical diagnostic model for predicting NS complicated by NPM by integrating multidimensional data, including hematological indicators and clinical symptoms, to facilitate early diagnosis and rational use of antimicrobial treatment.

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Materials and Methods

Study Design and Population

A retrospective study was conducted on neonates hospitalized at the Neonatal Department of Zhengzhou University Affiliated Children's Hospital between January 2016 and October 2024. NS cases were identified through International Classification of Diseases, 10th Revision (ICD-10) codes P36.0-P36.9, systematically retrieved from the hospital's electronic medical record (EMR) system. Initially, a total of 1698 suspected cases were identified. After applying detailed inclusion and exclusion criteria (outlined below), 535 cases were ultimately included in the final analysis.

The diagnosis of NS was established based on clinical manifestations and laboratory findings,[11] requiring fulfillment of all following criteria: (1) Presence of at least two abnormal clinical manifestations, including thermoregulatory instability (core temperature ≥38.0°C or ≤36.0°C), circulatory abnormalities (heart rate >160 bpm or <80 bpm, marbled skin pattern, cold extremities), respiratory symptoms (dyspnea, apnea, cyanosis), gastrointestinal manifestations (poor feeding, abdominal distension, vomiting, jaundice), and other systemic presentations (lethargy, edema, oliguria, hemorrhagic tendency); (2) Laboratory confirmation through either of the following: ≥ 2 positive non-specific hematological parameters (abnormal white blood cell count, elevated immature-to-total neutrophil ratio, elevated C-reactive protein or procalcitonin levels, thrombocytopenia), detection of pathogenic bacterial DNA in blood specimens, or positive blood culture results.

All included neonates underwent LP. The indications for lumbar puncture[11] (any one of the following three criteria): (1) positive blood culture; (2) clinical manifestations with at least two positive nonspecific infection markers; (3) poor response to anti-infective treatment. The LP procedure was performed within one week of the neonates' admission.

The definitive diagnosis of NPM relies on the investigation of CSF. For neonates within 28 days of birth, the diagnosis of purulent meningitis can be established when any one of the following criteria is satisfied:[12] (1) a positive CSF culture for pathogenic bacteria; (2) an elevated CSF white blood cell count (≥20 cells/mm^3) with a predominance of polymorphonuclear leukocytes (>50%), coupled with a low CSF glucose concentration (<2.2 mmol/L or <40% of serum glucose) or elevated CSF protein content (>1.7 g/L).

Inclusion criteria: Neonates aged ≤ 28 days who met the diagnostic criteria for NS. Exclusion criteria: (1)Neonates with congenital genetic metabolic disorders, bilirubin encephalopathy, congenital brain developmental malformations, malignant tumors, intracranial space-occupying lesions and hydrocephalus; (2)Neonates who developed other intracranial infectious diseases (such as tuberculous, viral, or cryptococcal meningitis) during hospitalization or treatment; (3) Neonates with incomplete clinical or laboratory data; (4) Neonates whose families chose to withdraw treatment or refused lumbar puncture during hospitalization.

The study adhered to the ethical principles outlined in the Declaration of Helsinki and received approval from the Hospital Ethics Review Board of Henan Children's Hospital (2023-H-K45). Data collection was retrospective, with strict anonymization protocols ensuring confidentiality. Due to the study's retrospective design, the requirement for informed consent was waived, as confirmed by the Hospital Ethics Review Board of Henan Children's Hospital (2023-H-K45).

Data Collection

The following data were obtained from the hospital's EMR system: (1) Demographic and admission data, including age, gender, weight, respiratory rate, and heart rate; (2) Perinatal-related indicators, including mode of delivery, history of hypoxia or asphyxia, preterm birth status, presence of premature rupture of membranes for ≥ 18 hours, maternal age, history of gestational diabetes, respiratory tract infections during pregnancy and gynecological inflammation; (3) Clinical symptoms, including fever, poor response, jaundice, and seizures. Fever was defined as a body temperature higher than 38°C and poor response was defined as lethargy and reduced activity and feeding; (4) Laboratory test results. All vital signs and laboratory data included in this study were measured within the first 24 hours after admission. In cases where measurements were taken multiple times within 24 hours, only the first recorded values were considered.

Statistical Analysis

Statistical analysis was performed using SPSS 27.0 software. R software (version 4.2.3) was used to randomly divide all study subjects into training and validation sets at a 7:3 ratio. The training set was used to construct the nomogram

predictive model, and the validation set was used to assess the model's performance. Both the training and validation sets were further divided into NPM and non-NPM groups based on the presence or absence of purulent meningitis. For continuous variables, data following a normal distribution were expressed as mean ± standard deviation, and inter-group comparisons were performed using independent sample *t*-tests. Non-normally distributed data were expressed as median (M) and interquartile range (P25, P75), with comparisons between groups conducted using the Mann–Whitney *U*-test. Categorical data were expressed as rates [n (%)], and differences between groups were compared using the chi-squared (χ^2) test. Variables with statistically significant differences underwent univariate and multivariate logistic regression analyses to identify independent risk factors for NPM in neonates with sepsis. A nomogram predictive model was constructed using R software (version 4.2.3). The model's performance was evaluated using the Hosmer-Lemeshow test and receiver operating characteristic (ROC) curve. All statistical tests were two-sided, and a P value of < 0.05 was considered statistically significant.

Results

General Information

A total of 535 pediatric patients with NS were included. In the NPM group, there were 143 cases, and in the non-NPM group, there were 392 cases. There was no statistical significance between the two groups in terms of perinatal indicators ($P > 0.05$), as shown in Table 1. The training set comprised 375 cases, and the validation set comprised 160 cases. No significant differences were found between the variables in the training and validation sets ($P > 0.05$), as shown in Table 2.

Comparison of Clinical Data Between NPM and Non-NPM Groups in the Training Set

A total of 375 cases of NS were included in the training set, with 100 cases in the NPM group and 295 cases in the non-NPM group. Compared to the non-NPM group, the NPM group had 86 (86%) cases of fever and 7 (7%) cases of seizures, which were both higher than in the non-NPM group ($P < 0.05$). The NPM group also had higher values for age, heart rate, red blood cell (RBC), fibrinogen (FBG), alkaline phosphatase (ALP), and total bilirubin (TBIL) than the non-NPM group ($P < 0.05$), while activated partial thromboplastin time (APTT) and prothrombin time (PT) were lower in the NPM group compared to the non-NPM group ($P < 0.05$), as shown in Table 3.

Table 1 Perinatal Characteristics of the Entire Study Cohort

Variables	NPM (n = 143)	Non-NPM (n = 392)	P
Cesarean section, n (%)	68(47.6%)	185(47.2%)	0.941
Premature birth, n (%)	12(8.4%)	55(14.0%)	0.081
Hypoxic asphyxia, n (%)	7(4.9%)	33(8.4%)	0.170
PROM ≥ 18h, n (%)	3(2.1%)	20(5.1%)	0.130
Birth weight (kg)	3.3(3.0, 3.5)	3.2(2.8, 3.5)	0.193
Maternal age (years)	27(24, 30)	25(28, 31)	0.425
Diseases during pregnancy, n (%)			
Respiratory tract infection	7(4.9%)	27(6.9%)	0.403
Gestational diabetes mellitus	4(2.8%)	20(5.1%)	0.254
Gynecological inflammation	5(3.5%)	15(3.8%)	0.859

Abbreviations: NPM, neonatal purulent meningitis; PROM, premature rupture of membranes.

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Table 2 Comparison of Clinical Data Between the Training Set and the Validation Set

Variables	Training Set (n = 375)	Validation Set (n = 160)	P
NPM, n (%)	100(26.7%)	43(26.9%)	0.999
Male, n (%)	230(61.3%)	96(60.0%)	0.847
Age (days)	13(8, 19)	13(8, 18)	0.700
Symptoms, n (%)			
Fever	245(65.3%)	110(68.8%)	0.506
Poor response	101(26.9%)	42(26.2%)	0.955
Jaundice	77(20.5%)	41(25.6%)	0.235
Seizures	12(3.2%)	6(3.8%)	0.951
Heart rate (bpm)	152(142, 165)	154 (145, 163)	0.983
Respiratory rate (rate/minute)	50(43, 57)	50 (43, 56)	0.514
Body weight (kg)	3.30(2.90, 3.67)	3.33(3.00, 3.70)	0.447
Biochemical parameters			
PCT (ng/mL)	0.24(0.11, 1.01)	0.28(0.14, 1.08)	0.214
APTT (S)	39.7(34.4, 47.3)	40.4(34.0, 50.4)	0.379
PT (S)	12.7(11.5, 14.0)	12.7 (11.6, 14.7)	0.337
NEU (10^6 cells/L)	4.7(2.8, 8.4)	4.9(3.0, 7.9)	0.557
PLT (10^9 cells/L)	298(190, 394)	291(174, 374)	0.414
RBC (10^{12} cells/L)	3.8(3.4, 4.4)	3.9 (3.3, 4.4)	0.563
WBC (10^9 cells/L)	9.9 (7.2, 13.8)	10.2 (7.4, 15.6)	0.543
FBG (g/L)	2.5 (1.8, 3.2)	2.4 (1.9, 3.2)	0.736
Lac (mmol/L)	2.1(1.4, 3.2)	2.1 (1.4, 3.4)	0.831
ALB (g/L)	30.5(27.5, 33.5)	30.8(27.3, 34.3)	0.670
ALP (U/L)	151.9(118.5, 193.9)	152.6 (122.7, 191.4)	0.676
ALT (U/L)	28.2(22.0, 39.2)	27.2 (21.6, 37.3)	0.499
AST (U/L)	36.1(27.7, 51.4)	36.3 (27.3, 53.5)	0.601
LDH (U/L)	367.4(303.6, 486.0)	379.5 (321.4, 506.4)	0.217
TBIL (μmol/L)	86.3(35.3, 176.2)	117.0 (37.8, 211.7)	0.157

Abbreviations: NPM, neonatal purulent meningitis; PCT, procalcitonin; APTT, activated partial thromboplastin time; PT, prothrombin time; NEU, neutrophil; PLT, platelet; RBC, red blood cell; WBC, white blood cell; FBG, fibrinogen; Lac, lactate; ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; TBIL, total bilirubin.

Factors Selection for the Predictive Model

Univariate analysis further showed that fever, jaundice, seizures, TBIL, ALP, FBG, heart rate, and age were related to the occurrence of NPM in NS ($P < 0.05$), as shown in Table 4. Variables with statistical significance in the univariate analysis were included in a logistic regression model for multivariate analysis. The results showed that fever, seizures, tachycardia, and decreased levels of ALP and TBIL were independent risk factors for the occurrence of NPM (P <

Table 3 Comparison of Clinical Data Between the NPM Group and Non-NPM Group in the Training Set

Variables	NPM (n = 100)	Non-NPM (n = 275)	P
Male, n (%)	62(62%)	168(61.1%)	0.873
Age (days)	14.5 (10.0, 20.8)	13.0 (8.0, 18.0)	0.009
Symptoms, n (%)			
Fever	86(86%)	159(57.8%)	< 0.001
Poor response	22(22%)	79(28.7%)	0.194
Jaundice	13(13%)	64(23.3%)	0.029
Seizures	7(7%)	5(1.8%)	0.029
Heart rate (bpm)	155 (146, 168)	151 (140, 162)	0.002
Heart Rate Status, n (%)			0.031
Tachycardia (≥ 160 rate/minute)	44(42%)	82(29.8%)	
Bradycardia (< 100 rate/minute)	0(0%)	3(1.1%)	
Respiratory rate (rate/minute)	52 (44, 58)	50.00(43, 56)	0.432
Body weight(kg)	3.35 (3.04, 3.70)	3.25 (2.90, 3.70)	0.091
Laboratory indicators			
PCT (ng/mL)	0.28 (0.12, 1.44)	0.23 (0.11, 0.88)	0.076
APTT (S)	37.9 (33.0, 44.5)	40.4 (35.2, 47.6)	0.038
PT (S)	12.1 (11.1, 13.4)	12.9 (11.7, 14.2)	< 0.001
NEU (10^9 cells/L)	4.3 (2.7, 8.2)	4.9(2.8, 8.7)	0.423
PLT (10^9 cells/L)	316.0(191.8, 415.8)	293.0 (187.0, 391.0)	0.587
RBC (10^{12} cells/L)	3.6 (3.2, 4.3)	3.9 (3.4, 4.4)	0.038
WBC (10^9 cells/L)	9.8 (7.0, 13.2)	10.0(7.3, 14.2)	0.333
FBG (g/L)	2.7(2.1, 3.6)	2.4 (1.7, 3.1)	0.004
Lac (mmol/L)	2.0 (1.5, 3.3)	2.1 (1.4, 3.2)	0.826
ALB (g/L)	30.5(28.1, 32.7)	30.6 (27.2, 34.0)	0.688
ALP (U/L)	131.2(108.6, 165.1)	157.7 (126.5, 205.2)	< 0.001
ALT (U/L)	32.3 (22.4, 40.3)	27.7 (21.3, 39.1)	0.089
AST (U/L)	39.0(30.2, 56.6)	35.4 (27.4, 49.7)	0.123
LDH (U/L)	380.5 (277.9, 500.9)	365.2 (304.7, 480.1)	0.907
TBIL (μmol/L)	47.0 (24.1, 109.5)	110.7 (40.8, 199.3)	< 0.001

Abbreviations: NPM, neonatal purulent meningitis; PCT, procalcitonin; APTT, activated partial thromboplastin time; PT, prothrombin time; NEU, neutrophil; PLT, platelet; RBC, red blood cell; WBC, white blood cell; FBG, fibrinogen; Lac, lactate; ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; TBIL, total bilirubin.

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Table 4 Univariate Logistic Regression Analysis of NS Complicated with NPM

Variables	OR	95% CI	P
Age (days)	1.05	1.01, 1.08	0.011
Fever, n (%)	4.48	2.43, 8.28	<0.001
Jaundice, n (%)	0.49	0.26, 0.94	0.032
Seizures, n (%)	4.07	1.26, 13.12	0.019
Heart rate (bpm)	1.02	1.01, 1.04	0.002
FBG (g/L)	1.31	1.07, 1.61	0.009
ALP (U/L)	0.990	0.985, 0.995	<0.001
TBIL (μmol/L)	0.995	0.992, 0.997	<0.001

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; FBG, fibrinogen; ALP, alkaline phosphatase; TBIL, total bilirubin.

Table 5 Multivariate Logistic Regression Analysis of NS Complicated with NPM

Variables	β	OR	95% CI	P
Fever, n (%)	0.998	2.713	1.400, 5.257	0.003
Seizures, n (%)	1.321	3.747	1.034, 13.581	0.044
Heart rate (bpm)	0.018	1.018	1.002, 1.034	0.028
ALP (U/L)	−0.010	0.990	0.985, 0.995	< 0.001
TBIL (U/L)	−0.004	0.996	0.993, 0.999	0.004

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; ALP, alkaline phosphatase; TBIL, total bilirubin.

0.05), as shown in Table 5. Through ROC curve analysis, we determined the cutoff values for the continuous variables in the model: ALP of 137.85 U/L, TBIL of 109.8 μmol/L, and heart rate of 142.5 bpm.

Establishment of the Predictive Model

A nomogram was drawn based on the five significant variables from the multivariate logistic regression analysis, as shown in Figure 1. The nomogram is used by drawing a vertical line upward for each variable to determine the corresponding score. The total score is then summed and a vertical line is drawn from the total score to the final probability axis to determine the risk of NPM occurrence.

Validation and Evaluation of the Predictive Model

The area under the ROC curve (AUC) for the model derived from the training set was 0.765 (95% CI: 0.711–0.819), and when the data from the validation population were incorporated into the established predictive model, the AUC of the ROC curve was 0.713 (95% CI: 0.625–0.800), both indicating that the model has good predictive ability, as shown in Figure 2. The Hosmer-Lemeshow goodness-of-fit test showed that the model had a good fit ($\chi^2 = 8.963$, $P = 0.345$). The calibration curve of the nomogram model was plotted, showing that the calibration curves for both the training set and the validation set were close to the ideal curve, suggesting good predictive performance of the model, as shown in Figure 3. Decision curve analysis indicated that the clinical application value of the nomogram model is relatively high, as shown in Figure 4.

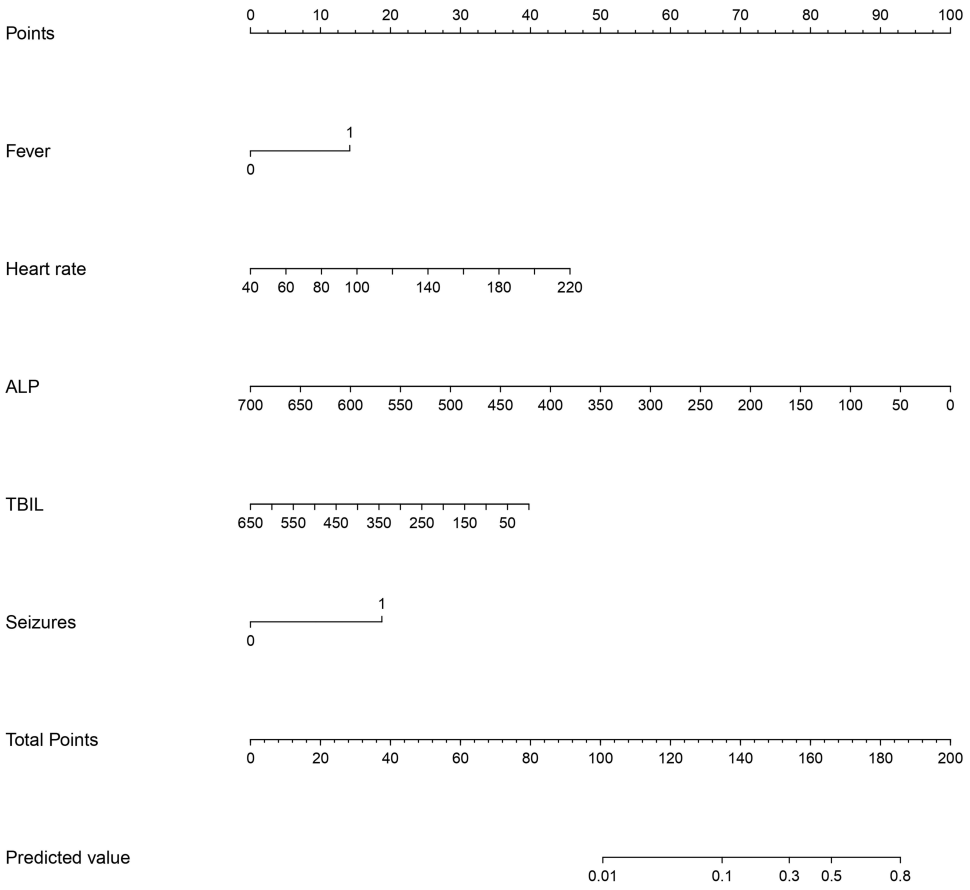

Figure 1 Nomogram prediction model for the risk of NS complicated by NPM. The corresponding scores are obtained based on the variables, and the total score is calculated by summing the individual scores. The total score corresponds to the risk axis, which allows the determination of the risk of NS complicated by NPM.
Abbreviations: ALP, Alkaline phosphatase; TBIL, Total bilirubin; NS, neonatal sepsis; NPM, neonatal purulent meningitis.

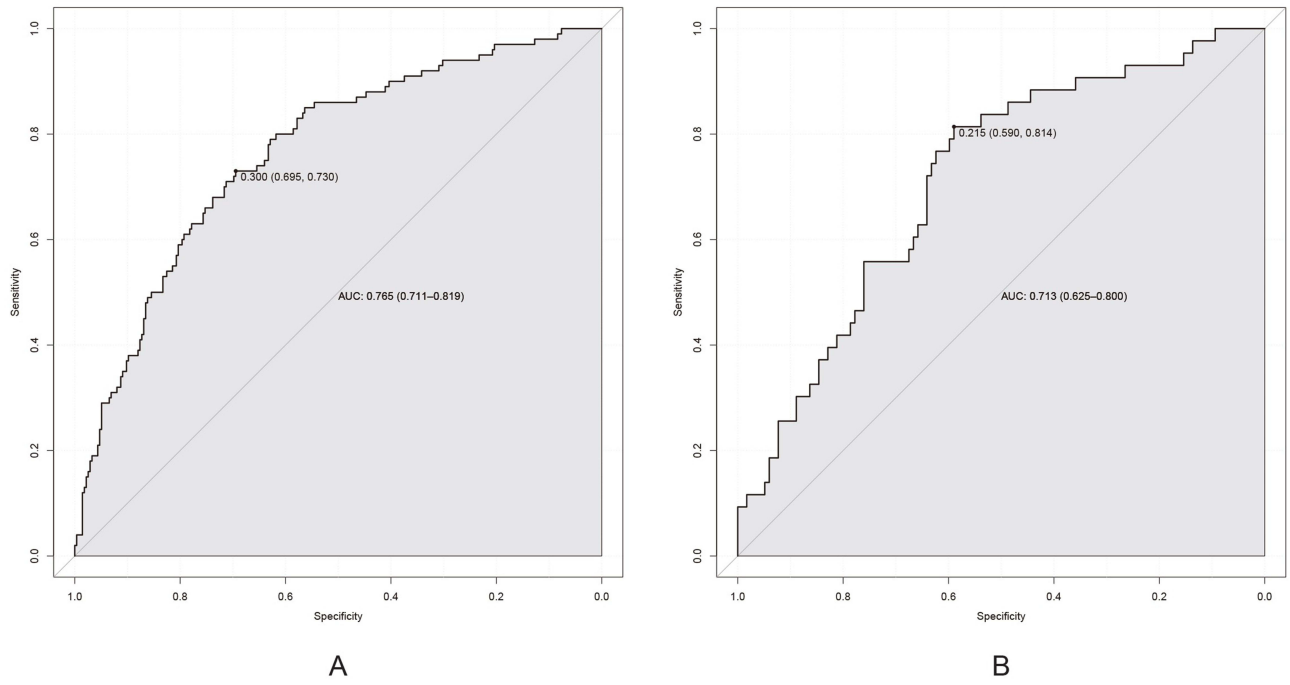

Figure 2 ROC curve of the nomogram prediction model. The AUC values for predicting the occurrence of NPM in neonatal sepsis (NS) in the training set (**A**) and validation set (**B**) are 0.765 and 0.713, respectively, indicating good discriminatory ability of the model.

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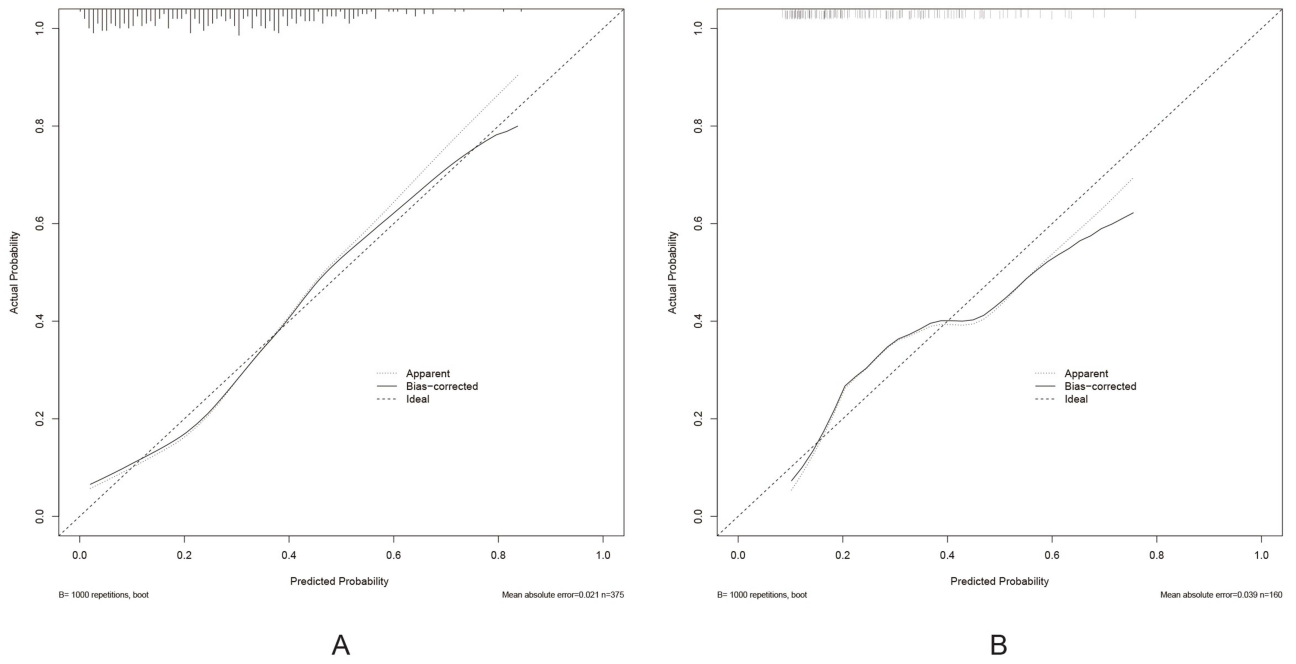

Figure 3 Calibration curve of the nomogram prediction model. The x-axis represents the predicted probability, while the y-axis represents the actual probability. The closer the calibration curve is to the ideal curve, the better the model's calibration. In this study, the calibration curves for both the training set (**A**) and validation set (**B**) of the nomogram model are close to the ideal curve, indicating that the model has good predictive performance.

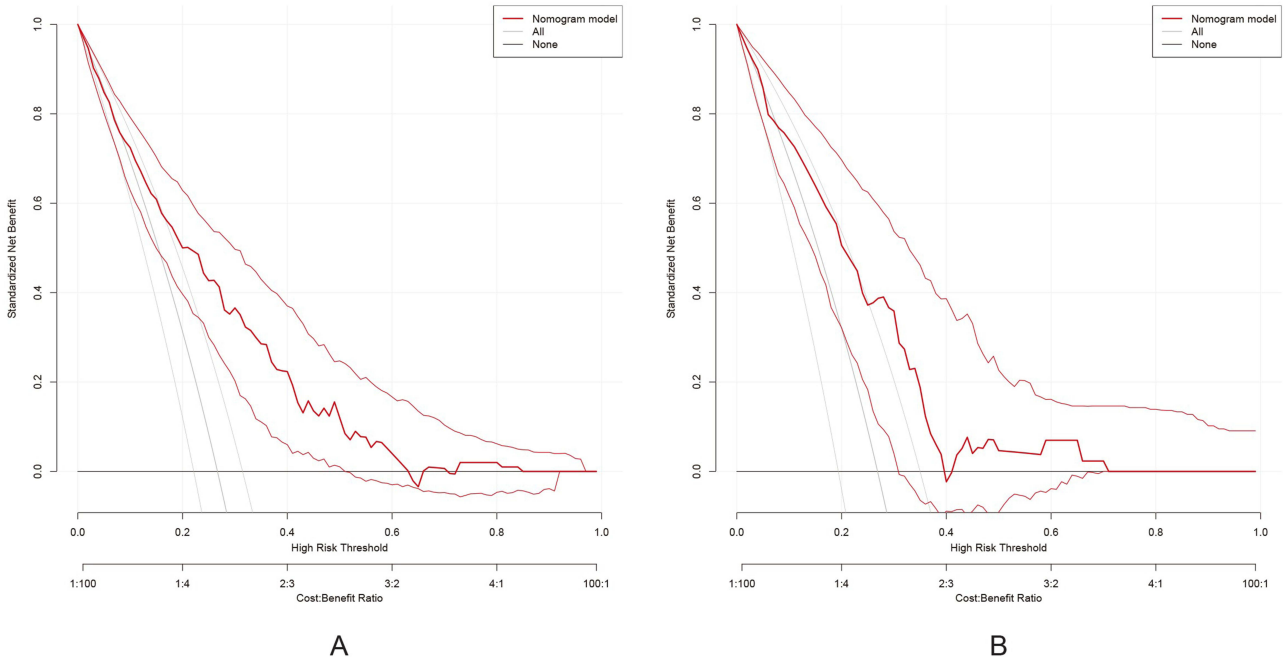

Figure 4 Decision curve analysis of the nomogram prediction model. The black line (labeled "None") represents no intervention for all NS patients, with a net benefit of 0. The gray line (labeled "All") indicates interventions for all NS patients, reflecting the standardized net benefit under this strategy. The red line (labeled "Nomogram model") demonstrates the standardized net benefit of the nomogram model in predicting the risk of NPM in NS patients. In both the training set (**A**) and validation set (**B**), the red line remains above the black and gray lines across most risk thresholds, indicating that the predictive model possesses high clinical applicability.

Discussion

NPM can present with atypical clinical manifestations, typically including fever, poor responsiveness, tense or bulging anterior fontanel, poor complexion, feeding difficulties, hyperbilirubinemia, and changes in muscle tone. These symptoms often overlap with those of NS.[13] Due to the underdevelopment of the neonatal nervous system, poor muscle development, and the open cranial sutures, the characteristic signs of meningeal irritation and intracranial hypertension are not evident. Moreover, the clinical similarities between the two conditions make it challenging to identify whether NS is complicated by NPM in the early stages. Based on the results of multivariate logistic regression analysis, this study developed a nomogram predictive model that includes five independent risk factors (fever, seizures, heart rate, ALP, and TBIL), which was subsequently validated. The model shows that fever, seizures, and heart rate are positively correlated with the occurrence of purulent meningitis, while ALP and TBIL levels are negatively correlated. The nomogram visualizes the complex statistical model, helping clinicians to predict the risk of NS complicated by NPM at an early stage. It provides both theoretical support and practical evidence for the early screening of NPM.

This study summarized the four most common clinical symptoms observed in pediatric patients with NS upon admission to our hospital: fever, poor responsiveness, jaundice, and seizures, and analyzed them. The results indicated that fever and seizures are independent risk factors for NS complicated by NPM ($p < 0.05$). Some studies have pointed out that 80.4% of children with purulent meningitis exhibit both fever and neurological symptoms, which is consistent with the findings of this study.[14] Recent research has shown that fever has a high sensitivity in the early diagnosis of NPM, especially when other typical symptoms are absent. Fever can serve as an important indication for lumbar puncture and cerebrospinal fluid examination.[15] The American Academy of Pediatrics' guidelines for the management of febrile infants recommend that infants aged 8–21 days with fever (≥ 38.0°C) should undergo a comprehensive evaluation, including cerebrospinal fluid culture. For infants aged 22–28 days with fever (> 38.0°C) and abnormal inflammatory markers, cerebrospinal fluid should be collected for analysis and culture.[16] Seizures are a relatively specific clinical manifestation of NPM.[17,18] This study also shows that seizures are an important independent risk factor for the occurrence of NPM, which is consistent with previous research. Studies have indicated that children with septic meningitis often present with tachycardia, and changes in heart rate are closely related to the severity of the infection and prognosis.[19] Therefore, for neonates presenting with fever of unknown origin, seizures, and other high-risk factors, early relevant examination and treatment should be conducted to improve the prognosis of the affected children.

Research has shown that ALP reduces inflammation by dephosphorylating and detoxifying endotoxins, and by converting ATP released during cellular stress into adenosine, which has anti-inflammatory and tissue-protective effects. This process helps alleviate the systemic inflammatory response caused by sepsis and improves organ function.[20,21] Brichacek et al found that ALP participates in the immune balance of sepsis by regulating T cell subpopulations.[22] Moreover, the study also found that ALP helps maintain the integrity of the blood-brain barrier and may have a protective effect on neuroinflammation caused by sepsis, thereby playing a protective role in preventing the onset and development of meningitis.[23] After using a nonspecific alkaline phosphatase inhibitor on human cerebral microvascular endothelial cell lines (hCMEC/D3 cells) and primary mouse brain microvascular endothelial cells (BMECs), the barrier function was significantly impaired.[24] Our study suggests that a decrease in ALP levels may be one of the risk factors for NS complicated by purulent meningitis. Compared to neonates without purulent meningitis, a significant decrease in ALP levels may reflect blood-brain barrier damage and immune dysregulation, which could create favorable conditions for the development of meningitis. Although this conclusion requires further clinical and experimental validation, it offers a new perspective on understanding the role of ALP in NS complicated by purulent meningitis and provides theoretical support for the clinical application of ALP as a potential biomarker.

In 1987, Stocker et al discovered that bilirubin is an endogenous antioxidant that can protect lipids from oxidative stress damage.[25] Since then, research on bilirubin in oxidative stress-related diseases has received increasing attention. Several studies have pointed out that bilirubin affects the progression of diseases related to oxidative stress, such as cardiovascular and respiratory diseases, by regulating inflammation and inhibiting oxidative reactions.[26–28] Research has found that in pediatric respiratory infections, total bilirubin and indirect bilirubin levels are significantly reduced, possibly related to inflammation and oxidative stress responses, suggesting that bilirubin levels could serve as

a reference indicator for clinically assessing the degree of inflammation and antioxidant capacity in the body.[29] The results of this study indicate that bilirubin levels are negatively correlated with the occurrence of NPM, suggesting that bilirubin may play a potential protective role in the prevention and treatment of septic NPM. This finding suggests that bilirubin could serve as a biomarker for sepsis-related complications and may play a role in immune regulation and anti-inflammatory processes.

This study included perinatal-related indicators; however, these factors were not selected as predictive factors. Some studies have pointed out that assessing maternal risk factors alone to suspect meningitis and perform lumbar puncture results in a low detection rate, which is consistent with the findings of this study.[7] Although some infection-related laboratory tests were also included, none were ultimately selected as risk factors. The results of this study indicate that no significant differences were found in white blood cells (WBC) and neutrophil count levels between the NPM and non-NPM groups. During bacterial infections, especially in severe cases, procalcitonin (PCT) levels tend to rise rapidly as part of the body's inflammatory response.[30] Previous studies have demonstrated that PCT can be a good supplemental biomarker with high diagnostic accuracy in detecting bacterial meningitis in children.[31] However, in the present study involving NS, no statistically significant difference in PCT levels was observed between the groups with NPM and those without purulent meningitis (non-NPM). This finding suggests that PCT may have limited diagnostic value in differentiating neonates with sepsis who have concurrent purulent meningitis. Consequently, further research is required to more comprehensively assess the diagnostic utility of PCT in this context. Additionally, due to the low blood culture positivity rate in the included patients, blood culture results were not included as study variables.

There are several limitations with our study: (1) While we considered multiple potential influencing factors, there may still be other clinical characteristics or laboratory indicators that were not accounted for, which could affect the further optimization of the model. Additionally, the lack of age-based subgroup analysis makes it difficult for us to fully understand the role of the physiological fluctuations of neonatal biomarkers with age in the development of sepsis-associated purulent meningitis. (2) The diagnostic criteria for NS used in this study may have certain limitations, potentially leading to missed diagnoses or false positives. Similarly, the diagnostic accuracy of NPM also presents challenges. Future studies should consider incorporating follow-up adjustments for potential misdiagnoses to enhance the accuracy of the model. (3) This study is a single-center retrospective study, which inevitably introduces potential biases. Additionally, the lack of external data to validate the model may limit its generalizability and statistical power. Future multicenter studies are required to validate and optimize the algorithm across diverse populations and clinical settings.

Conclusions

This study developed and validated a nomogram predictive model based on clinical features and laboratory indicators, including fever, seizures, heart rate, ALP, and TBIL. The model can provide a probabilistic assessment of the risk of NS complicated by NPM, and it has demonstrated good predictive ability and clinical applicability.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author Zhipeng Jin.

Ethics Approval and Consent to Participate

The study was conducted according to the guidelines of the Declaration of Helsinki and was approved the Hospital Ethics Review Board of Henan Children's Hospital (2023-H-K45). We confirmed that all the data were anonymized and maintained with confidentiality; therefore, the requirement for informed consent has been waived because of the retrospective nature of the current study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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