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Original Article

Factors for poor outcomes of neonatal bacterial meningitis: a retrospective multicenter study

Lan Shao[1], Dongdong You[2], Yunpeng Shao[3], Huanhuan Xu[4], Feng Li[5]

[1]Department of Paediatrics, The Jingmen Central Hospital, The Jingmen Central Hospital affiliated to Jingchu University of Technology, Jingmen, China; [2]Department of Neonatology, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China; [3]Department of Blood Purification, The Jingmen Central Hospital, The Jingmen Central Hospital affiliated to Jingchu University of Technology, Jingmen, China; [4]Second Department of Blood Donation Service, Wenzhou Central Blood Station, Wenzhou, China; [5]Department of Pediatric Neurology, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China.

ABSTRACT

Background. Neonatal bacterial meningitis remains a severe infectious disease associated with substantial mortality and long-term neurological sequelae. This study aimed to identify factors associated with poor outcomes and to determine independent prognostic predictors in neonates with bacterial meningitis.

Methods. This retrospective multicenter cohort study included neonates diagnosed with bacterial meningitis. Clinical characteristics, laboratory findings, microbiological data, treatment responses, and outcomes were analyzed. Univariate and multivariable logistic regression analyses were performed to identify factors associated with poor outcomes.

Results. A total of 85 neonates were included in the final analysis. 31 neonates (36.5%) experienced poor outcomes, including death or long-term neurological sequelae. In multivariable analysis, the presence of neurological signs at admission (odds ratio [OR]: 7.315; 95% confidence interval [CI]: 1.875–28.535) and the development of acute neurological complications during hospitalization (OR: 7.541; 95% CI: 2.045–27.807) were the only factors independently associated with poor outcomes. Several variables, including elevated cerebrospinal fluid protein levels, early administration of blood-brain barrier (BBB)-permeable antibiotics prior to lumbar puncture, and adequate response to initial antimicrobial therapy, were significantly associated with outcomes in univariate analyses but did not retain statistical significance after multivariable adjustment.

Conclusions. Neurological involvement at presentation and acute neurological complications are key independent predictors of poor outcomes in neonatal bacterial meningitis. Other clinical and laboratory variables may reflect disease severity or early clinical course and may assist in early risk stratification.

Key words: neonatal bacterial meningitis, prognosis, neurological complications, cerebrospinal fluid, outcomes.

Neonatal bacterial meningitis (NBM) continues to pose a serious clinical burden worldwide, with a particularly high disease severity and fatality rate in resource-limited settings.[1] Survivors of NBM frequently experience unfavorable neurological outcomes, and previous studies have reported that up to half of affected neonates may develop moderate to severe long-term disabilities, including impairments in language, hearing, vision, motor function, and cognition.[2] In addition, a proportion of survivors, estimated at approximately 5-20%, may subsequently develop epilepsy during later childhood or adolescence.[3]

✉ Feng Li ▪ lilifefe@163.com

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Early recognition of neonates with NBM at risk for poor outcomes is crucial for ensuring timely management and identifying those who require long-term follow-up and early intervention. Although several studies on NBM have been conducted, data on long-term epidemiological trends and prognostic factors remain limited.[4,5] This retrospective study analyzed six years of epidemiological data on culture-confirmed NBM from two medical centers in Eastern China, aiming to identify predictors of poor outcomes and support the early identification of high-risk neonates.

Materials and Methods

This retrospective multicenter study reviewed the inpatient electronic medical records of neonates diagnosed with neonatal bacterial meningitis (NBM) who were admitted to the neonatal intensive care units of Yuying Children's Hospital and the Department of Pediatrics, Jingmen Central Hospital from January 2017 to December 2022, as well as their outpatient follow-up electronic medical records. This study protocols were approved by the Yuying Children's Hospital Ethics Committee (date: 01.01.2021, number: 2021-K-167-02). Inpatient data collection encompassed demographic data, clinical characteristics, laboratory findings and additional assessments for each case. Demographic data included age at onset, sex, weight at admission, gestational age, and maternal and perinatal conditions. The clinical characteristics documented included detailed body temperature profiles (including peak and nadir values), initial clinical presentations (such as poor feeding, irritability, lethargy, vomiting, seizures), neurological symptoms and signs at admission, and antibiotic exposure prior to and during hospitalization.

Laboratory findings included a complete blood count (CBC), C-reactive protein (CRP), procalcitonin (PCT) levels, blood cultures, as well as cerebrospinal fluid (CSF) analysis, which consisted of a white blood cell count and differential, protein concentration, glucose level, Gram staining, and bacterial culture. Additional assessments consisted of cranial magnetic resonance imaging (MRI), hearing evaluations, and documentation of acute neurological complications during hospitalization. All clinical, laboratory, imaging, and treatment-related data were retrospectively extracted from electronic medical records using a standardized data collection form by trained investigators at each participating center.

The follow-up duration was at least 2 years for preterm infants and at least 1 year for term infants and was conducted through scheduled outpatient clinic visits. Follow-up data primarily focused on neurodevelopmental outcomes and long-term neurological sequelae associated with bacterial meningitis.

Inclusion criteria

1. Clinical diagnosis of NBM confirmed by CSF Gram-stained smear or CSF bacteriological culture.
2. Onset of NBM within the first 28 days of life.
3. Gestational age greater than 34 weeks and birth weight above 1500 grams.

Exclusion criteria

1. Recent neurosurgical interventions, such as CSF shunts or reservoirs.
2. Presence of acquired or congenital anatomical defects.
3. Immunological abnormalities.

Definitions and clarifications applied in this study

1. We defined CSF pleocytosis as a CSF white blood cel (WBC) count >16 cells per mm^3 for infants ≤ 28 days.[6]
2. An abnormal CSF profile was defined as a positive Gram-stain result, CSF pleocytosis, neutrophil predominance on the CSF WBC

differential (>50% neutrophils), an elevated CSF protein level (>128 mg/dL for infants ≤ 28 days),or a low CSF glucose level (<25 mg/dL for infants ≤ 28 days of age).[6]

3. Bacterial meningitis was defined as either a positive CSF culture yielding a pathogenic organism or a positive CSF Gram stain demonstrating bacteria (e.g., Gram-positive cocci, Gram-negative rods). For cases diagnosed solely by Gram staining, the diagnosis required both exclusion of contamination by laboratory assessment and the presence of an abnormal CSF profile.[6]

4. For infants with traumatic lumbar punctures (ie, CSF RBC count >10 000 cells per mm^3), we used an RBC/WBC correction factor of 1000:1 to determine the corrected CSF WBC count.[7]

5. Neurological sequelae were defined as impairments persisting for more than six months, including intellectual or motor deficits and cranial nerve dysfunction (e.g., hearing loss, visual impairment, facial or oculomotor nerve palsy). Intellectual and motor development was evaluated using the Gesell Developmental Diagnosis Scale (GDDS). The GDDS assesses five developmental domains: adaptability, gross motor, fine motor, language, and personal-social behavior. For each domain, a developmental quotient (DQ) is calculated as the ratio of developmental age to chronological age multiplied by 100. A total DQ score is derived by averaging the domain scores. A DQ score <85 was defined as developmental delay. The GDDS has been widely applied in pediatric neurodevelopmental assessment and has demonstrated acceptable reliability and validity in clinical practice.[8] Muscle strength, muscle tone, and cranial nerve dysfunction were assessed through physical examination and relevant instrumental tests. Secondary epilepsy was diagnosed based on medical history, clinical manifestations, and electroencephalography findings.

6. An adequate response to initial antimicrobial therapy was defined as an afebrile period of 48 consecutive hours (maximum tympanic temperature ≤ 37.5 °C), negative meningeal irritation signs, a CRP level ≤ 20 mg/L, and a neutrophil count ≤ 10,000/mm^3 within the first 3-5 days of treatment.[9,10]

7. Patients who died or developed neurological sequelae were regarded as having a poor outcome.

8. Cases with fatal outcomes were not included in the analysis of antibiotic duration and recurrence. Those who were lost to follow-up were excluded.

9. Neonatal fever (rectal temperature):
Low-grade fever: 38.0-38.4 °C,
Moderate fever: 38.5-38.9 °C,
High fever: 39.0-40.0 °C,
Hyperpyrexia: > 40.0 °C.

10. Neonatal hypothermia (rectal temperature):
Mild hypothermia: 36.0-36.4 °C,
Moderate hypothermia: 32.0-35.9 °C,
Severe hypothermia: < 32.0 °C.
Temperature instability:
Maximum rectal temperature ≥ 39.0 °C,
Minimum rectal temperature < 36 °C.

11. Early-onset meningitis was defined as bacterial meningitis occurring within the first 7 days of life, whereas late-onset meningitis referred to cases diagnosed after 7 days of age, in accordance with commonly used neonatal infection classifications.[11]

Statistical analysis

Continuous variables with a normal distribution were expressed as means ± standard deviations, whereas non-normally distributed variables were presented as medians with interquartile ranges (IQRs) (median [Q1, Q3]). Categorical variables were summarized as frequencies and percentages.

Comparisons between groups were performed using the independent-samples t test for normally distributed continuous variables, the Mann–Whitney U test for non-normally distributed continuous variables, and the chi-square test for categorical variables, as appropriate.

Variables included in the univariate analysis were selected a priori based on previous literature and clinical relevance to neonatal bacterial meningitis. Univariate logistic regression analysis was performed to identify variables associated with poor outcomes. Variables with a p value <0.05 in univariate analysis were subsequently entered into the multivariable logistic regression model to determine factors independently associated with poor outcomes.

Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. All statistical tests were two-sided, and a p value <0.05 was considered statistically significant. Statistical analyses were conducted using SPSS software (version 23.0).

Results

Patient characteristics

Between January 2017 and December 2022, a total of 92 neonates hospitalized at the neonatal intensive care units of Yuying Children's Hospital and the Department of Pediatrics, Jingmen Central Hospital met the diagnostic criteria for bacteriologically confirmed bacterial meningitis. Seven neonates (7.6%) were lost to follow-up; subsequent analyses were conducted on the remaining 85 neonates.

Among these 85 neonates, the mean gestational age was 36.8 ± 1.73 weeks (range: 34–40 weeks). The median age at symptom onset was 6 days after birth (IQR: 2–15; range: 0–28 days), with 43 (50.6%) classified as early-onset meningitis. The median duration of illness before admission was 12 hours (IQR: 7.5–23.5; range: 2–48 hours). The mean admission weight was 3.36 ± 0.64 kg (range: 1.9–5.1 kg), and 46 neonates (52.9%) were male. A total of 22 neonates (25.9%) had identifiable maternal or intrapartum risk factors, with one (12.2%) presenting with two such factors. These included premature rupture of membranes (n = 10, 11.8%), intrapartum fever (n = 7, 8.2%), prolonged labor (n = 2, 2.4%), antepartum hemorrhage (n = 2, 2.4%), and meconium-stained amniotic fluid (n = 2, 2.4%).

Clinical manifestations and neurological signs

Clinical symptoms were generally nonspecific and atypical. The most common manifestation was abnormal body temperature. Fever was observed in 78 neonates (91.8%), of whom 38 (44.7%) had high fever/hyperpyrexia. Hypothermia was present in 20 neonates (23.5%), including 19 with mild hypothermia and 1 with moderate hypothermia. Both high fever/hyperpyrexia and hypothermia were recorded in 9 cases (10.6%). Only 5 neonates (5.9%) maintained body temperature within the normal range. Other common symptoms included poor feeding in 41 (48.2%), irritability in 20 (23.6%), lethargy in 15 (17.6%), seizures in 11 (12.9%), and jaundice in 11 (12.9%). Less frequent symptoms (<10% each) were vomiting, dyspnea, cyanosis, irregular respiration, gaze preference, ocular deviation, and stupor. Neurological signs were present in 25 neonates (29.4%), including bulging or tense fontanelle in 20 (23.5%), abnormal muscle tone (hypertonia or hypotonia) in 11 (12.9%), and nuchal rigidity in 3 (3.5%).

Microbiological findings

A total of 51 neonates were caused by Gram-positive organisms, including group B *Streptococcus* (GBS, n = 22, 25.9%), *Streptococcus pneumoniae* (n = 7, 8.2%), *Staphylococcus aureus* (n = 6, 7.1%), *Enterococcus* spp. (n = 4, 4.7%), and unspecified Gram-positive cocci (n = 12, 14.1%). The remaining 34 cases were caused by Gram-negative bacteria, including *Escherichia* *coli* (n = 20, 23.5%), *Enterobacter* spp. (n = 1, 1.2%), *Haemophilus influenzae* (n = 1, 1.2%), and unspecified Gram-negative rods (n = 12, 14.1%). The most frequently isolated pathogens were GBS and *E. coli*.

Cerebrospinal fluid (CSF) findings

Among the 85 neonates, 83 (97.6%) exhibited elevated CSF total leukocyte counts (>20/mm³). Neutrophil predominance (>70%) and elevated CSF protein levels (>1.0 g/L) were each observed in 80 cases (94.1%), while decreased CSF glucose concentrations (<2.2 mmol/L) were noted in 68 cases (80.0%).

Timing and administration of antibiotics

Among the 85 neonates, 13 received immediate intravenous administration of standard-dose antibiotics at their outpatient visit, all of which were cefotaxime, a third-generation cephalosporin with good blood-brain barrier (BBB) penetration. After hospital admission, all neonates underwent lumbar puncture as the first procedure, and empirical antimicrobial therapy (initial antimicrobial therapy) was initiated immediately after the CSF routine results became available (approximately 1 hour later). Antibiotic selection and dosing followed the neonatal bacterial meningitis guidelines: ampicillin (150-200 mg/kg/day) plus cefotaxime (100-200 mg/kg/day) in 73 cases, and vancomycin (30-45 mg/kg/day) plus cefotaxime (150-200 mg/kg/day) in 12 cases. Following the CSF culture or Gram-stained smear results, the antibiotic regimen was maintained if an adequate clinical response was achieved; in cases of an inadequate clinical response, treatment was adjusted according to the findings of the CSF Gram stain or culture.

Response to initial antimicrobial therapy and treatment duration

Among the 85 neonates, 54 (63.5%) exhibited an adequate clinical response to initial antimicrobial therapy, while the remaining 31 (36.5%) showed an inadequate response and subsequently underwent repeat lumbar puncture. Excluding the three fatal cases, the median duration of antibiotic therapy was 23 days (IQR: 18.5–33.5; range: 14–76 days), with 28 neonates (34.1%) receiving treatment for 30 days or more.

Acute neurologic complications

Complications during hospitalization occurred in 33 (38.8%) neonates, including subdural effusion, defined on MRI as CSF-like signal intensity without diffusion restriction (n = 11, 12.9), hydrocephalus (n = 11, 12.9), brain abscess (n = 9, 10.6%), symptomatic seizure-like episodes (n = 9, 10.6%), subdural empyema, defined on MRI as subdural collections with restricted diffusion on diffusion-weighted imaging (n = 8, 9.4%), unilateral hearing loss (n = 6, 7.1%), intracerebral hemorrhage (n = 4, 4.7%), and ventriculitis (n = 2, 2.4%).

Outcomes

Long-term neurological sequelae were identified based on clinical evaluation and GDDS assessment during follow-up. Excluding the three fatal cases, 28 of the 82 surviving neonates (34.1%) developed at least one neurological sequela, including hypertonia (n = 14, 17.1%), paresis (n = 7, 8.5%), unilateral hearing loss (n = 6, 7.3%), secondary epilepsy (n = 5, 6.1%), motor developmental delay (n = 1, 1.2%), and global developmental delay (n = 1, 1.2%). The remaining 54 neonates (65.9%) achieved complete recovery.

Factors associated with outcomes

Table I compares the clinical characteristics between neonates with good outcomes (n = 54) and those with poor outcomes (n = 31). In univariate analyses, several factors were significantly associated with poor outcomes, including the presence of neurological signs at admission ($p < 0.001$), elevated initial CSF protein levels ($p = 0.036$), lack of BBB-permeable antibiotic use before lumbar puncture (p = 0.019), inadequate response to initial antimicrobial therapy (p = 0.002), and the occurrence of acute neurological complications during hospitalization (p < 0.001). Receiver operating characteristic (ROC) analysis demonstrated that a CSF protein level > 3.08 g/L was the optimal cutoff value for discriminating poor outcomes, with a sensitivity of 41.9% and a specificity of 87.0%.

Table I. Comparison of clinical characteristics in neonates with bacterial meningitis based on different outcomes.

Variables	Neonates with good outcomes (n=54)	Neonates with poor outcomes (n=31)	P value
Sex, male	31 (57.4%)	15 (48.4%)	0.500
Age at onset (days)	6 (2.75–15)	10 (1–16)	0.851
Gestational age (weeks)	36.96±1.78	36.61±1.67	0.375
Weight on admission (g)	3.42±0.62	3.25±0.68	0.252
Positive maternal or labor factors	8 (15.4%)	8 (24.2%)	0.230
Maximum rectal temperature (°C)	38.89±0.556	39.01±0.74	0.369
High fever or hyperpyrexia	20 (37.0%)	18 (58.1%)	0.099
Hypothermia	12 (22.2%)	8 (25.8%)	0.913
Temperature instability	5 (9.26%)	4 (12.9%)	0.873
Duration of illness before admission (h)	12 (7.75–22.25)	12 (6–24)	0.562
Neurological signs positive	8 (14.8%)	17 (54.8%)	<0.001**
Peak blood parameters before antibiotic use			
TLC (10^6/mL)	16.41±7.08	18.38±10.94	0.315
Neutrophil (%)	0.674±0.167	0.664±0.199	0.810
CRP (mg/L)	51.09±47.37	69.44±52.26	0.102
PCT (ng/mL)	3.00±2.88	2.94±1.89	0.918
Initial blood pathogens			
Positive culture	34 (63%)	19 (61.3%)	0.878
Negative culture	20 (37%)	12 (38.7%)	
Initial CSF parameters			
CSF-TLC (cell/mL)	3323.43±5297.33	2976.35±4170.96	0.755
CSF-Neutrophil (%)	0.779±0.167	0.750±0.233	0.509
CSF glucose (mmol/L)	1.879±0.558	1.620±0.671	0.060
CSF protein (g/L)	2.047±1.525	2.852±1.912	0.036*
Initial CSF pathogens			
Positive culture	20 (74.1%)	19 (61.3%)	0.218
Gram-stained smear (Gram-positive)	32 (59.3%)	22 (71.0%)	0.280
Use of BBB-permeable antibiotics before LP	12 (22.2%)	1 (3.2%)	0.019*
Adequate response to initial antibiotic therapy	41 (75.9%)	13 (41.9%)	0.002*
Complications	10 (18.5%)	23 (74.1%)	<0.001**

Data presented as n (%), median (Q1-Q3) or mean ± standard deviation; BBB, blood-brain barrier; CRP, C-reactive protein; CSF, cerebrospinal fluid; Neutrophil (%), absolute neutrophil count/total leukocyte count ratio; PCT, Procalcitonin; TLC, total leukocyte count; *p<0.05; **p<0.01.

Table II. Multivariate logistic regression analysis to identify risk factors for poor outcomes in neonates with bacterial meningitis.

Variables	B	Standard error	Wald	Odds ratio	95% CI	P value
Neurological signs	1.990	0.649	8.211	7.315	1.875-28.535	0.004**
CSF protein (g/L) > 3.08	0.229	0.731	0.098	1.258	0.300-5.274	0.754
Use of BBB-permeable antibiotics before LP	-1.081	1.137	0.904	0.339	0.037-3.150	0.342
Adequate response to initial antibiotic therapy	-0.840	0.690	1.482	0.432	0.112-1.668	0.223
Complications	2.020	0.666	9.209	7.541	2.045-27.807	0.002**

BBB, blood-brain barrier; CI, confidence interval; CSF, cerebrospinal fluid; LP, lumbar puncture; *p<0.05; **p<0.01.

As shown in Table II, in the multivariable logistic regression analysis, only the presence of neurological signs at admission (OR: 7.315; 95% CI: 1.875–28.535) and the occurrence of acute neurological complications during hospitalization (OR: 7.541; 95% CI: 2.045–27.807) remained independently associated with poor outcomes.

Discussion

This retrospective cohort study provides a comprehensive overview of NBM, with particular emphasis on clinical presentation, etiological patterns, treatment response, and prognostic factors. Our findings highlight the persistent diagnostic and therapeutic challenges of NBM, largely attributable to its nonspecific early manifestations and the high risk of long-term neurological morbidity.

Consistent with previous reports, the majority of clinical manifestations in our cohort were nonspecific, with abnormal body temperature, poor feeding, and irritability being the most frequent presentations.[12,13] Classical neurological signs, including lethargy, focal seizures, vomiting, and abnormal muscle tone, were relatively infrequent but were closely associated with severe disease.[11,14] These observations underscore the diagnostic difficulty of NBM and emphasize the indispensable role of CSF analysis and microbiological testing for definitive diagnosis.[15] Clinicians should therefore maintain a high index of suspicion for NBM in neonates presenting with sepsis-like features, even in the absence of overt meningeal signs.[12,13]

The reported frequency of fever in NBM varies across studies, ranging from approximately 67.9%[12] to 84.1%.[16] In our cohort, the rate was higher (91.8%), which may reflect referral bias to tertiary centers and the relatively small sample size. Notably, hypothermia occurred in 17.6% of cases, and 8.2% of neonates experienced both hyperpyrexia and hypothermia during the course of illness, indicating that temperature instability is not uncommon in NBM, consistent with the findings of Haque et al.[17] Despite these abnormalities, a small proportion (5.9%) of neonates in our study maintained entirely normal body temperatures, reinforcing that the absence of fever does not exclude the diagnosis of NBM.

Regarding microbiological findings, GBS and *E. coli* were the leading pathogens, together accounting for nearly half of all cases. This distribution is consistent with epidemiological patterns reported in high-and middle-income regions, likely reflecting vertical transmission from maternal colonization.[18,19] The relatively high proportion of GBS meningitis suggests that gaps may exist in the implementation of maternal screening, risk stratification, and intrapartum antibiotic prophylaxis.[20]

Typical CSF abnormalities in NBM include neutrophilic pleocytosis (80–95%), elevated protein, and decreased glucose.[21,22] However, normal reference values for CSF vary with gestational and postnatal age, complicating both diagnosis and monitoring.[15,23] In our study, several culture-proven cases had normal CSF white cell counts, protein, or glucose levels, consistent with findings by Garges et al. and others, which demonstrate that meningitis cannot be excluded based on a single CSF parameter.[24-26] Despite these limitations, CSF culture, microscopy, and biochemical analysis remain the diagnostic gold standard, while next-generation sequencing may serve as a valuable adjunct in complex or culture-negative cases.[5,27,28]

Importantly, in multivariable logistic regression analysis, only the presence of neurological signs at admission and the occurrence of acute neurological complications during hospitalization remained independently associated with poor outcomes. Neurological abnormalities at presentation, although relatively infrequent, were strongly associated with adverse prognosis (OR: 7.315; 95% CI: 1.875–28.535), supporting previous reports that early central nervous system involvement reflects more severe disease and a higher risk of irreversible brain injury.[29,30]

Acute neurological complications during hospitalization, including subdural effusion, hydrocephalus, brain abscess, ventriculitis, intracranial hemorrhage, seizure-related events, and hearing impairment, were independently associated with poor outcomes (OR: 7.541; 95% CI: 2.045–27.807). Nearly all infants who developed long-term neurological sequelae experienced at least one acute neurological complication during the acute phase, emphasizing the critical importance of early neuroimaging, close neurological monitoring, and timely intervention to mitigate secondary brain injury.[31]

Several variables, including elevated CSF protein levels (>3.08 g/L),[32-34] early administration of BBB–permeable antibiotics,[35,36] and a favorable initial response to antimicrobial therapy, were associated with outcomes in univariate analyses[37] but did not retain statistical significance after multivariable adjustment. These findings are consistent with previous reports suggesting that such factors may reflect disease severity, timing of diagnosis, or early clinical course rather than serving as independent prognostic determinants.

Despite advances in antimicrobial therapy and neonatal intensive care, 34.1% of surviving infants in our cohort developed long-term neurological sequelae, a prevalence consistent with the 20-50% range reported in previous studies.[38] These sequelae included abnormalities in muscle tone, paresis, hearing impairment, epilepsy, and developmental delay, underscoring the necessity of structured neurodevelopmental follow-up, routine audiological screening, and early rehabilitative interventions for survivors of NBM.

Several limitations of this study should be acknowledged. First, the retrospective design may limit causal inference and generalizability, and the availability of clinical data depended on the completeness of medical records. In addition, data from the most recent three years were not available, which may have limited the representativeness of current clinical practices and treatment strategies. Second, neurodevelopmental outcomes were assessed using the GDDS, rather than more comprehensive neuropsychological assessment tools, which may have resulted in underestimation of subtle cognitive or behavioral impairments. Moreover, the duration of follow-up was limited to at least one year for term infants, and although preterm infants were followed for a longer period, some neurodevelopmental sequelae may manifest later in childhood and therefore could have been missed. Third, the relatively small sample size may have limited the statistical power to identify additional factors independently associated with poor outcomes. Finally, potential selection bias and information bias inherent to multicenter retrospective studies cannot be completely excluded, including referral bias to tertiary centers and variability in diagnostic and management practices across institutions.

Conclusions

In this multicenter retrospective study, neurological signs at admission and acute neurological complications during hospitalization were independently associated with poor outcomes in neonatal bacterial meningitis. Other factors, including elevated CSF protein levels, early administration of BBB-permeable antibiotics, and response to initial therapy, were associated with outcomes in univariate analyses but did not retain independent significance after multivariable adjustment. These findings underscore the importance of early neurological assessment, close monitoring for complications, and structured long-term follow-up in affected neonates.

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Ethical approval

This study was conducted in accordance with the International Conference on Good Clinical Practice Standards and the Declaration of Helsinki. All study protocols were approved by the Ethics Committee of The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University (date: 01.01.2021, number: 2021-K-167-02). The requirement for informed consent from study participants or their guardians was waived due to the de-identification of information in this retrospective study. Additionally, the study was registered with the Chinese Clinical Trial Registry (ChiCTR-INR-17012884).

Author contribution

The authors confirm contribution to the paper as follows: Study conception and design: SL, LF; data collection: YDD, SYP, XHH, LF; analysis and interpretation of results: SL, YDD, SYP, XHH; draft manuscript preparation: SL, LF. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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