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Clinical Characteristics, Antimicrobial Resistance, Risk Factors for Infection and Mortality in Neonatal Bloodstream Infection: A Retrospective Cohort Study

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Abstract

Objective

With continuous advances in modern medical care, neonatal survival rates have improved significantly. Bloodstream infection (BSI) is a common and severe infectious disease in neonates and a major cause of neonatal death and long-term neurological sequelae, including brain injury and developmental delay. This study aimed to analyze the clinical characteristics, antimicrobial resistance profiles, risk factors for infection, and mortality predictors of neonatal BSI, thereby providing evidence to reduce its incidence and case fatality rate.

Methods

Blood culture specimens from 227 neonates diagnosed with BSI hospitalized at Jiangxi Maternal and Child Health Hospital between January 2021 and December 2025 were collected, yielding 228 pathogenic isolates. Data on maternal pregnancy status and neonatal clinical characteristics were recorded. Pathogen distribution, antimicrobial susceptibility, risk factors for infection, and factors associated with clinical outcomes were analyzed.

Results

Among the 227 neonates with BSI, 77.5% (176/227) were preterm, and the mortality rate was 17.6% (40/227). Gram-negative bacteria were the predominant pathogens. The top five isolates were Klebsiella pneumoniae (30.7%), Escherichia coli (26.0%), Enterococcus faecalis (12.3%), Staphylococcus aureus (3.9%), and Enterococcus faecium (3.5%). Antimicrobial resistance analysis showed that the carbapenem resistance rates of K. pneumoniae were 17.1% for imipenem and 12.9% for ertapenem, while all E. coli isolates remained susceptible. All Enterobacterales isolates were susceptible to cefoperazone/sulbactam and amikacin. Multivariate analysis identified parenteral nutrition (OR = 3.890, 95%CI: 1.581–10.366, P = 0.004), severe thrombocytopenia (< 50×10^9/L) (OR = 3.666, 95%CI: 1.014–13.762, P = 0.048), and moderate-to-severe thrombocytopenia (50–100×10^9/L) (OR = 2.755, 95%CI: 1.071–7.148, P = 0.035) as independent risk factors for K. pneumoniae BSI. Regarding mortality, multivariate analysis showed that heart rate abnormality was an independent risk factor for death (OR = 2.341, 95%CI: 1.013–5.562, P = 0.049); hypoxemia was of marginal significance (OR = 4.043, 95%CI: 1.109–20.251, P = 0.053). Pathogen type (Gram-negative bacteria: OR = 1.438, P = 0.346; Gram-positive bacteria: OR = 0.765, P = 0.488) was not significantly associated with death.

Conclusion

In our region, Gram-negative bacteria predominate in neonatal BSI, and carbapenem resistance in K. pneumoniae is a serious concern. Parenteral nutrition and thrombocytopenia are independent risk factors for K. pneumoniae BSI. Heart rate abnormality is an independent predictor of neonatal death, whereas the pathogen type itself is not significantly associated with mortality. Clinical decisions should focus more on infection-induced organ dysfunction rather than the specific pathogen. Strict control of indications for parenteral nutrition and continuous monitoring of carbapenem-resistant organisms should be strengthened.

Introduction

Bloodstream infection (BSI) refers to a severe infectious disease caused by invasion of pathogenic microorganisms into the bloodstream, which may further progress to bacteremia, sepsis, septic shock, and multiple organ dysfunction, with a high case fatality rate[1,2]. Neonates, especially preterm and low birth weight infants, are at particularly high risk of BSI due to their immature immune system and incomplete skin and mucosal barrier function. Studies have shown that the incidence and mortality of BSI in neonates are significantly higher than in other age groups, making it one of the most severe types of healthcare-associated infection in neonatal intensive care units (NICUs)[3].

In recent years, advances in perinatal medical care and the widespread use of invasive procedures (e.g., endotracheal intubation, central venous catheterization, umbilical arterial/venous catheters) and broad-spectrum antibiotics have been associated with an increasing risk of neonatal BSI[4]. Meanwhile, antimicrobial resistance has become a growing concern, particularly the increasing detection rates of extended-spectrum β-lactamase (ESBL)-producing Enterobacterales and carbapenem-resistant Enterobacterales (CRE), which have led to higher failure rates of empirical antibiotic therapy and substantially increased treatment difficulty[5,6].

Currently, large-scale, multicenter, systematic epidemiological data on the pathogen spectrum and antimicrobial resistance profile of neonatal BSI in China remain limited. Due to regional differences in economic development, antibiotic use strategies, and infection control measures, the distribution and resistance characteristics of pathogens vary considerably across areas[7,8]. As a major province in central China, the current etiological status and resistance trends of neonatal BSI in Jiangxi Province have not been systematically reported.

Therefore, this retrospective study analyzed the clinical data of neonates with blood culture-confirmed BSI at Jiangxi Maternal and Child Health Hospital from January 2021 to December 2025. We systematically described the pathogen composition, antimicrobial resistance profiles of major Gram-negative bacilli and Gram-positive cocci, and risk factors for infection and mortality, aiming to provide evidence-based support for the development of preventive strategies, optimization of empirical antibiotic therapy, and rational antimicrobial use for neonatal BSI in this region, ultimately reducing its incidence and mortality.

Materials and Methods

Study Design and Patient Enrollment

This retrospective cohort study included neonates admitted to the NICU, Department of Neonatology, or Department of Obstetrics at Jiangxi Maternal and Child Health Hospital between January 2021 and December 2025 who were diagnosed with BSI. Inclusion criteria were: age at admission ≤ 28 days, at least one positive blood culture during hospitalization, fulfillment of BSI diagnostic criteria[6], and availability of complete clinical and laboratory data. Exclusion criteria included incomplete or missing medical records, blood culture positivity considered to represent contamination or colonization, and all cases of recurrent infection. Infants were classified into survival and death groups based on prognosis.

Clinical Data Collection

Clinical data of the neonates were retrospectively collected from the electronic medical record system. Documented information included maternal perinatal status (fetal distress, premature rupture of membranes, oligohydramnios), neonatal general characteristics (sex, gestational age, birth weight, cesarean section delivery, preterm status), infection-related characteristics (age at infection < 7 days or ≥ 7 days, presence of concomitant abdominal infection, central nervous system infection, or respiratory infection, and pathogen species). Clinical manifestations (abdominal distension, tachypnea, cyanosis, decreased oxygen saturation, pallor, heart rate abnormality), laboratory parameters (C-reactive protein, platelet count, jaundice, anemia), and invasive procedures or treatments (indwelling central venous catheter, total parenteral nutrition, other indwelling devices/non-autologous materials, postnatal surgery, use of invasive devices such as ventilators or ECMO, blood product transfusion) were also recorded. Observed complications included purulent meningitis (corresponding to central nervous system infection), necrotizing enterocolitis (corresponding to enteritis), intraventricular hemorrhage (corresponding to subependymal hemorrhage), septic shock, and capillary leak syndrome. In addition, comorbidities such as patent ductus arteriosus, respiratory failure, and pneumonia were documented. Clinical outcomes were categorized as follows: patients who were cured or improved at discharge according to medical records were classified as survivors, while the death group comprised in-hospital deaths with BSI as the primary cause of death, as well as infants who were discharged after aggressive treatment and resuscitation failed to maintain vital signs and were confirmed to have died within one week of discharge during follow-up.

Microbiological Methods

Blood samples were collected from infants with signs of infection before antibiotic administration. Isolate identification and antimicrobial susceptibility testing were performed using the fully automated microbial mass spectrometry system AUTOFMS1000 (Autobio, Zhengzhou, China) and the VITEK-2 fully automated bacterial identification and susceptibility system (bioMérieux Inc., France), following standard

operating procedures for bacterial isolation. Quality control strains included E. coli ATCC 25922 and ATCC 35218, S. aureus ATCC 29213, ATCC BAA-1026, ATCC BAA-976, and ATCC BAA-977, Pseudomonas aeruginosa ATCC 27853, E. faecalis ATCC 51299, and Streptococcus pneumoniae ATCC 49619 (provided by the National Clinical Laboratory Center, Beijing, China). Testing protocols were customized according to the antibiotic classes used, and all susceptibility results were interpreted according to the breakpoints recommended by the Clinical and Laboratory Standards Institute[9].

Statistical Analysis

Data analysis was performed using R software (version 4.4.1). Normally distributed demographic and descriptive continuous variables were presented as mean (standard deviation, SD); non-normally distributed data were presented as median (interquartile range, IQR). Categorical variables were expressed as percentages. Comparisons between categorical variables were performed using the chi-square test; comparisons of medians or means between two groups were performed using the Mann-Whitney U test or Student's t-test, depending on data distribution. A P-value ≤ 0.05 was considered statistically significant. Risk factors were identified by univariate logistic regression analysis, and all statistically significant variables were entered into multivariate models to explore independent risk factors.

Results

Patient Characteristics

Between January 1, 2021, and December 31, 2025, bacterial growth was detected in 228 culture samples obtained from 227 patients. After culture and identification, duplicate strains were excluded, yielding 228 pathogenic isolates. Among the neonates, 130 (57.3%) were male and 97 (42.7%) were female. According to the definition of preterm birth, 176 (77.5%) were preterm and 51 (22.5%) were full-term. Ninety-two neonates (40.5%) were aged < 7 days at infection, and this proportion was significantly lower in the preterm group than in the full-term group (30.7% vs. 74.5%, P < 0.001). A total of 134 (59.0%) were delivered by cesarean section. Mean gestational age was 32.2 ± 4.7 weeks (range: 22.1–41.6 weeks), and mean birth weight was 1777.6 ± 954.7 g (range: 450–4100 g). Additionally, there were 32 cases (14.1%) of fetal distress, 82 (36.1%) of premature rupture of membranes, and 55 (24.2%) of oligohydramnios. Most neonates had at least one underlying condition, including jaundice (134, 59.0%), anemia (150, 66.1%), patent ductus arteriosus (60, 26.4%), respiratory failure (155, 68.3%), pneumonia (100, 44.1%), enteritis (51, 22.5%), and intraventricular hemorrhage (53, 23.3%). The primary infection foci were the respiratory system (110, 48.5%), central nervous system (56, 24.7%), and abdomen (45, 19.8%). The most common invasive procedures and medical devices were indwelling central venous catheter (143, 63.0%) and parenteral nutrition (145, 63.9%). Of the 227 neonates, 187 survived, yielding a BSI-attributable mortality rate of 17.6% (Table 1).

Table 1
Characteristics of Neonatal in 227 BSI Episodes, 2021–2025

Characteristics	N(%)
Total	227(100)
Gender	
Male	130(57.3)
Female	97(42.7)
Age	
≤37 w	176(77.5)
>37 w	51(22.5)
Age at infection	
≤ 7 d	92(40.5)
> 7 d	135(59.5)
Cesarean section	134(59.0)
Gestational Age	
≥37 w	52(22.9)
34–37 w	19(8.3)
32–34 w	30(13.2)
28–32 w	85(37.4)
<28 w	41(18.1)
Body Weight	
≥2.5 Kg	49(21.6)
1.5–2.5¯Kg	54(23.8)
<1.5 Kg	124(54.6)
Complications of pregnancy	
Fetal distress	32(14.1)
Premature rupture of membrane	82(36.1)
Oligohydramnios	55(24.2)
Underlying diseases	

Characteristics	N(%)
Jaundice	134(59.0)
Anemia	150(66.1)
Patent Ductus Arteriosus	60(26.4)
Respiratory failure	155(68.3)
Pneumonia	100(44.1)
Enteritis	51(22.5)
Neonatal subependymal hemorrhage	53(23.3)
Types of infectious foci	
Respiratory tract infection	110(48.5)
Central nervous system infection	56(24.7)
Intra-abdominal infection	45(19.8)
Urinary tract infection	4(1.7)
Other infections	3(1.3)
Healthcare-associated factors	
Indwelling CVC	143(63.0)
Other indwelling device/non-native material	148(65.2)
Receiving TPN	145(63.9)
Postnatal surgical intervention	14(6.2)
Using Ventilator or ECMO device	153(67.4)
Blood tranfusion	139(61.2)
Survival	187(82.4)

Bloodstream Infection Pathogens and Antimicrobial Resistance

A total of 228 culture samples were analyzed, including one polymicrobial infection and 227 monomicrobial infections. The most frequently isolated BSI pathogens were K. pneumoniae (30.7%), E. coli (26.0%), E. faecalis (12.3%), S. aureus (3.9%), E. faecium (3.5%), and S. agalactiae (3.1%). The distribution of all pathogens detected in blood cultures is presented in Supplementary Table 1.

The antimicrobial resistance patterns of common Gram-negative bacilli are shown in Table 2. Both K. pneumoniae and E. coli exhibited high resistance rates to ampicillin (94.3% and 93.2%, respectively). K.

pneumoniae showed higher resistance rates to cefazolin (84.3%) and cefuroxime (84.3%) compared with E. coli (74.6% and 55.9%, respectively). Carbapenem resistance was observed only in K. pneumoniae (imipenem: 17.1%, ertapenem: 12.9%), whereas all E. coli isolates were fully susceptible. Similarly, no E. coli isolates were resistant to piperacillin/tazobactam or cefoperazone/sulbactam, whereas K. pneumoniae showed a resistance rate of 25.7% to piperacillin/tazobactam. E. coli exhibited higher resistance rates to levofloxacin (42.4% vs. 11.4%) and ciprofloxacin (52.5% vs. 45.7%) than K. pneumoniae. Notably, all E. coli isolates were susceptible to nitrofurantoin (0% resistance), whereas the resistance rate of K. pneumoniae to nitrofurantoin was as high as 65.7%. Furthermore, both species were fully susceptible (0% resistance) to cefoperazone/sulbactam and amikacin.

Table 2
Antimicrobial resistance patterns of major Gram-negative bacilli

Predominant Gram-negative bacilli (n: 129)	***K. Pneumoniae* (n: 70)**	***E. Coli* (n: 59)**
Ampicillin	66 (94.3)	55 (93.2)
Cefazolin	59 (84.3)	44 (74.6)
Cefuroxime	59 (84.3)	33 (55.9)
Ampicillin/Sulbactam	54 (77.1)	34 (57.6)
Trimethoprim/Sulfamethoxazole	54 (77.1)	23 (39)
Ceftriaxone	52 (74.3)	42 (71.2)
Nitrofurantoin	46 (65.7)	0
Ceftazidime	44 (62.9)	12 (20.3)
Aztreonam	36 (51.4)	19 (32.2)
Ciprofloxacin	32 (45.7)	31 (52.5)
Cefepime	31 (44.3)	6 (10.2)
Amoxicillin/Clavulanate	22 (31.4)	14 (23.7)
Piperacillin/Tazobactam	18 (25.7)	0
Imipenem	12 (17.1)	0
Ertapenem	9 (12.9)	0
Gentamicin	8 (11.4)	13 (22)
Levofloxacin	8 (11.4)	25 (42.4)
Cefotetan	4 (5.7)	0
Tobramycin	1 (1.4)	3 (5.1)
Cefoperazone/Sulbactam	0	0
Amikacin	0	0

The resistance patterns of common Gram-positive cocci are shown in Table 3. All isolates were fully susceptible to vancomycin, tigecycline, and nitrofurantoin (0% resistance). E. faecalis showed resistance rates of 32.1% to erythromycin, tetracycline, quinupristin/dalfopristin, and gentamicin, and was fully susceptible to penicillin G and ampicillin. E. faecium exhibited the highest resistance rate to erythromycin (75.0%), and also showed considerable resistance to penicillin G (62.5%) and ampicillin (50.0%). S. aureus was susceptible to all tested antibiotics except for erythromycin, tetracycline,

ciprofloxacin, and levofloxacin, for which the resistance rate was 11.1%. S. agalactiae demonstrated high resistance rates to erythromycin (85.7%) and tetracycline (57.1%), but was fully susceptible to penicillin G and ampicillin.

Table 3
Antimicrobial resistance patterns of major Gram-positive cocci

Common Gram-positive cocci (n: 52)	***E. Faecalis*(n: 28)**	***S. aureus*(n: 9)**	***E. Faecium*(n: 8)**	***S. Agalactiae*(n: 7)**
Erythromycin	9 (32.1)	1 (11.1)	6 (75)	6 (85.7)
Tetracycline	9 (32.1)	1 (11.1)	0	4 (57.1)
Quinupristin/Dalfopristin	9 (32.1)	1 (11.1)	0	0
Gentamicin	8 (28.6)	0	0	NA
Streptomycin	4 (14.3)	NA	0	NA
Ciprofloxacin	2 (7.1)	1 (11.1)	3 (37.5)	NA
Levofloxacin	2 (7.1)	1 (11.1)	3 (37.5)	1 (14.3)
Linezolid	2 (7.1)	0	0	0
Penicillin G	0	6 (66.7)	5 (62.5)	0
Ampicillin	0	NA	4 (50)	0
Nitrofurantoin	0	0	0	0
Vancomycin	0	0	0	0
Tigecycline	0	0	0	0

Risk Factors for Common BSI Pathogens

To identify risk factors associated with common BSI pathogens in neonates, a case-control study was performed. Univariate analysis revealed that parenteral nutrition, thrombocytopenia (severe, moderate-to-severe, and mild-to-moderate), preterm birth, age < 7 days, and low birth weight were significantly associated with K. pneumoniae BSI (Table 4). Multivariate analysis identified parenteral nutrition (OR: 3.890, 95% CI: 1.581–10.366, P = 0.004), severe thrombocytopenia (< 50×10⁹/L) (OR: 3.666, 95% CI: 1.014–13.762, P = 0.048), and moderate-to-severe thrombocytopenia (50–100×10⁹/L) (OR: 2.755, 95% CI: 1.071–7.148, P = 0.035) as independent risk factors for K. pneumoniae BSI.

Table 4
Risk factor analysis for Klebsiella pneumoniae bloodstream infection

Variable	Univariate OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Parenteral nutrition	4.940 (2.447–10.891)	< 0.001	3.890 (1.581–10.366)	**0.004**
Severe thrombocytopenia (< 50×10⁹/L)	3.412 (1.098–10.635)	0.031	3.666 (1.014–13.762)	**0.048**
Moderate-to-severe thrombocytopenia (50–100×10⁹/L)	2.957 (1.271–6.843)	0.011	2.755 (1.071–7.148)	**0.035**
Mild-to-moderate thrombocytopenia (100–150×10⁹/L)	2.559 (1.172–5.529)	0.017	2.214 (0.930–5.259)	0.07
Patent ductus arteriosus	0.548 (0.266–1.072)	0.089	0.441 (0.194–0.950)	0.91
Age < 7 days	0.401 (0.211–0.735)	0.004	0.444 (0.186–1.007)	0.057
Preterm birth	5.257 (2.164–15.751)	< 0.001	3.633 (0.818–18.183)	0.098
Low birth weight (1500-2500g)	8.171 (3.010-26.428)	< 0.001	1.762 (0.347–8.739)	0.484
Very low birth weight (< 1500g)	3.888 (1.546–11.902)	0.008	0.333 (0.059–1.767)	0.195

For E. faecalis BSI, univariate analysis showed significant associations with abdominal distension (OR: 2.557, 95% CI: 1.130–6.192, P = 0.029), tachypnea (OR: 10.055, 95% CI: 2.061–181.539, P = 0.025), hypoxemia (OR: 3.798, 95% CI: 1.495–11.667, P = 0.009), preterm birth (OR: 9.060, 95% CI: 1.854–163.676, P = 0.033), age < 7 days (OR: 0.148, 95% CI: 0.035–0.440, P = 0.002), patent ductus arteriosus (OR: 3.476, 95% CI: 1.282–12.174, P = 0.026), pneumonia (OR: 7.054, 95% CI: 2.026–44.593, P = 0.009), parenteral nutrition (OR: 19.319, 95% CI: 3.990–348.029, P = 0.004), use of other devices (OR: 3.868, 95% CI: 1.428–13.536, P = 0.016), postoperative status (OR: 2.723, 95% CI: 1.069–8.380, P = 0.052), and very low birth weight (OR: 12.121, 95% CI: 2.453–219.698, P = 0.016) (Table 5). However, none of these variables remained statistically significant in multivariate analysis (all P > 0.05), likely due to the small sample size (only 28 cases in the E. faecalis group). The multivariate OR for parenteral nutrition was 6.148 (95% CI: 0.620–171.845, P = 0.180).

Table 5
Risk factor analysis for Enterococcus faecalis bloodstream infection

Variable	Univariate OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Parenteral nutrition	19.319 (3.990-348.029)	0.004	6.148 (0.620-171.845)	0.18
Very low birth weight (< 1500g)	12.121 (2.453-219.698)	0.016	0.516 (0.016–31.891)	0.726
Hypoxemia	3.798 (1.495–11.667)	0.009	1.799 (0.606–6.456)	0.321
Patent ductus arteriosus	3.476 (1.282–12.174)	0.026	0.903 (0.253–3.819)	0.88
Pneumonia	7.054 (2.026–44.593)	0.009	2.530 (0.488–25.553)	0.335
Abdominal distension	2.557 (1.130–6.192)	0.029	1.216 (0.480–3.234)	0.684
Tachypnea	10.055 (2.061-181.539)	0.025	1.187 (0.065–45.784)	0.915
Other medical devices	3.868 (1.428–13.536)	0.016	1.295 (0.390–5.229)	0.69
Age < 7 days	0.148 (0.035–0.440)	0.002	0.358 (0.073–1.273)	0.147
Postoperative status	2.723 (1.069–8.380)	0.052	1.671 (0.581–5.616)	0.367
Preterm birth	9.060 (1.854-163.676)	0.033	0.695 (0.049–22.858)	0.805

Risk Factors for Mortality in Neonatal BSI

The mortality and survival rates among neonates with BSI were 17.6% (40/227) and 82.4% (187/227), respectively. A retrospective cohort analysis was performed to identify risk factors for death. Univariate logistic regression showed that the following factors were significantly associated with neonatal death: tachypnea (OR: 7.515, 95% CI: 2.193–47.211, P = 0.007), cyanosis (OR: 3.523, 95% CI: 1.679–7.968, P = 0.001), hypoxemia (OR: 11.944, 95% CI: 4.131–50.679, P < 0.001), pallor (OR: 3.113, 95% CI: 1.545–6.324, P = 0.001), heart rate abnormality (OR: 4.826, 95% CI: 2.378–10.105, P < 0.001), preterm birth (OR: 4.259, 95% CI: 1.452–18.199, P = 0.020), anemia (OR: 2.821, 95% CI: 1.248–7.254, P = 0.019), patent ductus arteriosus (OR: 2.825, 95% CI: 1.378–5.759, P = 0.004), intraventricular hemorrhage (OR: 3.553, 95% CI: 1.715–7.341, P < 0.001), respiratory failure (OR: 7.212, 95% CI: 2.486–30.651, P = 0.001), enteritis (OR: 2.183, 95% CI: 1.020–4.548, P = 0.039), central venous catheter (OR: 2.739, 95% CI: 1.250–6.678, P = 0.017), invasive ventilation (OR: 11.896, 95% CI: 3.496–74.506, P < 0.001), blood product transfusion (OR: 7.183, 95% CI: 2.738–24.723, P < 0.001), extremely low birth weight (< 1000 g) (OR: 17.370, 95% CI: 4.481–115.590, P < 0.001), and very low birth weight (1000–1500 g) (OR: 4.700, 95% CI: 1.238–30.814, P = 0.047) (Table 6). Pathogen type analysis showed that neither Gram-negative (OR: 1.438, 95% CI:

0.691–3.177, P = 0.346) nor Gram-positive (OR: 0.765, 95% CI: 0.346–1.594, P = 0.488) infection was significantly associated with death; there were only 4 cases of fungal infection with no deaths. Multivariate logistic regression revealed that after adjustment for other confounders, heart rate abnormality remained an independent risk factor for death (OR: 2.341, 95% CI: 1.013–5.562, P = 0.049), while hypoxemia showed marginal significance (OR: 4.043, 95% CI: 1.109–20.251, P = 0.053). Invasive ventilation, blood product transfusion, intraventricular hemorrhage, respiratory failure, cyanosis, and low birth weight were not statistically significant in multivariate analysis (all P > 0.05).

Table 6
Risk factors for mortality in neonatal bloodstream infection

Variable	**Univariate OR (95% CI)**	***P*-value**	**Multivariate OR (95% CI)**	***P*-value**
Heart rate abnormality	4.826 (2.378–10.105)	< 0.001	2.341 (1.013–5.562)	0.049
Hypoxemia	11.944 (4.131–50.679)	< 0.001	4.043 (1.109–20.251)	0.053
Invasive ventilation	11.896 (3.496–74.506)	< 0.001	3.260 (0.758–23.048)	0.156
Blood products	7.183 (2.738–24.723)	< 0.001	2.333 (0.654–10.169)	0.217
Intraventricular hemorrhage	3.553 (1.715–7.341)	< 0.001	1.803 (0.769–4.169)	0.169
Respiratory failure	7.212 (2.486–30.651)	0.001	1.612 (0.359–10.229)	0.567
Cyanosis	3.523 (1.679–7.968)	0.001	1.297 (0.521–3.355)	0.581
Extremely low birth weight (< 1000g)	17.370 (4.481–115.590)	< 0.001	0.882 (0.091–9.869)	0.914
Very low birth weight (1000-1500g)	4.700 (1.238–30.814)	0.047	0.320 (0.036–3.255)	0.304

Discussion

This study systematically analyzed the clinical characteristics, pathogen distribution, antimicrobial resistance profiles, risk factors for infection, and mortality predictors in 227 neonates with BSI at Jiangxi Maternal and Child Health Hospital from 2021 to 2025. The main findings include: (1) K. pneumoniae (30.7%) and E. coli (26.0%) were the predominant pathogens, with Gram-negative bacteria predominating; (2) carbapenem resistance was observed only in K. pneumoniae (imipenem 17.1%, ertapenem 12.9%), whereas all E. coli isolates remained fully susceptible; (3) parenteral nutrition and thrombocytopenia were independent risk factors for K. pneumoniae BSI; and (4) heart rate abnormality

was an independent predictor of mortality (OR = 2.341, P = 0.049), while the pathogen type itself was not significantly associated with death. These findings provide important evidence-based support for optimizing preventive strategies and clinical management of neonatal BSI in our region.

Our study found that Gram-negative bacteria dominated the pathogen spectrum of neonatal BSI, with K. pneumoniae (30.7%) and E. coli (26.0%) being the most frequently isolated organisms. This finding is highly consistent with global epidemiological trends in neonatal BSI. A multicenter study of pediatric BSI in China by Xu et al. (2016–2022), which included nearly 40,000 bloodstream isolates, confirmed that E. coli and K. pneumoniae were the most common Gram-negative pathogens in the neonatal group, and reported a carbapenem-resistant K. pneumoniae (CRKP) detection rate of 31.4% in neonates, significantly higher than the 24.7% observed in older children[10]. Compared with the CRKP resistance rate in our study (17.1%), this indicates substantial regional differences in resistance levels.

Nguyen et al. from Vietnam also demonstrated a shift toward Gram-negative predominance in neonatal sepsis in Southeast Asia, closely related to local antibiotic use patterns and transmission of resistant bacteria[11]. Ferreira et al., in a 7.5-year observational study in a Brazilian NICU, reported that previous use of carbapenems was a significant risk factor for Gram-negative BSI (OR = 514.4, P < 0.01)[12]. This finding echoes the considerable carbapenem resistance rate observed in K. pneumoniae in our study (17.1%), suggesting that antibiotic selective pressure plays a critical role in the emergence and spread of resistant strains.

In our study, the isolation rate of E. faecalis (12.3%) was significantly higher than that of E. faecium (3.5%), whereas the detection rates of S. aureus (3.9%) and S. agalactiae (3.1%) were relatively low. A single-center study from Taiwan, China, including 109 pediatric enterococcal bacteremia cases between 2009 and 2019, with a substantial proportion of neonates, similarly indicated that E. faecalis was more common in neonates, consistent with our observation [13]. Okike et al. reported that neonatal enterococcal bacteremia was associated with high rates of complications and mortality, especially when complicated by meningitis (OR = 3.2, P = 0.04) [14]. Notably, only four cases of fungal infection (1.8%) were detected in our study, with no deaths. This proportion is lower than the 8.3% detection rate of Candida species reported in the NeoSEAP multicenter study from Southeast Asia, which also noted concerning resistance rates[11]. The low detection rate of fungal infections in our study may be related to regional antifungal prophylaxis strategies, NICU environmental factors, or the sensitivity of culture techniques.

The resistance analysis revealed highly concerning findings. K. pneumoniae has developed resistance to carbapenems (imipenem 17.1%, ertapenem 12.9%). A retrospective study of pediatric CRKP bacteremia showed that the 30-day mortality rate in neonates with CRKP bacteremia was as high as 39.4%, and an elevated Pitt bacteremia score was an independent risk factor for death (HR = 1.694, 95% CI: 1.313–2.186, P < 0.001)[15]. That study also found that in non-neonatal populations, higher platelet count (HR = 0.990), carbapenem use (HR = 0.212), and appropriate targeted antibiotic therapy (HR = 0.327) were associated with reduced mortality [15]. These findings corroborate our results showing thrombocytopenia

as a risk factor for infection and heart rate abnormality as a predictor of death. Ferreira et al. similarly pointed out that prior carbapenem use was a significant risk factor for Gram-negative BSI (OR = 514.4, P < 0.01), and prior use of fourth-generation cephalosporins was also significant (OR = 66, P < 0.01)[12]. Infection was significantly associated with prolonged hospital stay (10–39 days) and increased mortality (10%–29.9%), indicating that antibiotic selective pressure not only increases the detection rate of resistant strains but also directly affects clinical outcomes[12]. The NeoSEAP study revealed even more alarming resistance patterns: non-susceptibility to third-generation cephalosporins was 86.7% for K. pneumoniae and 46.4% for E. coli, while non-susceptibility to carbapenems was 17.1% and 15.4%, respectively[11]. These data suggest that WHO-recommended empirical antibiotic regimens have severely inadequate coverage in Southeast Asia. Studies on resistance in Enterobacterales have shown that the detection rate of ESBL-producing Enterobacterales in neonatal BSI continues to rise, posing a global public health threat[16]. Carbapenems are often used as the last therapeutic option for infections caused by ESBL-producing strains, but the emergence of carbapenem-resistant strains has left very limited treatment options[16]. The high resistance rate of K. pneumoniae to cephalosporins (84.3%) in our study suggests that ESBL-producing strains likely account for a considerable proportion.

Our results demonstrated that severe (< 50×10⁹/L) and moderate-to-severe (50–100×10⁹/L) thrombocytopenia are independent risk factors for K. pneumoniae BSI. Studies on neonatal thrombocytopenia have shown that necrotizing enterocolitis (OR = 2.25), early-onset sepsis (OR = 4.8), and late-onset sepsis (OR = 6.567) are major determinants of thrombocytopenia in neonates[17]. That study also found that severe intraventricular hemorrhage (OR = 4), pulmonary hemorrhage (OR = 20.9), and cardiovascular instability (OR = 5.76) were major predictors of death in infants with thrombocytopenia[17]. Studies on pediatric CRKP bacteremia similarly found that higher platelet count was associated with reduced 30-day mortality in non-neonatal populations (HR = 0.990, P = 0.010), and a monocyte count < 0.1×10⁹/L was a risk factor for septic shock (OR = 3.615)[15]. These findings indicate that platelet count is not only a marker of infection but also an important predictor of prognosis. A retrospective cohort study of neonatal thrombocytopenia also confirmed that severe sepsis (especially due to Gram-negative bacteria), pulmonary hemorrhage, and necrotizing enterocolitis are the leading causes of thrombocytopenia in neonates requiring transfusion[18]. That study also found that the incidence of thrombocytopenia was as high as 29.1% in the very low birth weight group and 27.7% in the preterm < 32 weeks group, emphasizing the important role of low birth weight and prematurity in the development of thrombocytopenia[18].

Our finding that parenteral nutrition is an independent risk factor for K. pneumoniae BSI (OR = 3.890, P = 0.004) has important clinical implications. A four-year surveillance study in a Turkish NICU showed that the use of parenteral nutrition was a significant risk factor for healthcare-associated infections (HAIs) (P < 0.001)[19]. In that study, BSI accounted for 53% of HAIs, the central line-associated BSI rate was 5.45/1000 catheter-days, and the most frequently isolated pathogens were Gram-positive bacteria (79.8%), followed by Gram-negative bacteria (17.8%) and Candida species (2.4%)[19]. Studies on the risks

of parenteral nutrition in neonates have indicated that parenteral nutrition is an independent risk factor for HAIs, catheter-related BSI, and clinical sepsis[20]. Many studies have confirmed that parenteral nutrition is associated with an increased risk of catheter-related infections, emphasizing the need to minimize its use and shorten its duration. The mechanisms by which parenteral nutrition increases infection risk may involve impaired intestinal barrier function leading to bacterial translocation, central line-associated infections, and potential suppression of immune function by nutritional components. Yang et al. reported that parenteral nutrition impairs host defense through multiple mechanisms, including inhibition of neutrophil function and alteration of gut microbiota composition[21].

Our study identified heart rate abnormality as an independent risk factor for neonatal death (OR = 2.341, P = 0.049), and hypoxemia showed marginal significance (OR = 4.043, P = 0.053). A South African multicenter study provided important comparative data[22]. That study included 907 neonatal BSI cases and found that the risk of death from Gram-negative BSI was 3.70 times that of Gram-positive BSI (95% CI: 1.46–9.39, P = 0.0059); the risk of death from late-onset sepsis was 2.42 times that of early-onset sepsis, and preterm infants had a 5.00-fold increased risk of death. The overall in-hospital mortality was 4.6%, while the crude mortality among neonates with confirmed BSI was 25.5%[22]. Notably, most neonatal deaths occurred in lower-tier hospitals, underscoring the urgency of strengthening infection prevention and control and resource allocation across all levels of healthcare facilities. Of interest, Gram-negative bacteria accounted for 63.2% of isolates in the South African study (K. pneumoniae 25.7%, Acinetobacter baumannii 19.2%), with extremely high resistance rates to multiple antibiotics (carbapenem resistance > 80% in A. baumannii). These findings are consistent with the Gram-negative predominance observed in our study; however, the South African study found a significant positive association between Gram-negative bacteria and mortality, whereas our study did not. This discrepancy may reflect regional differences in antibiotic treatment protocols, resistance patterns, and levels of NICU supportive care[22].

Studies on heart rate monitoring in neonatal sepsis have indicated that continuous heart rate monitoring combined with advanced analytical methods such as machine learning can enable early detection of sepsis[23]. These studies emphasize that subtle changes in heart rate variability may precede clinical signs, providing opportunities for early intervention. High-resolution continuous monitoring combined with advanced data analytics offers new approaches for improving outcomes in neonatal sepsis[23]. Studies on pediatric CRKP bacteremia provide complementary evidence: in neonates, a higher Pitt bacteremia score (reflecting illness severity) is an independent risk factor for 30-day mortality (HR = 1.694, P < 0.001)[15]. Collectively, these findings consistently indicate that disease severity (manifested as heart rate abnormalities, hypotension, altered mental status, etc.) and organ dysfunction are more important predictors of death than the specific pathogen type.

In our study, pathogen type (Gram-negative: OR = 1.438, P = 0.346; Gram-positive: OR = 0.765, P = 0.488) was not significantly associated with death. This negative finding contrasts with the South African study, which reported a significantly increased risk of death from Gram-negative infections[22]. Several possible

explanations may account for this discrepancy. First, differences in study populations: the South African study was conducted in lower-tier hospitals with potentially limited medical resources, intensive care capabilities, and antibiotic accessibility, leading to delayed or ineffective treatment for Gram-negative infections, whereas our study was performed at a tertiary hospital with a higher level of NICU supportive care. Second, differences in antibiotic availability and timeliness: the South African study had a higher proportion of multidrug-resistant organisms (carbapenem resistance > 80% in A. baumannii), while the CRKP resistance rate in our study (17.1%) was relatively lower. Third, differences in death definition and follow-up duration. The negative finding itself is of clinical importance: even in a setting where Gram-negative bacteria predominate and CRKP is present, timely antibiotic therapy and comprehensive organ support may render the pathogen type itself no longer an independent determinant of death. This highlights the critical role of comprehensive organ support in improving outcomes in the tertiary hospital NICU setting.

Demirbuğa et al. systematically evaluated risk factors for HAIs in the NICU and found that preterm birth ($P = 0.010$), birth weight ($P < 0.001$), mode of delivery ($P = 0.010$), length of hospital stay ($P = 0.004$), mechanical ventilation ($P = 0.009$), surgery ($P = 0.031$), parenteral nutrition ($P < 0.001$), and central venous catheter use ($P < 0.001$) were all significantly associated with HAIs[19]. Our finding that parenteral nutrition is an independent risk factor is consistent with these results. Based on pathogen spectrum and resistance data, Demirbuğa et al. recommended that NICUs develop empirical antibiotic regimens based on local epidemiology: for regions where Gram-negative bacteria predominate, empirical antibiotic choices covering Enterobacterales should be considered; for areas with a high prevalence of CRKP, novel β-lactamase inhibitor combinations might be considered[19]. A systematic review of the global burden of neonatal sepsis indicated that the incidence and mortality of neonatal sepsis remain high in low- and middle-income countries, and strengthening infection prevention and antimicrobial stewardship is key to improving outcomes[24]. The WHO global report on sepsis also emphasizes that establishing local pathogen surveillance systems and resistance databases is essential for guiding clinical treatment[25].

Limitations

This study has several limitations. First, as a single-center retrospective study, it is subject to potential selection and information biases, and the generalizability of the findings requires caution. Second, the sample sizes of the E. faecalis group ($n = 28$) and the fungal group ($n = 4$) were small, limiting the ability to detect statistically significant differences. Third, with only 40 deaths, the number of variables included in the multivariate models was limited (event-per-variable ratio approximately 4.4); although we controlled for this by selecting variables with the smallest P-values, model stability may still be affected. Fourth, vital sign data were collected retrospectively, and fine-grained indicators such as heart rate variability could not be continuously monitored.

Conclusions

This study found that parenteral nutrition and thrombocytopenia are independent risk factors for K. pneumoniae bloodstream infection, and that heart rate abnormality is an independent predictor of death in neonates with BSI, whereas the pathogen type itself is not significantly associated with mortality. In the NICU setting, clinical decisions should focus more on infection-induced organ dysfunction, particularly abnormalities in heart rate and oxygen saturation, rather than the specific pathogen, and should emphasize comprehensive supportive care and continuous vital sign monitoring in high-risk infants[26,27]. Future multicenter prospective studies integrating clinical, microbiological, and vital sign data are needed to develop predictive models for neonatal mortality. Bedside physiological indicators such as heart rate variability and oxygen saturation patterns hold promise for combination with laboratory parameters including platelet count and C-reactive protein to improve the accuracy of early warning and prognosis assessment. In addition, continuous surveillance of carbapenem-resistant K. pneumoniae and infection control strategies should be urgently strengthened[28].

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee (Medical Ethics Committee of Jiangxi Maternal and Child Health Hospital) with approval No. EC-KYZZ-20260412 and as our research was retrospective and primarily utilized existing medical records data, the data were anonymized during analysis, protecting the privacy of the participants and avoiding imposing additional risks or burdens on them. Therefore, the ethics committee waived the requirement for informed consent.

Consent for publication

All authors approved the final version and agreed to be responsible for the study.

Data availability

All data supporting the findings of this study are included in this article and its supplementary materials.

Competing interests

The authors declare no competing interests

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Authors' contributions

A.X: Conceptualization; Data interpretation; Writing-Original draft preparation; Software; Resources.

L.J, S.Z, X.L, Z.M, D,L: Methodology, Investigation; Supervision.

Y.H: Conceptualization; Writing-review & editing; Polishing the draft.

All authors reviewed the manuscript.

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