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Clinical Characteristic and Pathogen Spectrum of Neonatal Sepsis in Guangzhou City from June 2011 to June 2017

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Background: Preterm and low birth weight (birth weight <2500 g) neonates are vulnerable to sepsis, and the causative pathogens vary in different regions and times. The objective of this study was to identify common organisms leading to neonatal sepsis and identify the characteristic of patients infected with different bacteria, which may help in the selection of antibiotics for empirical treatment.

Material/Methods: We retrospectively collected the clinical and microbiological data of neonates with culture-proven sepsis in our clinical setting from June 2011 to June 2017. The demography, composition, and distribution of the pathogens and the clinical characteristic of the cases infected with different bacteria were analyzed.

Results: Of a total of 1048 bacteria that were isolated from patient samples, detailed clinical and microbiological data of 297 cases were available. *Escherichia coli*, *Klebsiella pneumoniae*, and *coagulase-negative Staphylococcus (co-NS)* were the top 3 isolated pathogens. *Streptococcus agalactiae* predominantly led to early-onset sepsis, while *K. pneumoniae* and *Staphylococcus aureus* mainly led to late-onset sepsis. *K. pneumoniae* was mainly acquired in the hospital. Leukopenia was more commonly seen than leukocytosis in our study, and patients infected with *K. pneumoniae* and *Candida spp* encountered more thrombocytopenia.

Conclusions: The results of our study revealed the composition of the pathogens of neonatal sepsis in our region and the clinical characteristic of sepsis caused by different bacteria; these data may help in the selection of antibiotics for empirical treatment of neonates with high risk of sepsis.

MeSH Keywords: Infant, Newborn • Premature Birth • Sepsis

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Background

Neonatal sepsis is defined as a systemic infection with bacteria, virus, or fungus with/without signs and symptoms of infection in the first 4-weeks of life (≤28 days) [1,2]. Although great improvements have been made in preventing and treating neonatal septicemia, it remains one of the most severe threats to the health of neonates, especially in developing countries. The prevalence of neonatal sepsis varies in different countries; in developed countries it is 1 to 10 cases per 1000 live births and in developing countries the incidence of neonatal septicemia increases to 49 to 170 cases per 1000 live births [3–5]. Depending on the time of onset, sepsis can be classified as early-onset sepsis or late-onset sepsis. Early-onset sepsis is defined as sepsis onset within 72 hours postnatal. Late-onset sepsis is sepsis happening more than 72 hours but no more than 28 days postnatal. The distinction has clinical relevance, as early-onset neonatal sepsis may be acquired before or during delivery while late-onset neonatal sepsis is mainly due to bacteria acquired from the hospital or community environment [1,6,7]. The pathogens of early-onset and late-onset neonatal sepsis are different. *Escherichia coli* and *Streptococcus agalactiae* are the most common organisms associated with early-onset neonatal sepsis; *coagulase-negative Staphylococcus (co-NS)* is the main pathogen of late-onset neonatal sepsis [6,8,9]. The spectrum of pathogens of neonatal sepsis varies among different settings and may change over time in the same setting [10–13].

Empirical antibiotic treatment is standard practice for neonates with high risk of sepsis, such as preterm labored infants, neonates born with premature rupture of membranes (PROM), and low birth weight (1501–2500 g) neonates or very low birth weight (≤1500 g) neonates [14–16]. The diversity of organisms causing sepsis varies in different regions and changes over time even in the same location, which makes the choice of antibiotics for empirical treatment challenging. In addition, early exposure or prolonged exposure to antibiotics may lead to poor prognosis for the neonate [17].

As far as we know, there is no national wide survey about the composition of the pathogens of neonatal sepsis in China. Two studies conducted in east and southwest of China revealed different pathogen spectrums causing neonatal septicemia. Studies in eastern China found that *Staphylococcus aureus, K. pneumoniae*, and *Acinetobacter baumannii* were the top 3 pathogens of neonatal sepsis, whereas studies in southwestern China revealed that *co-NS*, *E. coli* and *K. pneumoniae* were the top 3 pathogens [11,13]. The situation of neonatal sepsis in southern China is still unclear.

In the study presented here, we collected the clinical and microbiological data of neonates with blood culture proven bacteria sepsis in Guangdong women and children hospital, which is the main women and children healthcare center in south of China, located in Guangzhou City. We performed an analysis of the composition of pathogens and the distribution of pathogens among neonates with different clinical characteristic. We further analyzed the clinical characteristic of neonates infected with different bacteria, and the relationship of the time of hospitalized before a positive bacterial blood culture and the pathogens that lead to neonatal sepsis.

Material and Methods

Patients and population

This is a retrospective study aimed at addressing the composition of the pathogens and the clinical characteristics of neonatal sepsis in our clinical setting, which is a tertiary women and children care center in Guangzhou city in south China. This study was approved by the Ethics Committee of Guangdong Women and Children Hospital. The microbiological data of 1048 neonates with positive bacterial blood cultures during June 2011 and June 2017 were collected. Detail hospitalization data, clinical characteristics of 327 neonates, and the obstetric records of their mothers were collected. The inclusion criteria were as followed: 1) infants younger than 28 days post-partum; 2) with positive blood culture for bacteria; and 3) neonatal clinical data and mother's obstetric data could be accessed. Those with only 1 positive blood culture for *co-NS* without any symptoms of sepsis were excluded due to the possibility of contamination during sample handling.

Data collection and analysis

We collected the following data: the isolated species of the pathogen, the age of neonates at admission, positive blood culture for bacteria results, gestational age (GA), delivery mode, born body weight, the incidence of premature rupture of membranes (PROM) and intrauterine fetal distress (IFD), total leukocytes count (TLC), platelet count, hemoglobin (Hb) concentration, plateletcrit (PCT) and hs-CRP level at the time of the positive blood culture. The interval between admission and positive blood culture was calculated to try to explain whether the infection was a hospital-acquired infection or not. Data analysis was performed using Microsoft Excel 2010; the data are presented as frequencies. Chi-square test was performed to analysis the distribution of pathogens. To access the risk factors associated with infection with different pathogens, univariate and multivariate analysis were performed. Kruskal-Wallis and Mann-Whitney U tests were performed for continuous data in univariate analyses. The χ^2 test and Fisher exact test were performed for dichotomous data in univariate analyses. *P* value <0.05 was considered statistically

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significant. Multivariate analyses were performed separately by using logistic regression to analyze the risk factors of morbidity in preterm infants. Gender, gestation week, delivery mode, and birth weight were included in the analysis. $P<0.05$ was considered statistically significant.

Results

Demography of patients

From June 2011 to June 2017, there were 1048 neonates who had a history of positive blood culture for bacteria in our hospital; detailed microbiological and clinical data of 327 patients were collected. Thirty-five cases were excluded due to only one positive blood culture, and the contamination rate was 10.7%. The details of the demographics of the study patients can be seen in Table 1.

Table 1. Demographics of patients.

Characteristics	No. (%) (N=297)
Maternal data	
Gestational age	
Preterm (<37 weeks)	165 (55%)
Term (≥37 weeks)	132 (45%)
Mode of delivery	
Vaginal	177 (59%)
Caesarian section	120 (41%)
PROM	81 (27%)
Intrauterine distress	27 (9%)
Neonatal data	
Gender	
Male	188 (63%)
Female	109 (37%)
Age of BCP	
Early-onset (<72 hours)	82 (28%)
Late-onset (4–30 days)	215 (72%)
Birth weight	
VLBW (≤1500 g)	92 (31%)
LBW (1501–2500 g)	67 (23%)
Normal (>2500 g)	138 (46%)

PROM – premature rupture of membranes; BCP – bacterial cytological profiling; VLBW – very low birth weight; LBW – low birth weight.

Bacteria spectrum of neonatal sepsis

Among 1048 isolated pathogens, 432 (41%) were *co-NS*, 206 (20%) were *E. coli*, 126 (12%) were *K. pneumoniae*, 53 (5%) were *Enterococcus spp*, 52 (4.9%) were *S. agalactiae*, 47 (4.6%) were *S. aureus*, 34 (3.3%) were *Candida spp*, and 18 (1.7%) were *A. baumannii*. These bacteria were ranked the top 8 isolated pathogens of neonatal sepsis from June 2011 to June 2017 in our hospital (Figure 1A). Other bacteria accounted for 7.6% of all the isolates. The distribution of the pathogens of 297 neonates with detailed microbiology and clinical data were similar, except that *E. coli* was the most commonly seen pathogen among this population, followed by *K. pneumoniae*, and *co-NS* ranked the third most commonly seen isolated bacteria (Figure 1B).

Bacteria composition of neonatal sepsis with different clinical characteristic

In this study, 188 and 109 bacteria were isolated from male and female neonates, respectively, and the distribution of the pathogens varied among male and female infants (χ^2/P, 17.87/0.0126) (Table 2). *E. coli* (26%), *K. pneumoniae* (24%), *co-NS* (15%), and *Enterococcus spp* (12%) ranked as the top 4 isolated pathogens among male neonates, and *E. coli* (26%), *K. pneumoniae* (21%), *S. agalactiae* (18%), and *co-NS* (16%) were the most commonly seen pathogens in female infants (Table 2). The difference in the distributions of the pathogens was greater among preterm and term infants (χ^2/P, 42.96/<0.0001) (Table 2). For those infants with GA <37 weeks, *K. pneumoniae* (31%), *E. coli* (25%), and *Enterococcus spp* (13%) were the top 3 isolated pathogens, and for those with GA ≥37 weeks, *E.coli* (26%), *co-NS* (24%), and *S. agalactiae* (18%) were the most common (Table 2). Composition of the isolated bacteria varied between vaginal delivery and caesarian section (χ^2/P, 23.82/0.0012). *E. coli* (32%), *K. pneumoniae* (18%), *co-NS* (17%), and *S. agalactiae* (10%) were commonly seen in vaginally delivered infants, and *K. pneumoniae* (30%), *E. coli* (16%), *Enterococcus spp* (16%), and *co-NS* (13%) were the top 4 isolated pathogens in infants delivered by caesarian section (Table 2). In those infants whose mothers experienced PROM, *E. coli* (35%), *K. pneumoniae* (22%), and *Enterococcus spp* (14%) ranked as the top 3 isolated pathogens (Table 2). *K. pneumoniae* (26%), *E. coli* (19%), and *co-NS* (19%) were the top 3 isolated bacteria in neonates encountering intrauterine fetal distress (IFD) (Table 2). The composition of the pathogens was significantly different between early-onset sepsis and late-onset sepsis (χ^2/P, 62.75/<0.0001). For infants with early-onset sepsis, *E. coli* (32%) was the most commonly seen pathogen, followed by *S. agalactiae* (27%) and co-NS(17%), and for those with late-onset sepsis, *K. pneumoniae* (29%) was the most commonly seen pathogen followed by *E. coli* (23%)

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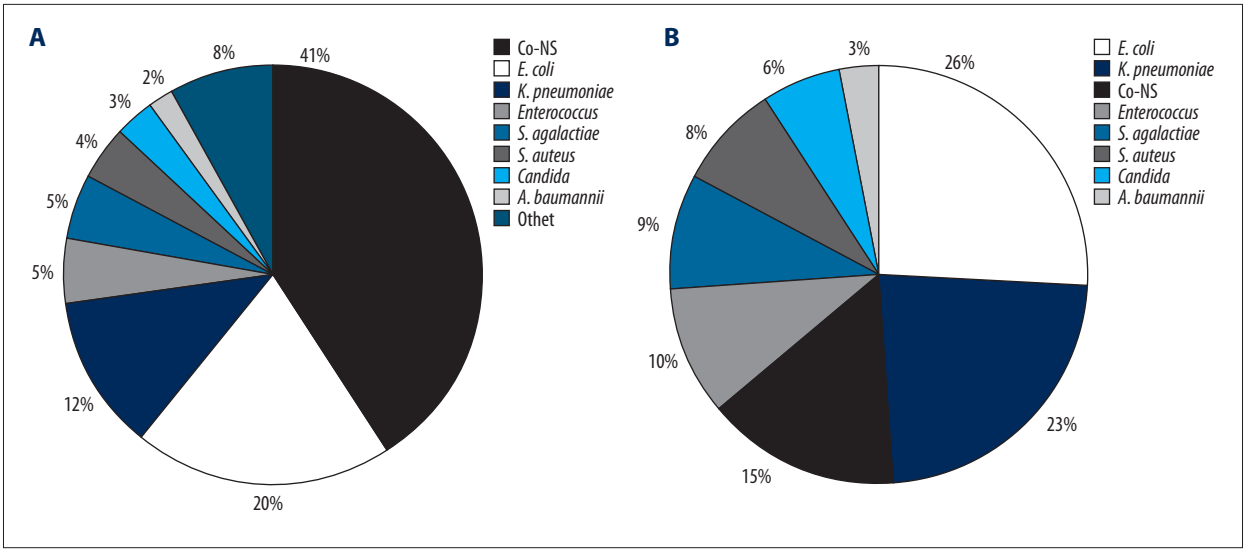

Figure 1. The distribution of the pathogens. (**A**) The distribution of the pathogens from 2011 to June 2017 before exclusion of "false positive" of *coagulase-negative Staphylococcus (co-NS)*. (**B**) The distribution of the pathogens with detail clinical and microbiological data after exclusion of "false positive" of *co-NS*.

and *co-NS* (15%) (Table 2). The spectrum of the pathogens was different among infants with different birth weight (χ^2/*P*, 58.67/<0.0001). *K. pneumoniae* (32%), *E. coli* (20%), *Enterococcus spp* (14%), and *Candida spp* (13%) were the most commonly seen pathogens in very low birth weight infants, and among low birth weight infants *E. coli* (36%), *K. pneumoniae* (29%), and *Enterococcus spp* (12%) were the top 3 isolated bacteria. In normal body weight neonates, *E.coli* (25%), *co-NS* (25%), *S. agalactiae* (15%), and *K. pneumoniae* (14%) were the most common isolated pathogens (Table 2).

Clinical characteristic of neonatal sepsis caused by different pathogens

We analyzed the laboratory findings of neonatal sepsis caused by different pathogens. We found that about 35% of neonatal sepsis patients experienced leukopenia (TLC <7500/uL), in contrast, only 4% of neonate patients experienced leukocytosis (TLC >25 000/uL), and 25% and 29% of neonate patients encountered anemia and thrombocytopenia, respectively. Leukopenia happened in more than 40% of neonatal sepsis patients caused by *E.coli, K. pneumoniae*, or *Candida spp*, and about 30% of cases caused by *co-NS*, *S. agalactiae*, or *Enterococcus spp* experienced leukopenia (Table 3); 22% of neonatal sepsis cases caused by *co-NS* encountered leukocytosis. Cases caused by *K. pneumoniae, Candida spp*, or *Enterococcus spp* encountered more anemia than cases caused by other pathogens; 53% and 65% of neonatal sepsis caused by *Candida spp* or *K. pneumoniae* experienced thrombocytopenia. In addition, thrombocytopenia caused by *Candida spp* or *K. pneumoniae* was more serious than that caused by other bacteria (Table 3). Neonatal sepsis cases caused by *K. pneumoniae, S. aureus*, or *E. coli* had higher C-reactive protein (CRP) levels; there was not significant different between cases caused by different pathogens in terms of procalcitonin (PCT) levels (Table 3).

Interval between admission and BCP (bacterial cytological profiling) of given pathogens

In this analysis, we tried to determine how the time of hospital stay correlated with the causative pathogen of neonatal sepsis. We found that all cases caused by *S. agalactiae* and more than 70% of cases caused by *E. coli*, *co-NS*, or *Candida spp* had positive blood cultures within 2 days after admission, while more than 60% of cases caused by *K. pneumoniae, Enterococcus spp*, or *A. baumannii* had positive blood cultures more than 3 days from admission.

Associated risk factors related to neonatal sepsis caused by a given pathogen

Risk factors associated with neonatal sepsis caused by a given pathogen were evaluated with univariate and multivariate analysis. Vaginal delivery and low birth weight were the risk factor for *E. coli* infection, with an adjusted odds ratio (AOR) of 2.43 (*P*=0.048) and 1.75 (*P*=0.038) (Table 4), respectively. These results indicated that neonates born by vaginal delivery were 2.43 times more likely to develop *E. coli*-related sepsis compare to other delivery methods, and neonates with birth weight <2500 g were 1.75 times more likely to develop *E. coli*-related sepsis compare to normal birth weight neonates. Low birth weight was a risk factor for *K. pneumoniae* infection, with an AOR of 3.078 (*P*=0.024) (Table 4), indicating that neonates with birth weight <2500 g were 3.078 times more likely to develop *K. pneumoniae*-related

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Table 2. Bacteria composition of neonatal sepsis with different clinical characteristics.

Species	*E. coli*	*K. pneumoniae*	Co-NS	Enterococcus	*S. agalactiae*	*S. aureus*	Candida	*A. baumannii*	Total	χ^2, *P*
Gender										
Male	48 (26%)	45 (24%)	29 (15%)	22 (12%)	8 (4%)	17 (9%)	11 (6%)	8 (4%)	188	17.87, 0.0126
Female	28 (26%)	23 (21%)	17 (16%)	9 (8%)	19 (18%)	6 (5%)	6 (5%)	1 (1%)	109	
Gestational age										
Preterm (<37 weeks)	41 (25%)	52 (31%)	14 (8%)	21 (13%)	8 (6%)	9 (5%)	15 (9%)	5 (3%)	165	42.96, <0.0001
Term (≥37 weeks)	35 (26%)	16 (12%)	32 (24%)	10 (8%)	19 (14%)	14 (11%)	2 (2%)	4 (3%)	132	
Mode of delivery										
Vaginal	57 (32%)	32 (18%)	30 (17%)	12 (7%)	18 (10%)	12 (7%)	13 (7%)	3 (2%)	177	23.82, 0.0012
Caesarian section	19 (16%)	36 (30%)	16 (13%)	19 (16%)	9 (8%)	11 (9%)	4 (3%)	6 (5%)	120	
PROM	28 (35%)	18 (22%)	10 (12%)	11 (14%)	8 (10%)	2 (2%)	3 (4%)	1 (1%)	81	
Intrauterine distress	5 (19%)	7 (26%)	5 (19%)	1 (4%)	3 (11%)	2 (7%)	2 (7%)	2 (7%)	27	
Age of BCP										
Early-onset (<72 hours)	26 (32%)	6 (8%)	14 (17%)	10 (12%)	22 (27%)	2 (2%)	1 (1%)	1 (1%)	82	62.75, <0.0001
Late-onset (4–30 days)	50 (23%)	62 (29%)	32 (15%)	21 (10%)	5 (2%)	21 (10%)	16 (7%)	8 (4%)	215	
Birth weight										
VLBW (≤1500 g)	18 (20%)	30 (32%)	7 (8%)	13 (14%)	2 (2%)	7 (8%)	12 (13%)	3 (3%)	92	58.61, <0.0001
LBW (1501–2500 g)	24 (36%)	19 (29%)	4 (6%)	8 (12%)	4 (6%)	3 (4%)	3 (4%)	2 (3%)	67	
Normal (>2500 g)	34 (25%)	19 (14%)	35 (25%)	10 (7%)	21 (15%)	13 (9%)	2 (2%)	4 (3%)	138	

PROM – premature rupture of membranes; BCP – bacterial cytological profiling; VLBW – very low birth weight; LBW – low birth weight.

sepsis compare to normal birth weight neonates. Low birth weight and vaginal delivery were risk factors for *Candida spp* infection, with AOR of 10.286 (*P*<0.001) and 2.22 (*P*=0.044) respectively (Table 4). These results suggest that neonates with birth weight <2500 g were 10.286 times more likely to develop *Candida spp*-related sepsis compared to normal birth weight neonates; in addition, neonates born by vaginal delivery were 2.22 times more likely to develop *Candida spp*-related sepsis compared to other delivery methods. Being male, preterm labor, and low birth weight neonates were at low risk of *S. agalactiae* infection, the AOR was 0.217 (*P*=0.041), 0.209 (*P*=0.047), and 0.218 (*P*=0.043) (Table 4), respectively. These results indicated that preterm male neonates with low birth weight were less likely to develop *S. agalactiae*-related sepsis.

Discussion

In this retrospective study, we presented the clinical and microbiological data of neonates with positive blood cultures for bacteria conforming sepsis. We first analyzed the composition of pathogens of neonatal septicemia. Among 1048 isolated pathogens, *co-NS* was the most commonly isolated bacteria, followed by *K. pneumoniae* and *E. coli*. This was in accordance with results from several previous studies [11,13,18,19].

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Table 3. Clinical characteristics of neonatal sepsis caused by different pathogens.

Species	*E. coli* (N=76)	*K. pneumoniae* (N=68)	Co-NS (N=46)	*Enterococcus* (N=31)	*S. agalactiae* (N=27)	*S. aureus* (N=23)	*Candida* (N=17)	*A. baumannii* (N=9)
hs-CRP level								
<6 mg/mL	32 (42%)	7 (10%)	18 (39%)	13 (42%)	14 (52%)	3 (13%)	7 (41%)	1 (11%)
6–50 mg/mL	25 (33%)	26 (38%)	26 (56%)	12 (39%)	10 (37%)	11 (49%)	8 (47%)	2 (22%)
>50 mg/mL	19 (25%)	30 (44%)	2 (4%)	6 (19%)	3 (11%)	8 (35%)	2 (12%)	3 (33%)
PCT level								
<0.1 ng/mL	9 (12%)	3 (4%)	3 (7%)	1 (3%)	0 (0%)	3 (13%)	2 (12%)	1 (11%)
0.1–0.5 ng/mL	18 (24%)	7 (10%)	14 (30%)	15 (48%)	6 (22%)	10 (43%)	8 (47%)	0 (0%)
>0.5 ng/mL	42 (55%)	47 (69%)	26 (57%)	12 (39%)	21 (78%)	8 (35%)	7 (41%)	5 (56%)
Routine blood test								
Leukopenia (TLC <7500/uL)	32 (42%)	28 (41%)	14 (30%)	10 (32%)	8 (30%)	3 (13%)	8 (47%)	2 (22%)
Leukocytosis (TLC >25 000/uL)	1 (1%)	4 (6%)	1 (2%)	1 (3%)	1 (4%)	1 (4%)	1 (6%)	1 (11%)
Anemia (Hb <90 g/L)	11 (14%)	27 (40%)	9 (20%)	11 (35%)	2 (7%)	6 (26%)	7 (41%)	0 (0%)
Thrombocytopenia (PLT <150 000/uL)	19 (25%)	36 (53%)	7 (15%)	6 (19%)	1 (4%)	3 (13%)	11 (65%)	3 (33%)
Mild	11 (14%)	6 (9%)	0	2 (6%)	1 (4%)	0	2 (12%)	3 (33%)
Moderate	4 (5%)	8 (12%)	5 (11%)	4 (13%)	0	0	3 (18%)	0
Severe	2 (3%)	10 (15%)	1 (2%)	0	0	3 (13%)	4 (23%)	0
Very severe	3 (4%)	11 (16%)	1 (2%)	0	0	0	2 (12%)	0

CRP – C-reactive protein; PCT – procalcitonin; TLC – total leukocytes count; Hb – hemoglobin; PLT – platelet count.

Co-NS is a commensal organism of the skin; positive blood cultures growing *co-NS* may be contamination due to inappropriate clinical procedures. Only a small percentage of blood cultures growing *co-NS* (ranging from 10% to 30%) are considered to be true positive results [18]. In our study, of the 134 cases infected with *co-NS* with detail clinical data, only 46 cases presented with symptoms of sepsis: persistent fever, significant change of WBC count, or increase of PCT or CRP level. The true positive rate of blood cultures growing *co-NS* was about 30% in our study. This rate may be an under estimation, as the immature immunity of neonates might lead to symptomless infections. Positive blood cultures growing *co-NS* should be dealt with prudently, as several studies have demonstrated that *co-NS* is one of the most commonly isolated organisms in neonatal intensive care unit [8,20–22]. Empirical antibiotic treatment is standard practice for neonates suspected of septicemia. Nonetheless, early antibiotic exposure remains controversial due to the possibility of creating an environment for emerging bacterial resistance and the potential for poor prognosis [12,23,24]. Thus, it is of great importance to identify which patients that need antibiotic treatment and what kind of antibiotics are most suitable. Isolation of organisms from blood culture is the gold standard for diagnosis of sepsis, but can be time-consuming and false-negative blood culture results make it difficult to guide the choice of antibiotics for empirical treatment.

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Table 4. Univariate and multivariate analysis on risk factors associated with indicated pathogen related neonatal sepsis.

Pathogen	Risk factor	Univariate analysis	*P*-value	Multivariate analysis	*P*-value
E. coli	Gender (Male)	1.039	0.863	0.967	0.782
	Gestational age (<37 weeks)	0.608	0.534	0.896	0.613
	Mode of delivery (vaginal)	3.157	0.007	2.436	0.048
	Birth weight (≤2500 g)	2.305	0.0289	1.756	0.038
K. pneumoniae	Gender (Male)	1.232	0.216	1.075	0.356
	Gestational age (<37 weeks)	1.398	0.148	1.137	0.281
	Mode of delivery (vaginal)	0.5	0.058	0.78	0.08
	Birth weight (≤2500 g)	3.547	0.017	3.078	0.024
Candida	Gender (Male)	1.106	0.659	1.006	0.775
	Gestational age (<37 weeks)	0.89	0.765	0.932	0.586
	Mode of delivery (vaginal)	2.781	0.027	2.22	0.044
	Birth weight (≤2500 g)	11.654	<0.001	10.286	<0.001
S. agalactiae	Gender (Male)	0.356	0.047	0.217	0.041
	Gestational age (<37 weeks)	0.261	0.047	0.209	0.047
	Mode of delivery (vaginal)	1.346	0.123	1.156	0.354
	Birth weight (≤2500 g)	0.314	0.056	0.218	0.043

In our study, we found that more male neonates were diagnosed with sepsis than female neonates (188 versus 109). This finding was consistence with the results of studies conducted in the USA [12,25]; we do not know the reason for this phenomenon. Except for the different incidence rates of sepsis, the distribution of *S. agalactiae* among genders has been found to be imbalanced. Female infants appear to be vulnerable to *S. agalactiae,* which is the most common pathogens of early-onset neonatal sepsis [9,12]. Here we found more than 80% of neonatal septicemia caused by *S. agalactiae* were classified as early-onset sepsis, and more than 70% of these cases were term, normal birth weight neonates and most were delivered vaginally. Penicillin may be considered preferentially for empirical treatment of such populations with suspected sepsis.

K. pneumoniae and *E. coli* were the most common isolated *Enterobacteriaceae* in our study, accounting for 48% of all the isolated pathogens. Vaginal delivery and low birth weight are the risk factor for *K. pneumoniae* and *E. coli* related sepsis. Previous studies demonstrated that most of isolated *K. pneumoniae* and *E.coli* from neonatal sepsis patients were ESBL (extended spectrum beta-lactamase) producing strains [2,26,27]. We found that about 62%of the isolated *K. pneumoniae* and *E. coli* are ESBL positive, thus we should consider this when choosing antibiotics for empirical treatment for patients with high risk of *K. pneumoniae* or *E. coli* sepsis. Fungi are common pathogens of neonatal sepsis, implicating in increasing number of systemic infections, usually acquired during prolonged hospital stay of preterm neonates [28]. It is the third most common cause of late-onset neonatal sepsis in low birth weight infants [29]. In our study, *Candida spp* accounted for 5% of isolated pathogens, significantly higher than the results of 2 other studies conducted in east and southwest China [11,13]. Very low birth weight and vaginal delivery are risk factor for *Candida spp* related neonatal sepsis. The isolation rate of *S. aureus* in our study was lower than that reported previously by others [13,26]. Different hygiene levels and different locations of studies may explain the differences in *S. aureus* isolation rates.

In our study, we found that infants infected with *K. pneumoniae, Enterococcus, S. aureus*, and *A. baumannii* had long hospital stays before a positive blood culture for bacteria, indicating that these pathogens were acquired in the hospital. *K. pneumoniae* is considered normal gastrointestinal flora and has recently been demonstrated as a significant cause of nosocomial infection. Particularly, preterm neonates are vulnerable to *K. pneumoniae*. Long hospital stays, prolonged intravenous access, endotracheal intubation, or other invasive procedures place preterm neonates at increased risk for hospital-acquired infections.

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Systemic bacterial infection may lead to malfunctions of the hemopoietic system. In our study, of the 297 cases with detailed clinical and microbiological data, 105 cases experienced leukopenia and only 11 cases experienced leukocytosis. This was not our expectation, as leukocytosis is considered one of the indices of sepsis [30]. Anemia and thrombocytopenia occurred in 73 and 89 cases of sepsis, respectively. These result demonstrated that the hemopoietic system was inhibited under condition of sepsis. In an immature neonatal hemopoietic system, LPS and toxins of the bacteria may be the reasons for hemopoietic malfunction. In our study, *S. aureus* led to less leukopenia than other bacteria. Sepsis caused by *K. pneumoniae* or *Candida* was accompanied by high incidence of anemia and thrombocytopenia. When dealing with neonatal sepsis patients, we should pay attention to hemopoietic changes and take necessary steps to improve the condition of patients.

As our retrospective study, we did not calculate the precise rate of sepsis. Though preterm labor, low birth weight and PROM have been shown to be risk factors for neonatal sepsis, in our study, we found little difference between term and preterm, as well as between low birth weight and normal birth weight; and PROM was only presented in about 25% of the cases. Differences in study design may explain the differences in study results. The obtain more detailed information related with these aspects of neonatal sepsis, a prospective study should be conducted in our hospital.

Though our study has several limitations, it also provides helpful information: it unveils the pathogen composition of neonatal sepsis in our region for the first time, which is of great help in preventing and treating neonatal sepsis. It may be used to guiding the selection of antibiotic for empirical treatment in case characteristic dependent manner.

Conclusions

The bacterial spectrum of neonatal sepsis varies among healthcare settings; thus, it is of great important to find out the bacterial spectrum of neonatal sepsis in a hospital setting for empirical treatment or preventing purposes. The risk factors associating with pathogen-specific sepsis are different based on the pathogen. It is important to consider the possible bacterial spectrum as it might help in choose appropriate treatments. Different pathogens may lead to different clinical manifestations, such as thrombocytopenia, and thus we might conduct appropriate precautionary treatment according to isolated pathogens.

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