Original Article

Changing trends in the bacteriological profiles and antibiotic susceptibility in neonatal sepsis at a tertiary children's hospital of China

Xiao-Juan Tang, Bin Sun, Xin Ding, Hong Li, Xing Feng

Neonatal Intensive Care Unit, Department of Neonatology, Children's Hospital of Soochow University, Suzhou, China

Contributions: (I) Conception and design: X Feng, XJ Tang; (II) Administrative support: B Sun, X Ding; (III) Provision of study materials or patients: XJ Tang, H Li; (IV) Collection and assembly of data: XJ Tang, H Li; (V) Data analysis and interpretation: XJ Tang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Professor Xing Feng, PhD. Chairman of the Pediatrics Branch of Jiangsu Medical Association, Department of Neonatology, Children's Hospital of Soochow University, Suzhou, China. Email: fengxing@suda.edu.cn.

Background: Sepsis is a major cause of neonatal morbidity and mortality in developing countries, and early-onset sepsis has poor outcomes. The causative bacteria vary depending on the geographical location of the hospital. This study aimed to determine the changing trends of causative bacteria and antibiotic susceptibility in the past decade.

Methods: This study retrospectively analyzed the blood culture of positive cases of early-onset sepsis admitted to the neonatal intensive care unit of our hospital between 2009 and 2018. The cases were divided into two phases, i.e., phase I (2009 to 2013) and phase II (2014 to 2018). Changing trends in the bacteriological profiles and antibiotic susceptibility were recorded and analyzed.

Results: A total of 1,479 causative bacteria were detected. Gram-positive bacteria were isolated in 74.92% of the cases, and coagulase-negative *Staphylococci* (CoNS) (63.22%) was identified as the common isolate. *Klebsiella pneumoniae* (10.01%) followed by *Escherichia coli* (8.72%) were the dominant Gram-negative bacteria. Comparative analysis showed a significant reduction in CoNS. Among Gram-negative bacteria, *K. pneumoniae* was initially predominant but was replaced by *E. coli* in phase II. Gram-positive bacteria showed relatively high susceptibility to aminoglycosides and quinolones. *K. pneumoniae* exhibited higher resistance to cephalosporin compared with *E. coli*. Reduced sensitivity against the first- and second-generation antibiotics was observed in phase II.

Conclusions: The etiological profile of neonatal sepsis (NS) has undergone a significant change in the last decade. Antibiotic resistance has increased, and continuous surveillance for antibiotic susceptibility is required to ensure efficient therapeutic outcomes.

Keywords: Bacteriocins; newborn; sepsis

Introduction

The microbial etiology of neonatal sepsis (NS) varies according to the geographical location of hospitals; as such, developing therapeutic interventions is challenging. NS is defined as a systemic infection, usually bacterial, viral, or fungal, that may occur with/without signs and symptoms of infection during the first 4 weeks of life (1). Early-onset sepsis is defined as sepsis occurring less than 7 days of age and often has worse prognosis than late-onset sepsis (≥7 days of age). Despite the improvements in NS treatment strategies, it remains a major threat to the health of neonates, particularly in developing countries (2). Several

studies have found changing trend in the bacterial etiology of NS in different periods (3-5). Early identification and treatment of NS are challenging due to variations in the microbial etiology of regions where hospitals are located. Periodic epidemiological surveys of NS can identify commonly encountered pathogens and their antibiotic susceptibility patterns in a neonatal setting.

Antibiotics are the standard therapy for high-risk patients with NS, including preterm infants and those who have ruptured membranes and low body weight. The diversity of organisms causing sepsis changes over time, which poses a challenge for selection of antibiotics for empirical treatment (3-6). Additionally, prolonged antibiotic exposure leads to poor prognosis in neonates. This study focused on determining the causative bacteria and antibiotic susceptibility of early-onset sepsis due to the differences in the etiology between early-onset and late-onset sepsis. Here, we investigated the trend in the etiology of NS and their antibiotic susceptibility pattern over the last decade in our hospital. We present the following article in accordance with the STROBE reporting checklist (available at http:// dx. doi. org/10. 21037/tp–20–115).

Methods

Pretreatment evaluation

We obtained data on blood cultures of patients with early-onset sepsis (<7 days of age) who were admitted to the neonatal intensive care unit at Children's Hospital of Soochow University between Jan 2009 and Dec 2018. The cases were divided into two phases, i.e., phase I (2009 to 2013) and phase II (2014 to 2018). Bacterial and demographic data were obtained and compared with microbial databases. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Clinical Trial Ethics Review Committee of Children's Hospital of Soochow University (No. 2019LW019) and individual consent for this retrospective analysis was waived.

We collected demographic and microbial data from ward admission and laboratory registers and validated these against the electronic microbial database. Blood cultures of patients who were potentially septic were assessed. The clinical outcome and duration of hospital stay were not assessed. Bacterial colonization data from vaginal swabs and antibiotic therapy during neonate delivery were unavailable.

NS was defined as neonates presenting with at least one of the following symptoms: fever (rectal temperature ≥38 ℃) or hypothermia (rectal temperature ≤36 ℃), white blood cell counts ≥30,000/mm or <5,000/mm or >25% immature cells, convulsions, lethargy, feeding or breathing problem, hypoglycemia, bulging fontanels, vomiting, and jaundice.

Blood cultures

Blood was sampled from the peripheral vein under aseptic conditions before antibiotic interventions. Blood (2 mL) was inoculated into the brain-heart infusion broth at 37 ℃. Sub-cultures were produced on blood and MacConkey's agar following 24 and 48 h of growth. Bacterial growth was identified through colony counting, Gram staining, slide agglutination, and biochemical properties. If no growth was evident after 48 h, then the growth period was extended to 7 days before being confirmed as sterile. Mixed bacterial flora or diphtheroid growth represented contamination. Coagulase-negative *Staphylococci* (CoNS) was considered pathogen only when isolated in paired cultures. All isolates were analyzed. Antimicrobial susceptibility was assessed using Kirby-Bauer disk diffusion method. Data were interpreted based on the criteria of the Clinical and Laboratory Standard Institute. The cultures with aerobic spores were considered contaminated. Gram-positive bacteria were tested against the following antimicrobials: oxacillin, erythromycin, ciprofloxacin, rifampin, linezolid, moxifloxacin, penicillin G, gentamicin, tetracycline, tigecycline, cefoxitin, vancomycin, and levofloxacin. Gram-negative bacteria were tested against the following antimicrobials: amikacin, ampicillin, aztreonam, ertapenem, ciprofloxacin, meropenem, piperacillin, piperacillin/tazobactam, gentamicin, cefepime, cefuroxime, cefoperazone/sulbactam, ceftriaxone, cefotaxime, ceftazidime, cefotetan, cefoxitin, imipenem, and levofloxacin.

Data analysis

The results of the laboratory investigations were recorded in a proforma and analyzed using SPSS version 17.0. Descriptive statistics were used to describe data distribution. Chi-square test was performed for categorical variables. P<0.01 was considered statistically significant.

Table 1 Changing trends in distributions of bacterial isolates between the two phases

Isolate	Total (%)	Phase I (%)	Phase II (%)	P
Gram-positive organisms	1,108 (74.92)	614 (81.22)	494 (68.33)	<0.01
Coagulase-negative *Staphylococci*	935 (63.22)	535 (70.77)	399 (55.19)	<0.01
Streptococcus	79 (5.34)	22 (2.91)	57 (7.89)	<0.01
Staphylococcus aureus	43 (2.91)	20 (2.66)	23 (2.18)	0.54
Enterococcus	43 (2.91)	29 (3.84)	14 (1.94)	<0.01
Listeria monocytogenes	8 (0.54)	8 (1.06)	0 (0)	<0.01
Gram-negative organisms	317 (21.43)	126 (16.67)	191 (26.42)	<0.01
Klebsiella pneumoniae	148 (10.01)	72 (9.52)	76 (10.51)	0.53
Escherichia coli	129 (8.72)	42 (5.56)	87 (12.03)	<0.01
Enterobacter	17 (1.15)	4 (0.53)	13 (1.80)	<0.01
Acinetobacter	10 (0.68)	2 (0.26)	8 (1.11)	<0.01
Pseudomonas	7 (0.47)	3 (0.39)	4 (0.55)	0.66
Klebsiella oxytoca	2 (0.14)	1 (0.13)	1 (0.14)	0.98
Salmonella	2 (0.14)	1 (0.13)	1 (0.14)	0.98
Citrobacter	1 (0.07)	0 (0)	1 (0.14)	0.31
Proteus	1 (0.07)	1 (0.13)	0 (0)	0.33
Fungus	54 (3.65)	16 (2.12)	38 (5.26)	<0.01
Total	1,479	756	723	

Results

Isolated organisms

Table 1 provides the detailed etiology of the 1,479 isolates, including Gram-positive bacteria (74.92%), Gram-negative bacteria (21.43%), and fungi (3.65%). CoNS were the most common organisms accounting for 63.15% of the isolates and mainly comprised *S. epidermidis* (57.49%, i.e., 537/934), *S. hemolyticus* (20.56%, i.e., 192/934), and *S. hominis* (10.49%, i.e., 98/934). Common Gram-negative bacteria were *Klebsiella pneumoniae* (10.01%) and *Escherichia coli* (8.72%). Among other Gram-positive bacteria, *Streptococcus* accounted for 5.34%, *Enterococcus* accounted for 2.91%, and *S. aureus* accounted for 2.91%. The table also shows the comparative analysis of the changing trends in bacteriological profiles in the two phases. Gram-positive bacteria were still the predominant isolates. However, the proportion decreased in phase II (P<0.01). CoNS were the most common organisms among Gram-positive bacteria, but their proportion significantly decreased in phase II (P<0.01). *K. pneumoniae* was the predominant pathogen

among Gram-negative bacteria in phase I. However, *E. coli* had replaced *K. pneumoniae* as the prevalent Gram-negative bacteria in phase II.

Antibiotic susceptibility

Table 2 shows the analysis of the antibiotic susceptibility of CoNS and *S. aureus*. CoNS were more susceptible to commonly used non-β-lactam antibiotics compared with oxacillin and penicillin. CoNS showed 95.1% resistance to penicillin G and 78.1% resistance to oxacillin. The percentages of susceptibility were 100% against linezolid, tigecycline, and teicoplanin; 76.96% against cefoxitin; and 58.04% against levofloxacin. *S. aureus* was more susceptible to commonly used non-β-lactam antibiotics compared with penicillin and cefoxitin. The results showed that *S. aureus* was fully susceptible to moxifloxacin, tigecycline, teicoplanin, and vancomycin followed by gentamicin (96.97%) and ciprofloxacin (91.30%), but less sensitive to cefoxitin (28.57%) and penicillin (18.18%). *Table 3* shows the susceptibility assessment of *K. pneumonia* and

Table 2 Antibiotic susceptibility of the major gram-positive bacteria

Antimicrobial	CoNS (%)	S. aureus (%)
Oxacillin	143/653 (21.90)	26/33 (78.79)
Cotrimoxazole	394/653 (60.34)	31/33 (93.94)
Erythromycin	152/653 (23.23)	18/33 (54.55)
Ciprofloxacin	265/453 (58.80)	21/23 (91.30)
Rifampicin	626/653 (95.87)	33/33 (100.00)
Linezolid	652/652 (100.00)	33/33 (100.00)
Moxifloxacin	502/653 (76.88)	33/33 (100.00)
Penicillin G	32/653 (4.90)	6/33 (18.18)
Gentamicin	518/653 (79.33)	32/33 (96.97)
Tetracycline	498/653 (76.26)	28/33 (84.85)
Tigecycline	378/378 (100.00)	21/21 (100.00)
Teicoplanin	276/276 (100.00)	11/11 (100.00)
Cefoxitin	157/204 (76.96)	6/21 (28.57)
Vancomycin	651/652 (99.85)	33/33 (100.00)
Levofloxacin	379/653 (58.04)	30/33 (90.91)

CoNS, coagulase-negative *Staphylococci*.

E. coli. For β-lactam antibiotics, *K. pneumoniae* showed the maximum susceptibility to ertapenem (100%), piperacillin/tazobactam (86.61%), meropenem (85.71%), and imipenem (82.93%) and had high resistance to ampicillin (100%), piperacillin (93.75%), cefuroxime (85.71%), and cefotaxime (85.0%). For non-β-lactam antibiotics, *K. pneumoniae* showed the maximum susceptibility to aminoglycosides and quinolones including amikacin (100%), ciprofloxacin (96.0%), and levofloxacin (93.90%). *E. coli* demonstrated high susceptibility to aminoglycosides, carbapenem, and quinolones but low susceptibility to ampicillin (27.43%) and piperacillin (28.57%). *E. coli* maintained relatively high susceptibility to most third-generation cephalosporins.

Table 4 presents the comparison of the antibiotic susceptibility of CoNS isolated between 2009 and 2018. The susceptibility of the isolates to ciprofloxacin, tetracycline, and levofloxacin significantly increased in phase II compared with that in phase I (P<0.01). By contrast, the antibiotic susceptibility of CoNS against cefoxitin decreased from 81.08% in phase I to 72.04% in phase II (P<0.01). *Table 5* summarizes the comparison of the antibiotic susceptibility of *S. aureus*. No significant difference in the susceptibility of the isolates was observed during the two phases. *K. pneumoniae* showed similar

Table 3 Antibiotic susceptibility of the major gram-negative bacteria

Antimicrobial	K. pneumoniae (%)	E. coli (%)
Amikacin	98/98 (100.00)	116/116 (100.00)
Ampicillin	0/123 (0)	31/113 (27.43)
Aztreonam	42/100 (42.0)	76/92 (82.61)
Ertapenem	83/83 (100.00)	92/92 (100.00)
Cotrimoxazole	61/100 (61.00)	42/92 (45.65)
Ciprofloxacin	96/100 (96.00)	55/92 (59.78)
Meropenem	36/42 (85.71)	64/65 (98.46)
Piperacillin	4/64 (6.25)	18/63 (28.57)
Piperacillin/tazobactam	110/127 (86.61)	114/117 (97.44)
Gentamicin	113/123 (91.87)	67/113 (59.29)
Cefepime	45/120 (37.50)	94/113 (83.19)
Cefuroxime	10/70 (14.29)	32/52 (61.54)
Cefoperazone/sulbactam	79/134 (58.96)	101/112 (90.18)
Ceftriaxone	20/99 (20.20)	53/83 (63.86)
Cefotaxime	6/40 (15.00)	22/39 (56.41)
Ceftazidime	42/123 (34.15)	91/114 (79.82)
Cefotetan	84/100 (84.00)	88/91 (96.70)
Cefoxitin	96/123 (78.05)	105/110 (95.45)
Imipenem	68/82 (82.93)	108/111 (97.30)
Levofloxacin	77/82 (93.90)	80/109 (73.39)

resistance to ampicillin and piperacillin. The resistance against second- and third-generation cephalosporins was significantly higher in phase II than that in phase I. *K. pneumoniae* showed high sensitivity toward amikacin and gentamicin among aminoglycosides throughout the study. The resistance to carbapenems and β-lactamase inhibitors significantly increased in phase II (*Table 6*). *Table 7* depicts the resistance patterns of *E. coli* over time. The resistance to ampicillin and piperacillin was comparable over the study period, whereas that to carbapenems and β-lactamase inhibitors increased gradually.

Discussion

Despite recent advances in health care, morbidity and

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Table 4 Trend of antibiotic susceptibility for CoNS between the two phases

Antimicrobial	Phase I (%)	Phase II (%)	P
Oxacillin	74/399 (18.55)	69/254 (27.17)	<0.01
Cotrimoxazole	239/399 (59.90)	155/254 (61.02)	0.78
Erythromycin	87/399 (21.80)	65/254 (25.59)	0.26
Ciprofloxacin	105/199 (52.76)	160/254 (62.99)	<0.01
Rifampicin	389/399 (97.49)	237/254 (93.31)	<0.01
Linezolid	398/398 (100.00)	254/254 (100.00)	
Moxifloxacin	301/399 (75.44)	201/254 (79.13)	0.28
Penicillin G	21/399 (5.26)	11/254 (4.33)	0.59
Gentamicin	312/399 (78.20)	206/254 (81.10)	0.37
Tetracycline	281/399 (70.43)	217/254 (85.43)	<0.01
Tigecycline	126/126 (100.00)	252/252 (100.00)	
Teicoplanin	112/112 (100.00)	164/164 (100.00)	
Cefoxitin	90/111 (81.08)	67/93 (72.04)	<0.01
Vancomycin	397/398 (99.75)	254/254 (100.00)	0.42
Levofloxacin	217/399 (54.39)	162/254 (63.78)	<0.01

Table 5 Trend of antibiotic susceptibility for *S. aureus* between the two phases

Antimicrobial	Phase I (%)	Phase II (%)	P
Oxacillin	17/19 (89.47)	9/14 (64.29)	0.08
Cotrimoxazole	18/19 (94.74)	13/14 (92.86)	0.82
Erythromycin	12/19 (63.16)	6/14 (42.86)	0.25
Ciprofloxacin	8/9 (88.89)	13/14 (92.86)	0.74
Rifampicin	19/19 (100.00)	14/14 (100.00)	
Linezolid	19/19 (100.00)	14/14 (100.00)	
Moxifloxacin	19/19 (100.00)	14/14 (100.00)	
Penicillin G	2/19 (10.53)	4/14 (28.57)	0.18
Gentamicin	18/19 (74.74)	14/14 (100.00)	0.38
Tetracycline	17/19 (89.47)	11/14 (78.57)	0.39
Tigecycline	7/7 (100.00)	14/14 (100.00)	
Teicoplanin	5/5 (100.00)	6/6 (100.00)	
Cefoxitin	1/7 (14.29)	5/14 (35.71)	0.31
Vancomycin	19/19 (100.00)	14/14 (100.00)	
Levofloxacin	17/19 (89.47)	13/14 (92.86)	0.74

Table 6 Trend of antibiotic susceptibility for *K. pneumoniae* between the two phases

Antimicrobial	Phase I (%)	Phase II (%)	P
Amikacin	37/37 (100.00)	61/61 (100.00)	
Ampicillin	0/57 (0)	0/66 (0)	
Aztreonam	7/34 (20.59)	35/66 (53.03)	<0.01
Ertapenem	34/34 (100.00)	49/49 (100.00)	
Cotrimoxazole	25/34 (73.53)	36/66 (54.55)	0.07
Ciprofloxacin	33/34 (97.06)	62/66 (93.94)	0.96
Meropenem	23/23 (100.00)	13/19 (68.42)	<0.01
Piperacillin	1/15 (6.67)	3/49 (6.12)	0.89
Piperacillin/tazobactam	61/61 (100.00)	49/66 (74.24)	<0.01
Gentamicin	51/57 (89.47)	62/66 (93.94)	0.37
Cefepime	13/57 (22.81)	32/63 (50.79)	<0.01
Cefuroxime	5/34 (14.71)	5/36 (13.89)	0.92
Cefoperazone/sulbactam	51/69 (73.91)	28/65 (43.08)	<0.01
Ceftriaxone	7/34 (20.59)	13/65 (20.00)	0.92
Cefotaxime	1/23 (4.35)	5/17 (29.41)	<0.01
Ceftazidime	16/57 (28.07)	28/66 (42.42)	0.13
Cefotetan	34/34 (100.00)	50/66 (75.76)	<0.01
Cefoxitin	53/57 (92.98)	43/66 (65.15)	<0.01
Imipenem	16/16 (100.00)	52/66 (78.79)	<0.01
Levofloxacin	15/16 (93.75)	62/66 (93.94)	0.98

mortality due to NS remain a major concern in neonates (7). NS may not have specific signs and symptoms; as such, a delay in diagnosis and treatment contributes to higher morbidity and mortality. Sepsis-related mortality is preventable with time-sensitive empiric antibiotic therapy, which is decided based on the periodic epidemiological survey of local bacterial flora and their antibiotic susceptibility patterns. Causative organisms vary in different regions. Therefore, epidemiologic studies are of great importance in each region. This study retrospectively analyzed the blood culture of positive cases of early-onset sepsis to determine the changing trends of causative bacteria and antibiotic susceptibility in the past decade.

Previous studies emphasized the pivotal role of Gram-negative bacteria, such as *E. coli* and *K. pneumoniae*, as NS-causing pathogens (8-10). However, the main NS-causing pathogens, based on reported cases in China, were Gram-positive organisms (11). In the present study,

Gram-positive bacteria were more common than Gram-negative bacteria during phases I and II. However, we observed a significant decrease in the number of Gram-positive bacteria during phase II. This decrease was mainly attributed to the decrease in CoNS and the increase in *E. coli*. Although the proportion of CoNS decreased over time, it remained the major pathogen, consistent with previous study (12). Identifying CoNS is often challenging because most CoNS-positive blood cultures are deemed contaminated (13,14). CoNS cause NS when medical devices penetrate the skin and mucosal barriers. The increasing use of invasive medical devices, including central venous catheters, has increased the prevalence of this strain. The National Institute of Child Health and Human Development Neonatal Research Network published specific criteria to define CoNS sepsis (15). Two positive blood cultures are required to diagnose culture-proven sepsis. In the present study, patients with CoNS

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Table 7 Trend of antibiotic susceptibility for *E. coli* between the two phases

Antimicrobial	Phase I (%)	Phase II (%)	P
Amikacin	41/41 (100.00)	75/75 (100.00)	
Ampicillin	11/38 (28.95)	20/75 (26.67)	0.79
Aztreonam	13/17 (76.47)	63/75 (84.00)	0.46
Ertapenem	20/20 (100.00)	72/72 (100.00)	
Cotrimoxazole	5/17 (29.41)	37/75 (49.33)	0.14
Ciprofloxacin	8/17 (47.06)	47/75 (62.67)	0.24
Meropenem	21/21 (100.00)	43/44 (97.72)	0.49
Piperacillin	1/6 (16.67)	17/57 (29.82)	0.49
Piperacillin/tazobactam	42/42 (100.00)	72/75 (96.00)	0.19
Gentamicin	19/38 (50.00)	48/75 (64.00)	0.15
Cefepime	27/38 (71.05)	67/75 (67.75)	<0.01
Cefuroxime	8/14 (57.14)	24/38 (63.16)	0.69
Cefoperazone/sulbactam	35/37 (94.59)	66/75 (88.00)	0.27
Ceftriaxone	5/8 (62.50)	48/75 (64.00)	0.93
Cefotaxime	13/21 (61.90)	9/18 (50.00)	0.46
Ceftazidime	27/39 (69.23)	64/75 (85.33)	<0.01
Cefotetan	16/16 (100.00)	72/75 (96.00)	0.42
Cefoxitin	35/35 (100.00)	70/75 (93.33)	0.12
Imipenem	36/36 (100.00)	72/75 (96.00)	0.23
Levofloxacin	30/34 (88.24)	50/75 (66.67)	<0.01

had positive paired blood cultures and were clinically symptomatic for sepsis, confirming the absence of contamination. The decline in the number of CoNS was probably due to improvements in aseptic and disinfection procedures. No significant differences in the number of *S. aureus* were found between the two phases. Furthermore, the proportion of *Streptococcus* species increased, which was contradictory to previous reports (16). Our study also demonstrated a significant decrease in the proportion and frequency of *Enterococcus* species. For Gram-negative organisms, *K. pneumoniae* was the predominant species initially in phase I but was replaced by *E. coli* in phase II. Meanwhile, the proportion and frequency of *Enterobacter* and *Acinetobacter* were significantly higher in phase II than those in phase I. These findings indicate a paradigm shift in the etiology of NS in recent years.

We also detected a significant change in the susceptibility to antibiotics during the last decade. Our results revealed

that Gram-positive bacteria exhibited the highest resistance to penicillin, oxacillin, and erythromycin and remained sensitive to vancomycin, tigecycline, and teicoplanin. CoNS exhibited approximately 90% resistance toward penicillin and oxacillin. Based on the results, the use of ampicillin, penicillin G, and first or second-generation cephalosporins, which were previously recommended as empiric antibiotics for the treatment of NS, is probably unnecessary due to their extremely low sensitivity. The WHO recommends first-line antibiotics, including ampicillin and aminoglycosides, for the treatment of NS (17,18). However, ampicillin showed alarming resistance in the present study. Meanwhile, considering the extensive use of third-generation cephalosporines, we observed high antimicrobial resistance among Gram-positive and Gram-negative bacteria, including rapid resistance in *K. pneumoniae* during phase II. The susceptibility to β-lactamase inhibitors also significantly decreased in *K. pneumoniae* during phase II.

A hospital used fluoroquinolones to treat Gram-negative infections until β-lactam plus β-lactamase inhibitors were available for management due to the high resistance observed to these antibiotics (19). This study found that Gram-negative bacteria remained highly sensitive to quinolones throughout the study period. Therefore, the therapeutic role of fluoroquinolones may gain considerable importance in the future.

Zaidi *et al.* (17) reviewed 11,471 blood cultures from developing countries in South-East Asia and recommended imipenem and amikacin for the initial treatment of suspected sepsis in hospitalized neonates. Amikacin is effective against Gram-negative bacteria but is rarely used for NS because it can cause kidney and ear-associated toxicity (11). In the present study, the carbapenem-resistance significantly increased in *K. pneumoniae* during phase II. The reduced susceptibility to meropenem and imipenem was attributed to their over-prescription in this population, emphasizing the importance of third-generation cephalosporin therapy for these patients. The proportion of *E. coli* significantly increased during phase II and showed a notable resistance pattern. *E. coli* was resistant to ampicillin and sensitive to cefoperazone/sulbactam, piperacillin/tazobactam, cefotetan, and cefoxitin, all of which are commonly administered antibiotics. According to our findings, the resistance of *E. coli* against cephalosporins remained relatively unchanged over the last decade. This change in the sensitivity pattern of antimicrobials could be attributed to the fact that microorganisms tend to become resistant to commonly used antibiotics while remain sensitive to the rarely used ones.

Conclusions

In recent years, microbial profiles in NS have significantly changed, including a reduction in CoNS and an increase in *E. coli*. An increasing trend of antibiotic resistance to commonly used and available drugs has been observed. The resistance toward carbapenems has considerably increased. Antibiotic susceptibility patterns should be assessed in different phases. Each hospital should implement a unique antibiogram program that assesses options for empirical antibiotic therapy. This study had certain limitations, most notably the lack of correlation of our findings to clinical features and the limited representativeness of the sample. However, efforts to change the bacteriological profiles and antibiotic susceptibility patterns over 10 years and the large sample size were the strengths of the study.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx. doi. org/10. 21037/tp-20-115

Data Sharing Statement: Available at http://dx. doi. org/10. 21037/tp-20-115

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx. doi. org/10. 21037/tp-20-115). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Clinical Trial Ethics Review Committee of Children's Hospital of Soochow University (No. 2019LW019) and individual consent for this retrospective analysis was waived.

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