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ORIGINAL RESEARCH

Antimicrobial Resistance Patterns and Epidemiological Distribution of Pathogenic Bacteria in the Pediatric Intensive Care Unit at Beijing Children's Hospital: A Decade-Long Retrospective Analysis (2014–2023)

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Objective: This study aimed to analyze the distribution characteristics and changes in antimicrobial resistance of pathogens in the Pediatric Intensive Care Unit (PICU) of Beijing Children's Hospital from 2014 to 2023 to guide the rational use of antibiotics and provide a scientific basis for hospital infection prevention and control, as well as public health policy formulation.

Methods: A retrospective cohort design was used to systematically analyze the clinical data and antibiotic sensitivity results of 4,468 children aged 0–17 years who were admitted to the PICU of Beijing Children's Hospital between 2014 and 2023.

Results: 6,079 strains of pathogenic bacteria were cultured and isolated. There were 4,276 strains of Gram-negative bacteria, including *Acinetobacter baumannii* (20.0%), *Pseudomonas aeruginosa* (15.2%), and *Klebsiella pneumoniae* (12.9%); There were 1,803 Gram-positive bacteria, including *Staphylococcus aureus* (11.3%) and coagulase-negative *Staphylococci* (CoNS) (7.9%). Between 2014 and 2023, the number of detected Gram-negative and Gram-positive bacteria showed a fluctuating upward trend. *A. baumannii* showed a resistance rate of over 70% to most antibiotics, *P. aeruginosa* exhibited a relatively high resistance rate to carbapenems, and *Escherichia coli* demonstrated a high resistance rate to third-generation cephalosporins, but a low resistance rate to carbapenems. Methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative *Staphylococci* (MRCNS) were highly resistant to most antibiotics but remained highly sensitive to linezolid and vancomycin. Carbapenem-resistance (CR) and difficult-to-treat resistance (DTR) phenotypes of *K. pneumoniae* showed a marked upward trend. In contrast, *E. coli, P. aeruginosa*, and *A. baumannii* exhibited fluctuating or relatively stable resistance to extended-spectrum cephalosporins (ECR) and fluoroquinolones (FQR).

Conclusion: This study revealed the distribution and antibiotic resistance trends of pathogens in the PICU of Beijing Children's Hospital, providing important evidence for empirical anti-infective treatment in clinical practice.

Keywords: antimicrobial resistance, children, multidrug-resistant, pathogenic bacteria, pediatric intensive care unit, PICU

Introduction

In the Pediatric Intensive Care Unit (PICU), infectious diseases caused by pathogens have become one of the key causes of rapid deterioration of the condition of critically ill children and even death.[1] Such infections not only significantly increase the complexity of clinical management but are also likely to induce end-organ damage, such as multiple organ

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dysfunction syndrome (MODS), through cascade reactions, forming a life-threatening vicious cycle. Notably, this type of infection is closely associated with poor prognosis in children, and its occurrence and development are often accompanied by a higher mortality rate, which poses a dual challenge to the critical care team's formulation of diagnosis and treatment strategies, as well as to the children's long-term quality of life. In the PICU, the risk of nosocomial infection in children is significantly increased because of the incomplete development of their immune function and the widespread use of invasive procedures, such as mechanical ventilation and central venous catheter placement.[2] Compared to children in regular wards, children in the PICU have a 2–5 times higher incidence of hospital-acquired infections.[3] The situation of hospital-acquired infections in the PICU, which is closely related to immune suppression, mucosal barrier damage, and increased risk of microbial colonization, is different from that in regular wards. This difference in the incidence and characteristics of infections has become a key factor affecting the success rate of critical care for critically ill children.[4]

The significant increase in infection risk not only increases the complexity of clinical interventions but also poses a serious challenge to the precision of infection prevention and control systems. Early precision antimicrobial therapy based on pathogen-related evidence has been proven to effectively reduce the mortality rate of critically infected children and become a key intervention node for improving prognosis.[5] However, global multicenter research data shows that the proportion of antibiotic use in the PICU has risen to 51%-76%, and this high-level use of antibiotics directly drives the rapid evolution of bacterial resistance.[6] It is worth noting that the detection rate of multidrug-resistant bacteria has been increasing year by year, and some strains have shown pan resistance characteristics, leading to a sharp narrowing of the range of clinically available antibiotics.[7] This vicious cycle of "treatment demand-antimicrobial resistance evolution" not only weakens the clinical efficacy of antibiotics, but also transforms infection control from a simple medical problem to a major challenge in the global public health field. There is an urgent need to establish a multidisciplinary collaborative antimicrobial management (AMS) system to overcome this dilemma.[8]

Globally, there is a significant regional heterogeneity in the pathogenic spectrum and antimicrobial resistance characteristics of Pediatric Intensive Care Unit (PICU). In developed countries in Europe and America, Gram-positive bacteria have become the main pathogenic bacterial group, with methicillin-resistant *Staphylococcus aureus* (MRSA) and *Streptococcus pneumoniae* being the most common. This distribution pattern is closely related to local antibiotic use patterns, infection prevention and control strategies, and population immune backgrounds.[9] In the Asian healthcare system, the epidemiological characteristics of pathogens in PICUs show a relatively different trend from those in Europe and America. Monitoring data from countries such as China and India indicate that Gram-negative bacteria have become the main pathogens causing PICU infections, mainly *Escherichia coli, Klebsiella pneumoniae*, and *Acinetobacter baumannii*. The significant differences in pathogen structure may be attributed to the high antibiotic exposure pressure in Asian medical institutions, the varying maturity of hospital infection prevention and control systems, and the characteristics of the community-acquired infectious disease spectrum.[10]

The China Bacterial Resistance Monitoring Report of 2023 shows that the detection rates of third-generation cephalosporin-resistant *E. coli* and *K. pneumoniae*, methicillin-resistant coagulase-negative staphylococci (MRCNS), carbapenem-resistant (CR)-*E. coli*, CR-*K. pneumoniae*, CR-*Pseudomonas aeruginosa*, and CR-*A. baumannii* in intensive care units are much higher than those in other wards. Therefore, long-term monitoring of the PICU pathogen spectrum is of great significance. Monitoring changes in antimicrobial resistance is also crucial for reducing the prevalence of drug-resistant bacteria and improving the treatment success rate. It is worth noting that, as a super-large city, Beijing has unique epidemiological characteristics among pediatric patients admitted to the PICU. The greater the complexity of underlying diseases, the higher the proportion of invasive procedures, and the longer the average hospital stay, the greater the diversity of the pathogen spectrum. However, there is still a lack of research on the long-term monitoring of pathogens and trends in antimicrobial resistance in PICUs in Beijing, and systematic analysis is urgently needed to fill this gap.

This study aims to analyze the distribution characteristics and changes in antibiotic resistance of pathogens in the PICU of Beijing Children's Hospital from 2014 to 2023. By doing so, it will not only guide the rational use of antibiotics in clinical practice but also provide a scientific basis for hospital infection prevention and control and the formulation of public health policies.

Material and Method

Object of Study

This study adopted a retrospective cohort design to conduct a systematic analysis of the clinical data of 4,468 children aged 0–17 who were hospitalized in the PICU of Beijing Children's Hospital between January 2014 and December 2023. All included cases had comprehensive epidemiological data records (including sex, age, and season of onset) and microbiological testing data.

Cultivation and Identification of Bacterial Strains

According to the clinical laboratory operating procedures, specimens submitted by patients, including respiratory tract specimens, blood, cerebrospinal fluid, urine, feces, pleural effusion, and wound secretions, were separated, purified, and cultured. Bacterial identification was carried out using a VITEK MS (BioMerieux, France).

Antibiotic Susceptibility Test

The first pathogenic bacteria isolated from the patients were employed for antimicrobial resistance analysis. A Vitek2-compact microbiological analyzer (BioMerieux, France) was utilized for susceptibility testing. For some bacteria that were not suitable for drug sensitivity testing, the K-B or E-test method was applied. The results of antibiotic susceptibility testing were interpreted in accordance with the CLSI guidelines (M100 34th edition). Quality control strains, including *E. coli* (ATCC 25922 and ATCC 35218), *P. aeruginosa* (ATCC 27853), *S. aureus* (ATCC 25923 and ATCC 29213), *E. faecalis* (ATCC 29212), and *S. pneumoniae* (ATCC 49619), were used for quality control purposes.

Definition of Resistance Phenotype of Gram-Negative Bacteria

The term difficult-to-treat resistance (DTR) was applied to isolates demonstrating in vitro non-susceptibility to all classes of β-lactam antibiotics, as well as to fluoroquinolone.[11] Carbapenem resistance (CR) refers to a lack of susceptibility to both imipenem and meropenem. Resistance to extended-spectrum cephalosporins (ECR) was characterized by in vitro resistance to ceftazidime, cefotaxime, and cefepime. Similarly, fluoroquinolone resistance (FQR) has been defined as resistance to both ciprofloxacin and levofloxacin.[12]

Data Analysis

WHONET 5.6 software was used to analyze the data. GraphPad Prism 9.0 software (GraphPad Software, Boston, MA, USA) was used for data collection and graph generation. Categorical variables were expressed as frequencies and percentages. For categorical data such as demographic characteristics, bacterial distribution, and antimicrobial resistance rates, intergroup comparisons were performed using the Chi-square (χ^2) test in IBM SPSS Statistics 23. All data were organized and tabulated using Microsoft Excel 2019. $P<0.05$ was considered statistically significant.

Results

Basic Information

The total number of samples included in this study was 6,079, with males constituting the majority, at 60.3%. Regarding age distribution, young children aged ≤ 1 year constituted the largest group, accounting for 2,967 cases (48.8%). Sample collection was more concentrated in winter, accounting for 28.1%. Chi-square goodness-of-fit tests indicated that the distributions of sex, age, and season were all statistically significant ($P<0.001$) (Table 1).

Specimen Source Distribution

From 2014 to 2023, 4,468 positive specimens were detected, mainly originating from the lower respiratory tract (51%) (Figure 1).

Table 1 Basic Characteristics of Pathogens in PICU from 2014 to 2023

Variable	Number (n=6079)	Ratio (%)	χ^2	*P* Value
Sex				
Males	3664	60.3	260.281	<0.001
Females	2415	39.7		
Age categories				
≤ 1 year	2967	48.8	3386.906	<0.001
> 1 year, ≤ 3 years	817	13.4		
> 3 years, ≤ 7 years	970	16.0		
> 7 years, ≤ 12 years	967	15.9		
> 12 years, <18	358	5.9		
Collecting season				
Spring	1504	24.7	36.203	<0.001
Summer	1477	24.3		
Autumn	1389	22.9		
Winter	1709	28.1		

Abbreviation: n, the number of strains.

The Distribution of Bacterial Species

There were 4,276 Gram-negative bacterial strains, with the top three being *A. baumannii* (20.0%), *P. aeruginosa* (15.2%), and *K. pneumoniae* (12.9%). There were 1,803 Gram-positive bacteria, with the top three being *S. aureus* (11.3%), coagulase-negative *Staphylococci* (CoNS) (7.9%), and *S. pneumoniae* (4.8%) (Table 2).

Distribution of Pathogenic Bacteria in Common Infection Routes

The specimens causing respiratory tract infection included sputum, throat swabs, and alveolar lavage fluid, and 4,244 strains of pathogenic bacteria were detected, mainly *A. baumannii* (24.7%), *P. aeruginosa* (19.6%), *K. pneumoniae* (14.6%), and *S. aureus* (13.4%). A total of 257 strains of pathogenic bacteria causing urinary infection were detected, mainly *Enterococcus faecium* (26.5%), *E. coli* (24.5%), and *K. pneumoniae* (15.6%). A total of 830 strains of pathogenic bacteria were detected in the specimens causing bloodstream infection, mainly *Staphylococcus epidermidis* (22.4%), *Staphylococcus hominis* (14.7%), *K. pneumoniae* (7.8%) and *S. aureus* (7.5%). Specimens causing sterile body fluid infection include peritoneal effusion, pleural effusion, cerebrospinal fluid, joint, bone marrow, and pericardial effusions, and in total, 211 strains of pathogenic bacteria were detected, including *A. baumannii* (15.2%), *K. pneumoniae* (12.8%), *E. faecium* (10.0%), and *S. aureus* (9.0%) (Figure 2).

The Trends of Gram-Negative Bacteria and Gram-Positive Bacteria in PICU

From 2014 to 2023, both Gram-positive and Gram-negative bacteria showed a fluctuating upward trend. Gram-negative bacteria remained consistently higher in number throughout this period. A nadir was observed in 2020 (269 and 559 isolates, respectively), followed by a rapid increase to a peak in 2023 (Figure 3).

Trends in the Main Isolated Strains in PICU

Except for 2023, the number of *A. baumannii* in 2014–2022 was always the highest. In 2020, the number of *A. baumannii, P. aeruginosa, K. pneumoniae*, and *S. aureus* was significantly lower than before. The annual detection

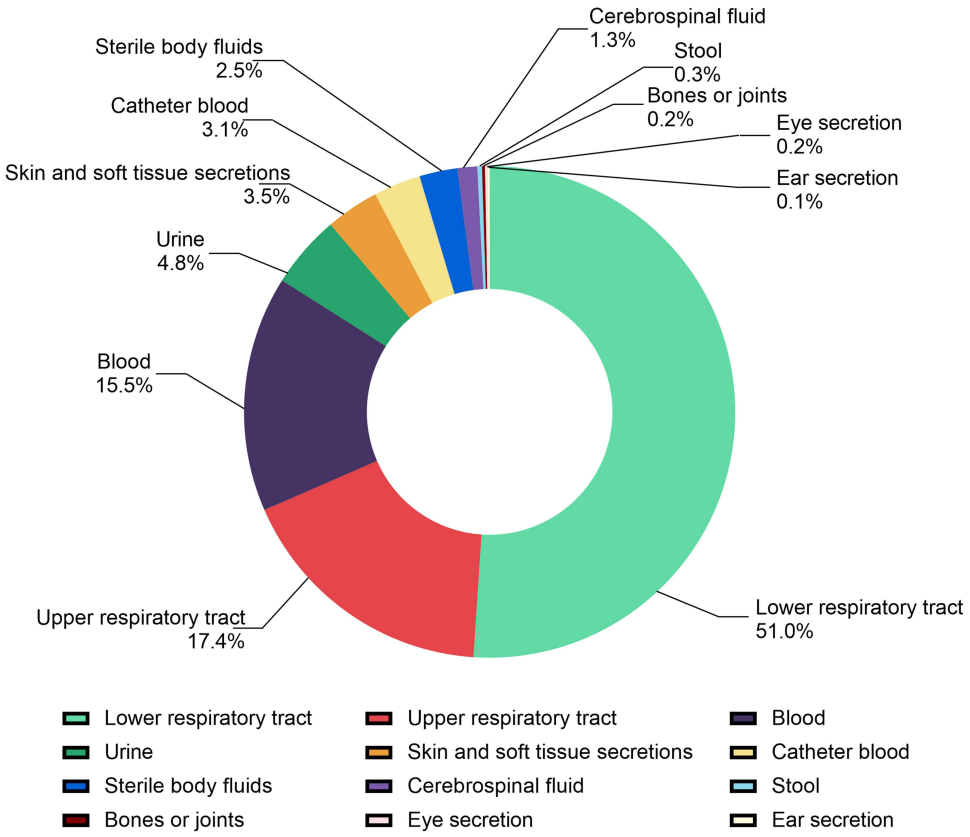

Figure 1 Composition ratio of 4468 positive specimens in PICU from 2014 to 2023.

rates for CoNS and *E. coli* were relatively stable Except for *A. baumannii* and *K. pneumoniae*, all other bacteria were detected by 2023 with the highest amount (Figure 4).

Comparison of Antibiotic Resistance Rates of S. aureus and CoNS

The penicillin resistance rates of *S. aureus* and CoNS were > 89%. The resistance rate of CoNS to most antibiotics was higher than that of *S. aureus*, particularly oxacillin (81.9% vs 32.4%), erythromycin (89% vs 73.1%), trimethoprim-

Table 2 Distribution of Bacterial Species from 2014 to 2023

Organisms	Number of Strains	% (n=6079)
Acinetobacter baumannii	1217	20.0
Pseudomonas aeruginosa	926	15.2
Klebsiella pneumoniae	785	12.9
Staphylococcus aureus	688	11.3
Coagulase-negative staphylococci	483	7.9
Streptococcus pneumoniae	293	4.8
Escherichia coli	290	4.8
Haemophilus influenzae	238	3.9

(*Continued*)

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Table 2 (Continued).

Organisms	Number of Strains	% (n=6079)
Stenotrophomonas maltophilia	208	3.4
Enterobacter cloacae	191	3.1
Enterococcus faecium	157	2.6
Serratia marcescens	71	1.2
Moraxella (Branh.) catarrhalis	56	0.9
Enterococcus faecalis	48	0.8
Burkholderia cepacia	46	0.8
Enterobacter aerogenes	31	0.5
Klebsiella oxytoca	31	0.5
Others*	320	5.3

Note: *Bacteria other than the list.

sulfamethoxazole (51.7% vs 19.9%), and levofloxacin (43.1% vs 4.2%). Both strains exhibited the highest sensitivity to linezolid and vancomycin. In addition, MRSA demonstrated significantly higher resistance rates than methicillin-susceptible *S. aureus* (MSSA) to penicillin G (100% vs 84.1%), tetracycline (39.2% vs 11.0%), clindamycin (66.5% vs 27.3%), and erythromycin (89.1% vs 65.5%), but lower resistance to gentamicin (5.0% vs 17.6%) and trimethoprim-sulfamethoxazole (5.0% vs 27.1%) (all $P<0.05$). MRCNS strains showed significantly higher resistance rates than MSCNS to the vast majority of the tested antimicrobial agents. The differences were particularly pronounced for ciprofloxacin (42.8% vs 1.5%), levofloxacin (52.1% vs 2.3%), and trimethoprim-sulfamethoxazole (59.0% vs 18.6%) (all $P<0.05$) (Table 3).

Distribution of MRSA and MRCNS

As shown in Figure 5, the number of MRCNS isolates was always higher than that of MRSA isolates, and the overall trend was relatively stable The proportion of MRCNS cases fluctuated between 70% and 90%, reaching a maximum of 88.1% in 2014 and a minimum of 71.4% in 2020. The proportion of MRSA has fluctuated between 20% and 40%, reaching a peak of 40.0% in 2018, and a minimum of 22.4% in 2022.

As shown in Figure 6, the detection rate of MRSA was the lowest in children aged 1–3 years (29.4%) and the highest in children aged <1 year (34.5%). The proportion of patients with MRCNS gradually decreased with age. However, in general, the distribution of MRSA and MRCNS at different ages was relatively stable with no statistically significant differences (all $P>0.05$) (Table 4).

Analysis of Antibiotic Susceptibility of Major Gram-Negative Bacteria

The resistance rate of *A. baumannii* to most antibiotics exceeded 70%, with extremely low rates of resistance to polymyxin (0.2%) and tigecycline (5.6%). The resistance rate of *P. aeruginosa* to most antibiotics was less than 10%, but the resistance rates to imipenem, meropenem, and aztreonam were 34.0%, 31.4%, and 26.9%, respectively. The resistance rates of *E. coli* to ampicillin (93.1%), cefuroxime (79.8%), and ceftriaxone (78.7%) were high, whereas those to amikacin (1.7%), imipenem (5.9%), and meropenem (5.9%) were low (Table 5).

Distribution of Common Antimicrobial Resistance Phenotypes in Major Gram-Negative Bacteria

The detection rates of the four antimicrobial resistance phenotypes of *A. baumannii* fluctuated between 2014 and 2023, and remained relatively high. Among them, CR-*A. baumannii* and extended-spectrum cephalosporin-resistant (ECR)-

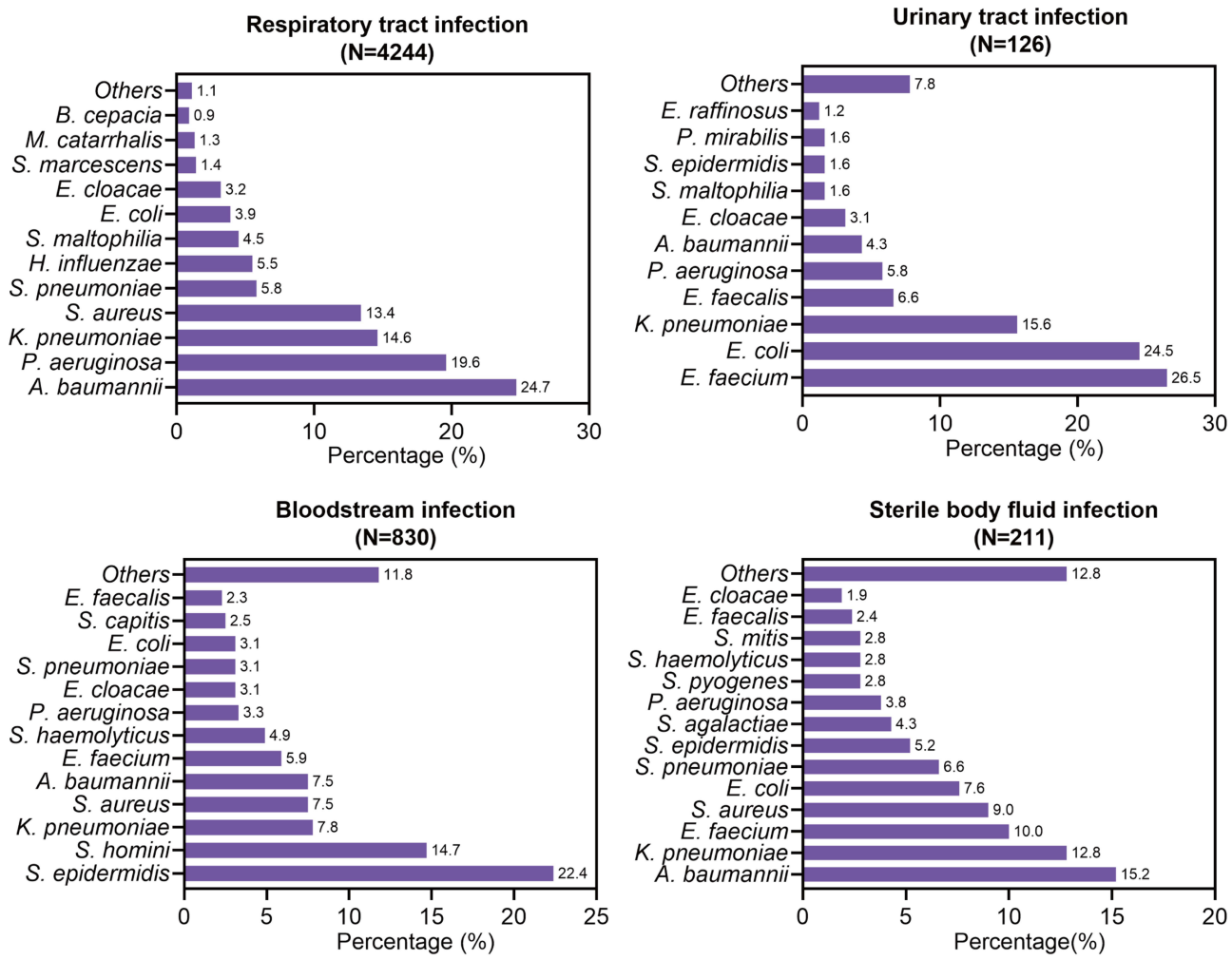

Figure 2 The distribution of pathogenic bacteria in different infection sites.

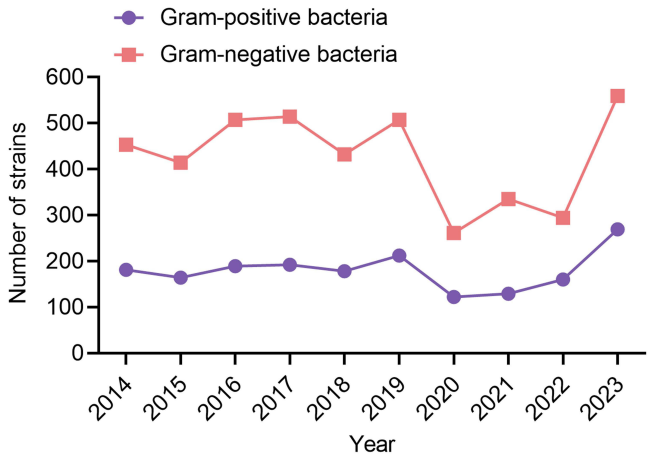

Figure 3 Trends in the number of Gram-negative and Gram-positive bacteria isolated from PICU patients from 2014 to 2023.

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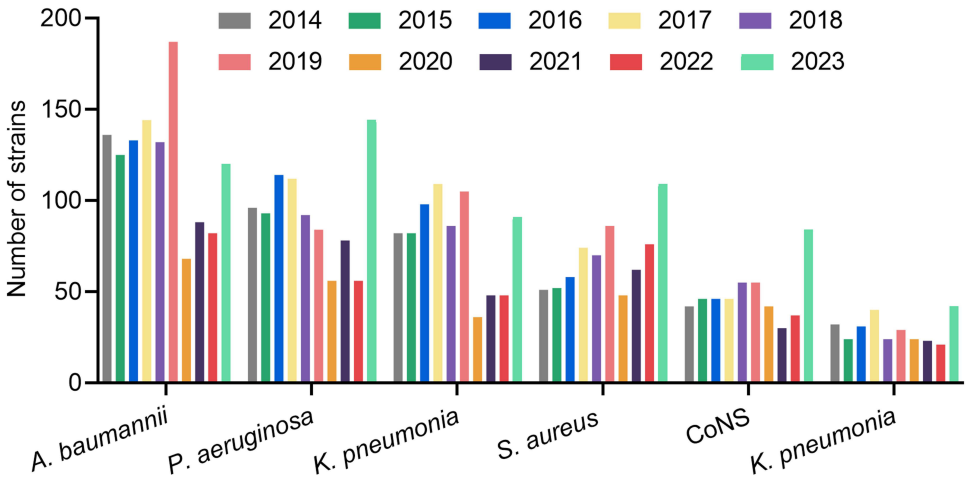

Figure 4 Distribution of the top six bacterial strains detected in PICU patients from 2014 to 2023.

A. baumannii had the highest detection rates in 2019, at 85.0% and 86.1%, respectively. DTR-*A. baumannii* and FQR-*A. baumannii* had the highest detection rate (80.5%) in 2022. The detection rates of DTR-*P. aeruginosa* and FQR-*P. aeruginosa* were less than below 10%. CR-*P. aeruginosa* showed a fluctuating downward trend from 2016 to 2023, with a lowest detection rate of 9.0% in 2023. The detection rate of ECR-*K. pneumoniae* was relatively high but decreased significantly from 81.3% in 2021 to 58.3% in 2022. CR-*K. pneumoniae* increased significantly from 2015 to 2018, and then showed a downward trend. DTR-*K. pneumoniae* and FQR-*K. pneumoniae* showed a rising trend in 2014–2018. The detection rate of ECR-*E. coli* fluctuated between 72.4% and 91.7%. FQR-*E. coli* showed an overall upward but fluctuating trend between 2015 and 2023, with the most significant increase in detection rate occurring in 2016 (from 16.7% to 51.6%). Both DTR-*E. coli* and CR-*E. coli* fluctuated between 0% and 16% with little overall change (Figure 7).

We compared the distribution of the four antimicrobial-resistance phenotypes in different age groups (Figure 8 and Table 4). Notably, the resistance rates for *A. baumannii* phenotypes — including DTR-*A. baumannii*, ECR-*A. baumannii*,

Table 3 Antimicrobial Resistance of *S. aureus* and *CoNS*

Antimicrobial Agents	Rate of Resistant (%)			*P* Value (MRSA vs MSSA)	Rate of Resistant (%)			*P* Value (MRCNS vs MSCNS)
	S. aureus (n=688)	MRSA (n=221)	MSSA (n=461)		CoNS (n=483)	MRCNS (n=390)	MSCNS (n=86)	
Penicillin G	89.2	100.0	84.1	<0.001	94.8	99.7	72.8	<0.001
Oxacillin	32.4	100.0	0.0	<0.001	81.9	100.0	0.0	<0.001
Gentamicin	13.6	5.0	17.6	<0.001	24.8	30.0	1.2	<0.001
Rifampin	2.0	5.9	0.2	<0.001	19.4	23.3	1.2	<0.001
Ciprofloxacin	4.4	7.4	2.4	0.002	34.9	42.8	1.5	<0.001
Tetracycline	20.8	39.2	11.0	<0.001	20.0	21.9	12.1	0.017
Levofloxacin	4.2	6.8	3.0	0.017	43.1	52.1	2.3	<0.001
Moxifloxacin	4.1	6.8	2.8	0.013	23.4	27.9	2.4	<0.001
Trimethoprim-Sulfamethoxazole	19.9	5.0	27.1	<0.001	51.7	59.0	18.6	<0.001
Clindamycin	39.9	66.5	27.3	<0.001	42.1	48.7	11.6	<0.001
Erythromycin	73.1	89.1	65.5	<0.001	89.0	92.3	75.6	<0.001
Linezolid	0.0	0.0	0.0	-	2.5	3.1	0.0	0.182
Vancomycin	0.0	0.0	0.0	-	0.0	0.0	0.0	-

Note: *P*-value not computable (denoted "-").
Abbreviations: MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; CoNS, coagulase-negative *Staphylococci*; MRCNS, methicillin-resistant coagulase-negative *Staphylococci*; MSCNS, methicillin-susceptible coagulase-negative *Staphylococci*.

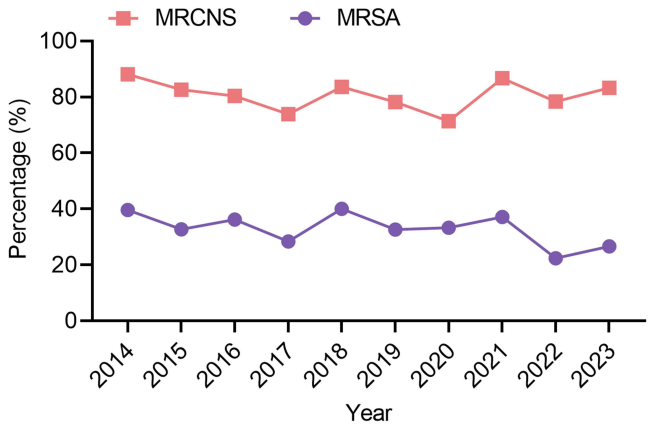

Figure 5 Trends in detection rates of MRSA and MRCNS in PICU from 2014 to 2023.
Abbreviations: MRSA, methicillin-resistant *S. aureus*; MRCNS, methicillin-resistant coagulase-negative *Staphylococci*.

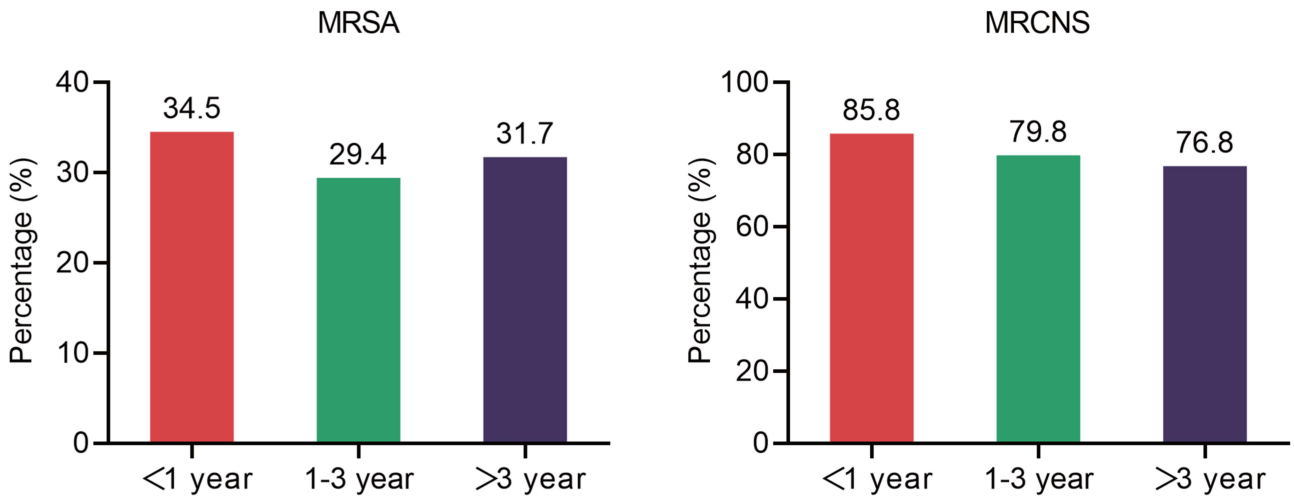

Figure 6 Distribution of MRSA and MRCNS in different age groups.
Abbreviations: MRSA, methicillin-resistant *S. aureus*; MRCNS, methicillin-resistant coagulase-negative *Staphylococci*.

CR-*A. baumannii*, and FQR-*A. baumannii*— consistently increased with age, showing significantly higher proportions in children older than 3 years compared to those under 1 year (all $P<0.05$). Conversely, ECR-*P. aeruginosa* and ECR-*K. pneumoniae* exhibited a declining trend with increasing age. Additionally, FQR-*E. coli* demonstrated a significant age-

Table 4 Statistical Analysis Results of Age Groups with Specific Antimicrobial Resistance Phenotypes

Specific Antimicrobial Resistance Phenotypes	Number (%)			χ^2	*P* Value	*P<0.05*
	<1 Year	1-3 Year	>3 Year			
MRSA	77(34.5)	42(29.4)	102(31.7)	1.118	0.572	-
MRCNS	151(85.8)	87(79.8)	152(76.8)	4.963	0.083	-
DTR-ABA	214(57.8)	223(66.6)	358(69.9)	14.161	0.001	+
ECR-ABA	269(72.7%)	264(78.8)	414(80.9)	8.541	0.014	+
CR-ABA	252(68.1)	259(77.3)	400(78.1)	12.933	0.002	+

(*Continued*)

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Table 4 (Continued).

Specific Antimicrobial Resistance Phenotypes	Number (%)			χ^2	*P* Value	*P<0.05*
	<1 Year	1-3 Year	>3 Year			
FQR-ABA	234(63.2)	241(71.9)	384(75.0)	14.708	0.001	+
DTR-PAE	14(4.7)	18(7.2)	15(4.0)	3.430	0.180	-
ECR-PAE	59(19.6)	51(20.5)	48(12.8)	8.333	0.016	+
CR-PAE	118(39.2)	89(35.7)	115(30.6)	5.615	0.060	-
FQR-PAE	6(2.0)	10(4.0)	12(3.2)	1.962	0.375	-
DTR-KPN	89(24.3)	44(23.5)	57(24.6)	0.066	0.968	-
ECR-KPN	311(85.0)	150(80.2)	173(74.6)	9.941	0.007	+
CR-KPN	135(36.9)	62(33.2)	81(34.9)	0.789	0.674	-
FQR-KPN	86(23.5)	53(28.3)	72(31.0)	4.372	0.112	-
DTR-ECO	10(6.7)	4(7.0)	2(2.4)	2.164	0.339	-
ECR-ECO	118(78.7)	47(82.5)	65(78.3)	0.432	0.806	-
CR-ECO	10(6.7)	5(8.8)	2(2.4)	5.472	0.066	-
FQR-ECO	54(36.0)	28(49.1)	46(55.4)	8.889	0.012	+

Abbreviations: MRSA, methicillin-resistant *S. aureus*; MRCNS, methicillin-resistant coagulase-negative *Staphylococci*; DTR, difficult to treat resistance; CR, carbapenem resistance; ECR, extended-spectrum cephalosporin resistant; FQR, fluoroquinolone resistance; ABA, *A. baumannii*; PAE, *P. aeruginosa*; KPN, *K. pneumoniae*; ECO, *E. coli*.

Table 5 Resistance of Four Major Gram-Negative Bacteria in PICU

Antimicrobial Agents	*A. baumannii* (n=1217)		*P. aeruginosa* (n=926)		*K. pneumonia* (n=785)		*E. coli* (n=290)	
	N	R (%)	N	R (%)	N	R (%)	N	R (%)
Ciprofloxacin	1217	70.5	917	3.1	785	26.1	288	44.1
Gentamicin	1217	75.6	918	7.0	785	41.9	104	41.3
Amikacin	1217	66.1	918	3.6	785	14.0	289	1.7
Meropenem	1217	74.6	918	31.4	784	35.5	289	5.9
Imipenem	1217	74.2	918	34.0	785	34.8	289	5.9
Cefepime	1216	77.3	917	14.3	784	71.0	289	64.0
Ceftazidime	1216	74.4	918	12.1	785	64.3	289	40.5
Aztreonam	–	–	918	26.9	433	71.4	104	51.0
Piperacillin-Tazobactam	1216	76.1	918	9.3	512	54.7	104	21.2
Ampicillin-sulbactam	1215	71.7	-	-	432	81.9	-	-
Trimethoprim-Sulfamethoxazole	1215	68.5	-	-	784	57.0	289	60.9
Levofloxacin	1206	67.1	-	-	428	32.7	102	57.8
Colistin	1198	0.2	-	-	-	-	-	-
Tetracycline	1045	67.9	-	-	-	-	-	-
Piperacillin	543	78.8	918	12.4	-	-	-	-
Tigecycline	409	5.6	-	-	367	0.0	-	-
Tobramycin	401	68.3	890	4.0	370	22.2	101	15.8
Cefoperazone-sulbactam	-	-	908	21.7	780	26.0	-	-
Cefuroxime	-	-	-	-	-	-	277	79.8
Cefatriaxone	401	73.1	-	-	724	78.3	286	78.7
Minocycline	401	22.9	-	-	-	-	-	-
Ampicillin	-	-	-	-	-	-	288	93.1
Amoxicillin-clavulanic acid	-	-	-	-	-	-	278	24.5
Cefoxitin	-	-	-	-	-	-	283	14.1

Abbreviations: n/N, number of strains; R, drug resistance rate; "–", Not detected.

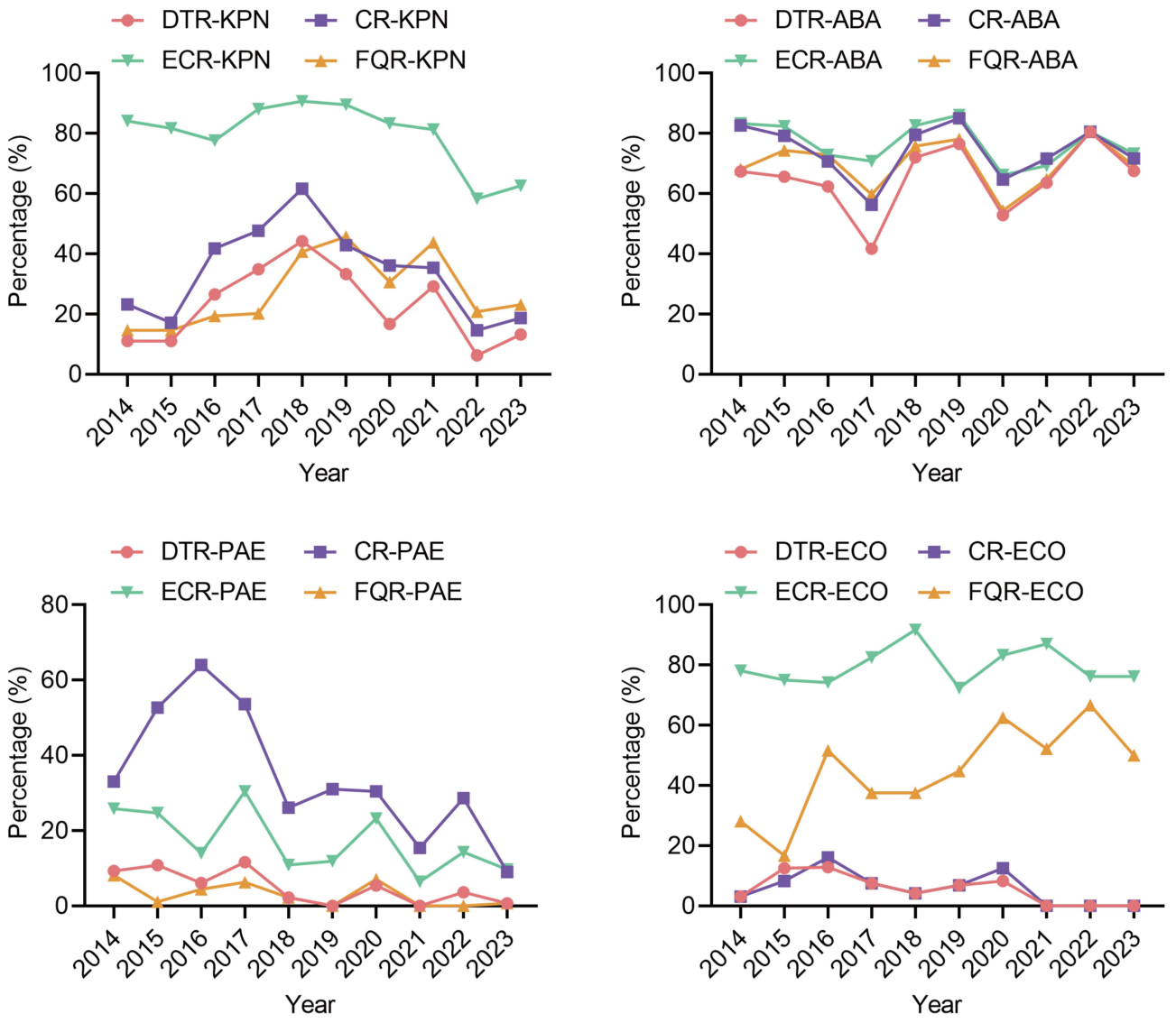

Figure 7 Trends in different resistance phenotypes of major Gram-negative bacteria from 2014 to 2023.
Abbreviations: DTR, difficult to treat resistance; CR, carbapenem resistance; ECR, extended-spectrum cephalosporin resistant; FQR, fluoroquinolone resistance. ABA, *A. baumannii*; PAE, *P. aeruginosa*; KPN, *K. pneumoniae*; ECO, *E. coli*.

dependent rise in resistance. In contrast, the prevalence of MRSA, MRCNS, DTR-*P. aeruginosa*, DTR-*K. pneumoniae*, DTR-*E. coli*, ECR-*E. coli*, CR-*P. aeruginosa*, CR-*K. pneumoniae*, CR-*E. coli*, FQR-*P. aeruginosa*, and FQR-*K. pneumoniae* did not differ significantly among the three age groups (all $P>0.05$).

Discussion

Infections in intensive care units (ICUs) pose a global challenge. The infection rate in developing countries is 8% higher than in developed nations. This situation is exacerbated by severe antimicrobial resistance, which not only increases patient mortality but also places a greater burden on public health systems, creating a vicious cycle.[13,14] Although China has introduced multiple policies in recent years regarding the clinical use of antimicrobial agents, the current state of drug resistance remains severe.

Respiratory infections are the most common type of hospital-acquired infections in ICUs.[15] This study reveals that the primary pathogens causing respiratory infections in PICU children are *A. baumannii* (24.7%), *P. aeruginosa* (19.6%), *K. pneumoniae* (14.6%), and *S. aureus* (13.4%). However, a study by Zhu et al showed that the most frequently detected

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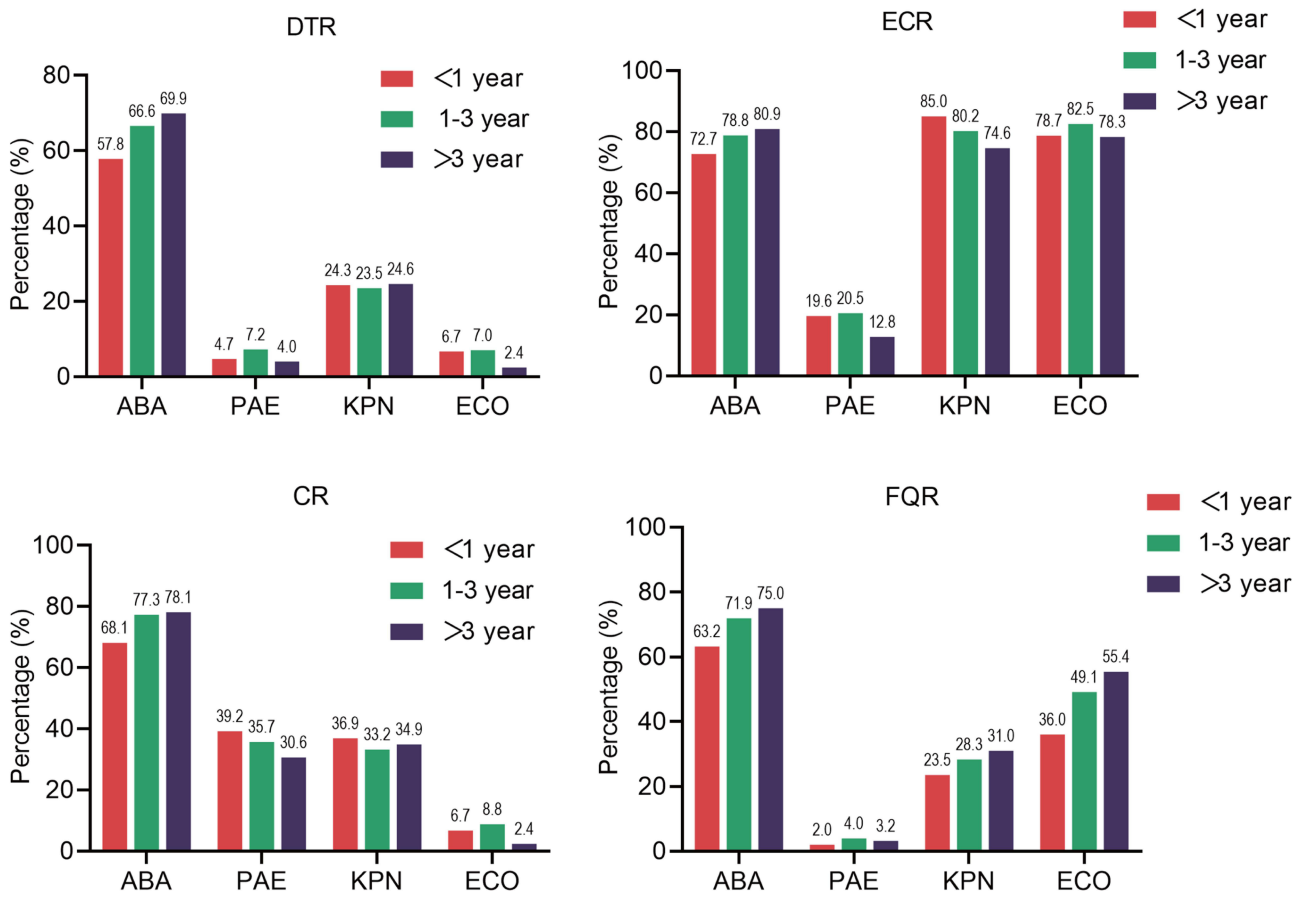

Figure 8 Distribution of four antimicrobial resistance phenotypes in different age groups.
Abbreviations: DTR, difficult to treat resistance; CR, carbapenem resistance; ECR, extended-spectrum cephalosporin resistant; FQR, fluoroquinolone resistance. ABA, *A. baumannii*; PAE, *P. aeruginosa*; KPN, *K. pneumoniae*; ECO, *E. coli*.

pathogens causing respiratory infections in children were *Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumoniae and S. aureus*,[16] which differs significantly from our data. *A. baumannii, P. aeruginosa*, and *K. pneumoniae* are typical pathogens causing hospital-acquired pneumonia in ICUs.[17] These bacteria possess strong acquired resistance mechanisms, such as carbapenemases in *A. baumannii* and porin mutations in *P. aeruginosa*.[18,19] They can also form biofilms and exhibit strong environmental adaptability. For instance, *A. baumannii* can survive on dry surfaces for months,[18] and *P. aeruginosa* can survive in disinfectants.[20] Thus, the epidemic nature of pathogenic bacteria in the ICU is essentially the result of a combination of host immune deficiencies, evolution of pathogen resistance, and exposure to a unique ICU environment.

This study shows that the primary pathogens causing urinary tract infections in the PICU were *E. faecium* (26.5%), *E. coli* (24.5%), and *K. pneumoniae* (15.6%). This is consistent with a previous finding that *E. coli* is the main pathogen in pediatric urinary tract infections.[21] However, the proportion of *E. faecium* in this study was relatively high, which may be due to the overuse of broad-spectrum antibiotics. This overuse leads to the dissemination and colonization of *E. faecium*, which is originally a commensal bacterium in human and animal intestines, significantly increasing the risk of infection. Additionally, PICU children often undergo urinary tract instrumentation or have abnormal urinary tract physiology, causing opportunistic pathogens like *E. faecium* to become one of the most common pathogens in hospital-acquired infections. Our study indicated that the main pathogens causing sterile body fluid infections in the PICU include *A. baumannii, K. pneumoniae, E. faecium*, and *S. aureus*. Alhibbu et al found that *K. pneumoniae* and *E. coli* were the dominant pathogens, with *K. pneumoniae* being the core pathogen common to both studies.[22] This suggests that the distribution of pathogens causing sterile body fluid infections varies across different populations or regions. This is

consistent with findings from a study on bacterial epidemiology in Chinese children from 2016 to 2020.[23] When CoNS are detected in blood cultures, contamination is typically considered. Owing to limitations in the research conditions, it is currently impossible to determine whether they are pathogenic.

S. aureus is a significant pathogen that causes suppurative infections in the skin, soft tissues, and other areas. The irrational use of antimicrobial agents has led to drug resistance, significantly increasing the difficulty of preventing and treating *S. aureus* infections.[24] One study indicated that children with sepsis caused by *S. aureus* account for 1% of all PICU admissions, and the mortality rate among these children is significantly higher than the overall PICU mortality rate.[25] Our study shows that the overall detection rate of MRSA over the past decade was 32.4%, but it exhibited a downward trend from 2022 to 2023. This decline is attributed to stricter isolation measures implemented for MRSA-infected or colonized patients, such as single-room isolation and restricted personnel movement, which effectively curbed the spread of the pathogen in the wards. A related study also supported this view.[26] Continued efforts to strengthen MRSA infection prevention and control in the PICU are necessary to reduce harm to children. Additionally, our data showed a high susceptibility of *staphylococci* to linezolid and vancomycin, which aligns with the current clinical treatment options for antimicrobial-resistant staphylococcal infections. Moreover, the prevalence level of MRSA in our data did not show significant age-related differences (P=0.572), which aligns with the findings in the Infectious Disease Surveillance of Pediatrics (ISPED) report.[23] Additionally, the overall MRSA detection rate in this study (31.9%) closely matches the five-year national average detection rate (35.0%) reported by ISPED. This consistency strongly confirms that MRSA remains an important and stable drug-resistant bacterium among Gram-positive cocci in pediatric infections in China.

Enterobacteriaceae are significant pathogens commonly isolated in clinical settings and, as previously mentioned, play an important role in various types of infections such as respiratory tract infections, urinary tract infections, and bloodstream infections. Carbapenems are commonly used in clinical practice to treat *Enterobacteriaceae* that produce extended-spectrum β-lactamases (ESBLs) and AmpC enzymes. However, the widespread use of these drugs led to the emergence of carbapenem resistance. In recent years, the detection rate of carbapenem-resistant bacteria in children has been increasing.[27] Our data show that, with the exception of CR-*E. coli*, the detection rates of CR-*A. baumannii*, CR-*P. aeruginosa*, and CR-*K. pneumoniae* in children admitted to the PICU (74.9%, 34.8%, and 35.4%, respectively) were significantly higher than the overall rates reported in Chinese children (45.6%, 12.8%, and 19.3%, respectively).[23] This indicates that the prevalence of carbapenem-resistant bacteria in the PICU is more severe and poses greater challenges compared to general pediatric wards.

The issue of multidrug-resistant bacterial infections has become increasingly prominent, posing a particular threat to children.[28] This study analyzed four resistance patterns among Gram-negative bacteria: DTR, CR, ECR, and FQR. Compared with the traditional classifications of multidrug-resistant (MDR) and extensively drug-resistant (XDR), this new categorization method more specifically reflects bacterial resistance to first-line clinical antibiotics that are highly effective and have low toxicity, thereby offering greater practicality and aiding clinicians in rapidly optimizing treatment regimens.[29] Our surveillance data revealed that the detection rates of all four resistance phenotypes in *A. baumannii* exceeded 67%, consistent with the global trend of increasing resistance in *A. baumannii*.[30,31] For *P. aeruginosa*, the detection rate of CR-*P. aeruginosa* was relatively high, which may be attributed to its diverse resistance mechanisms, including the production of metallo-β-lactamases, loss of porin proteins, and efflux pump mutations.[32–34] Notably, the detection rate of CR-*P. aeruginosa* varied significantly across regions, such as the United States (2%), Europe (30%), and South America (50%),[34,35] recent research findings underscore the importance of understanding local CR-*P. aeruginosa* epidemiology. Moreover, resistance in *K. pneumoniae* and *E. coli* is often mediated by highly transmissible epidemic plasmid genes, such as those encoding ESBLs and AmpC enzymes, and is associated with the widespread use of cephalosporins,[36] resulting in significantly higher detection rates of the ECR phenotype than those of other resistance types. Additionally, the prevalence of FQR-*E. coli* has shown a fluctuating upward trend in recent years. A study in the Seattle area reported that the detection rate of the *E. coli* clone ST1193 increased from 1.7% in 2015 to 4.3% in 2021.[37] These strains often carry multiple fluoroquinolone resistance genes and exhibit strong transmission capabilities, contributing to the overall fluctuating increase in resistance rates. The same study also noted that the co-resistance rate of fluoroquinolone-resistant *E. coli* to third-generation cephalosporins increased from 21.5% to 33.1%, likely due to the co-

localization of co-resistance genes (eg, blaCTX-M) and fluoroquinolone resistance genes on mobile genetic elements, leading to co-selection and co-transmission under cross-selective pressure. This is another significant factor driving the increased detection of FQR-*E. coli*.

Among *A. baumannii*, the detection rate of four drug-resistance phenotypes increased with age, which was consistent with the findings of Pan et al's study on CR-A. baumannii.[23] This is likely because infants under one year generally undergo fewer medical interventions, receive fewer types and lower frequency of antibiotics, thereby reducing the opportunities for colonization and infection by drug-resistant *A. baumannii*. In contrast, older children are more mobile within the hospital, increasing their exposure to complex populations and settings, thereby increasing the likelihood of encountering resistant *A. baumannii*.[38] Conversely, ECR-*P. aeruginosa* and ECR-*K. pneumoniae* showed a declining trend with increasing age (all $P<0.05$). This may be related to the immature immune system in infants and young children, potentially making them more susceptible to infections caused by specific resistant strains.[39] Furthermore, FQR-*E. coli* also exhibited a significant age-dependent increase ($P<0.05$), suggesting that the use of this antimicrobial class in older children may be driving the development of resistance.[40] There were no significant differences in the prevalence of other resistance phenotypes (DTR-*P. aeruginosa*, DTR-*K. pneumoniae*, DTR-*E. coli*, ECR-*E. coli*, CR-*P. aeruginosa*, CR-*K. pneumoniae*, CR-*E. coli*, FQR-*P. aeruginosa*, FQR-*K. pneumoniae*) among the three age groups. This indicates that these resistance mechanisms are distributed relatively uniformly within the pediatric population, without significant variation by age stage, potentially reflecting transmission dynamics linked to infection control factors that are not age-dependent.

The high colonization rate of resistant bacteria in the PICU and the associated high risk of outbreaks are major factors contributing to the increased incidence and mortality of sepsis in pediatric patients. This situation arises from multiple factors, including the prevalence of underlying diseases, immature immune function, frequent invasive procedures, prolonged exposure to broad-spectrum antibiotics, and cross-infection due to the high patient density. Therefore, stricter infection control measures should be implemented in the PICU. A comprehensive barrier strategy is recommended, including contact isolation, active screening of colonized patients, enhanced environmental cleaning and disinfection, and standardized antimicrobial use. These measures can effectively interrupt the transmission of resistant bacteria among individuals, and reduce the incidence of hospital-acquired infections.

In conclusion, this study analyzed the distribution of pathogens and trends in antimicrobial resistance over a ten-year period in the PICU of Beijing Children's Hospital, providing crucial evidence for empirical anti-infective therapy. For instance, clinicians may prioritize antibiotics targeting *A. baumannii* and *P. aeruginosa* in respiratory tract infections. For urinary tract infections, attention should be paid to the resistance profiles of *E. coli* and *E. faecium*. However, this study has certain limitations. As a single-center retrospective study, the results may be influenced by hospital-specific environments and clinical practices, and may not fully represent the pathogen distribution and resistance patterns in PICUs across China. Furthermore, this study did not delve into the specific resistance mechanisms of resistant bacteria, which will be addressed in future studies.

Ethics Statement

Our study is a retrospective analysis of anonymized microbiological and demographic data collected during routine hospital laboratory and infection control procedures. No patient interventions were performed, and no additional biological specimens were collected for this research.

In accordance with the International Ethical Guidelines for Health-related Research Involving Humans (Council for International Organizations of Medical Sciences-CIOMS) and the Chinese Regulation on the Management of Human Genetic Resources, this study did not require ethical approval. Therefore, an ethics waiver was granted by the Ethics Committee of Xinjiang Hospital of Beijing Children's Hospital (Waiver Approval Number: XJZZQETYY2025102401). The study utilized only anonymized data derived from standard clinical practice, presented minimal risk to subjects, and waiver of consent did not adversely affect the rights and welfare of the participants.

Author Contributions

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

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Disclosure

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

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