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Vital Surveillances

Surveillance of Multidrug-Resistant Bacterial Infections in Non-Adult Patients — Zhejiang Province, China, 2014–2019

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ABSTRACT

Introduction: Antimicrobial resistance has become a major public health threat globally. The prevalence of multidrug-resistant (MDR) bacterial infections increased substantially among inpatients under 18 years of age in recent years. In Zhejiang Province, China, the trends of drug-resistance in non-adult patients from 2014 to 2019 were monitored, aiming to determine the variation patterns and epidemiological features of MDR strains.

Methods: Patient data were collected from the Annual Review of Hospital Infection Resistance Survey in Zhejiang Province, 2014–2019. Statistical analysis was performed to analyze the pattern of distribution of five key bacterial pathogens in different age groups, ward settings, and bloodstream infections.

Results: From 2014 to 2019, a total of 30,163 multidrug-resistant strains were identified among 212,252 clinical isolates. The prevalence of extended spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E), carbapenem-resistant Enterobacteriaceae (CRE), carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), and methicillin-resistant *Staphylococcus aureus* (MRSA) were 40.6%, 2.3%, 14.7%, 9.0%, and 27.4%, respectively. The prevalence of these key pathogens was lower than that reported in the national surveillance system (China Antimicrobial Resistance Surveillance System and Infectious Diseases Surveillance of Pediatrics). The prevalence of ESBL-E and CRE decreased since 2015 but that of CRPA and MRSA increased from 2014 to 2018.

Conclusions: Despite an overall decrease in the prevalence of drug-resistant bacteria in 2019, the rising prevalence of MRSA and CRPA still warrant much attention. Multidrug-resistant bacteria prevention and control strategies should be adjusted in a timely manner based on the surveillance results.

The prevalence of bacterial resistance to antibiotics has risen globally since mid-1990s, posing a severe risk to public health (*1*). Multidrug-resistant (MDR) organisms, which were defined as a strain resistant to three or more classes of antimicrobial drugs within the antimicrobial spectrum, pose an increasing challenge to global health.

Despite the increasing global attention to MDR infection, little research has been conducted on MDR infections in non-adult populations. Few available data suggested that epidemiology, risk factors, and outcomes of MDR infections were comparable with those observed in adults (*2*).

Most of the MDR organisms in Chinese children showed decreasing trends in recent years, except for imipenem-resistant *Escherichia coli*, imipenem-resistant *Klebsiella pneumoniae,* and methicillin-resistant *Staphylococcus aureus* (MRSA) (*2*). It is undeniable that multidrug-resistant bacterial infections lead to longer hospital stays and higher mortality rate (*3*). Among them, carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), carbapenem-resistant Enterobacteriaceae (CRE), and extended spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E) were classified as critical priority pathogens and MRSA as high priority pathogen in the *Priority Pathogens List* of the World Health Organization (WHO). Infections caused by those key pathogens have aroused wide public concern.

Constant surveillance of the epidemiological trends of drug-resistant organisms is critical since MDR infections remain strongly associated with treatment failures and high mortality rates, particularly among pediatric patients. This report provides valuable information on MDR organism infections in non-adults in Zhejiang Province that could help facilitate better infection control and healthcare.

METHODS

Clinical data were obtained from the Annual Review of Hospital Infection Resistance Survey in Zhejiang Province, 2014–2019. Hospitals that participated in the study were distributed across 11 cities in Zhejiang Province: Hangzhou, Jiaxing, Huzhou, Shaoxing, Ningbo, Zhoushan, Taizhou, Jinhua, Quzhou, Lishui, and Wenzhou. Hospitals in China are classified into 3 categories (primary, secondary, and tertiary institutions) based on their medical service capacity. All the hospitals in the study were secondary or tertiary hospitals accredited to perform pathogen identification and anti-microbial susceptibility testing (Supplementary Table S1, available at http://weekly.chinacdc.cn/). The prevalence of CRE, ESBL-E, CRAB, CRPA, and MRSA isolates were determined by analyzing data exported from WHONET software (version 5.6, WHO) with SPSS software (version 23.0, SPSS Inc., Chicago, IL, USA). In group comparisons, Pearson's chi-square and Fisher's exact tests were used. In all models, there was statistical significance with $P<0.05$.

RESULTS

A total of 212,252 non-duplicate strains collected from 2014 to 2019 were analyzed in this study. Among them, 30,163 strains were found to be multidrug-resistant. These included 15,758 ESBL-producing strains of the Enterobacteriaceae family (ESBL-E, accounting for 40.6% of Enterobacteriaceae strains), 1,349 CRE (2.3% of Enterobacteriaceae), 881 CRAB (14.7% of *Acinetobacter baumannii*), 507 CRPA (9.0% of *Pseudomonas aeruginosa*), and 11,668 MRSA (27.4% of *Staphylococcus aureus*). MRSA and ESBL-E were the most common pathogens, accounting for 90.9% of all drug-resistant infections (52.2% for ESBL-E and 38.7% for MRSA infections). Sample characteristics were provided in the Supplementary Table S1.

The prevalences of CRAB, CRE, CRPA, MRSA, and ESBL-E recorded in different years were displayed in Figure 1. The prevalence of CRE decreased from 2.7% (95% CI 2.4%–3.0%) in 2016 to 2.1% (95% CI 1.9%–2.4%) in 2019, and the prevalence of ESBL-E also consistently declined from 42.7% (95% CI 41.2%–44.2%) in 2014 to 39.4% (95% CI 38.2%–40.6%) in 2019. The highest prevalence of CRAB (19.8%, 95% CI 17.6%–22.1%), was recorded in 2015, and a decrease was observed afterwards. It is worth noting that the prevalence of CRPA fluctuated during 2014–2016 and increased significantly from 7.18% (95% CI 5.2%–9.5%) in 2017 to 12.7% (95% CI 10.6%–15.0%) in 2019. MRSA appeared to be another emerging threat. The prevalence of MRSA increased significantly from 24.3% (95% CI 23.1%–25.6%) in 2014 to 29.2% (95% CI 28.2%–30.2%) in 2018 and remained at a high level (27.2%, 95% CI 26.3%–28.2%) after dropping in

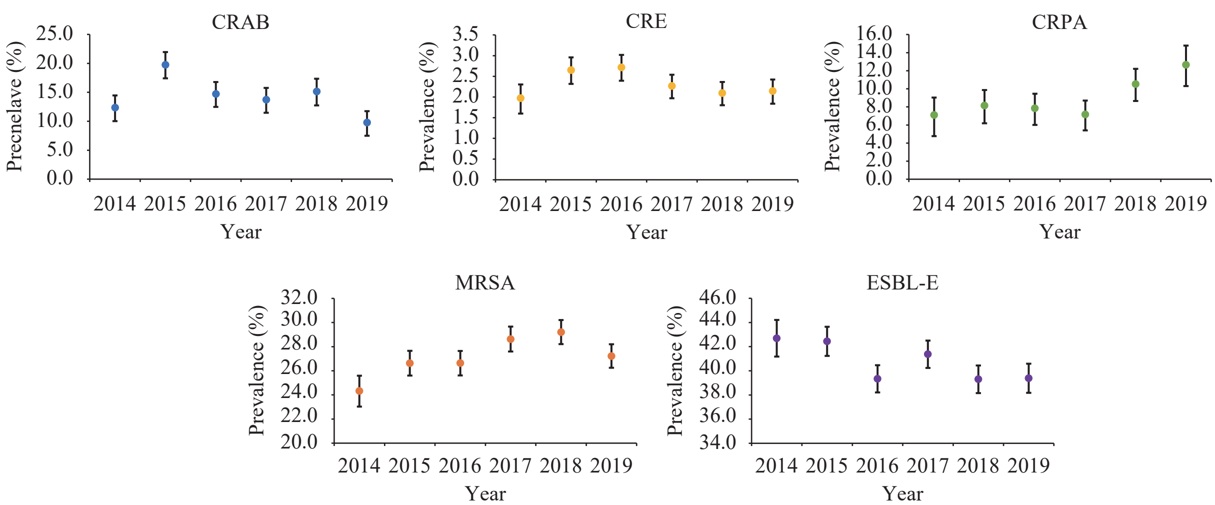

FIGURE 1. The prevalence of CRAB, CRE, CRPA, MRSA, and ESBL-E in non-adult patients — Zhejiang Province, 2014–2019.

Note: The error bars represent 95% CI of the prevalence.

Abbreviations: CRAB=carbapenem-resistant *Acinetobacter baumannii*; CRE=carbapenem-resistant Enterobacteriaceae; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; MRSA=methicillin-resistant *Staphylococcus aureus*; ESBL-E=extended-spectrum β-lactamase-producing Enterobacteriaceae.

TABLE 1. Prevalence and risk analysis of critical pathogens in intensive care unit (ICU) and non-ICU groups in non-adult patients — Zhejiang Province, 2014–2019.

Pathogens	ICU	2014				2015				2016			
		Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*
CRAB (n=889)	Yes	50	38.8 (30.3–47.7)	7.4 (4.7–11.5)	<0.001	113	50.5 (43.3–56.7)	6.7 (4.9–9.3)	<0.001	110	43.7 (37.4–50.0)	12.0 (8.2–17.5)	<0.001
	No	60	7.9 (6.1–10.0)	1		130	12.9 (10.9–15.2)	1		51	6.1 (4.5–7.9)	1	
CRE (n=6,278)	Yes	17	5.7 (3.3–8.9)	3.3 (2.0–5.6)	<0.001	54	7.1 (5.4–9.2)	3.3 (2.4–4.4)	<0.001	54	6.0 (4.5–7.7)	2.6 (1.9–3.5)	<0.001
	No	107	1.8 (1.5–2.2)	1		210	2.3 (2.0–2.6)	1		239	2.4 (2.1–2.7)	1	
CRPA (n=604)	Yes	18	31.0 (19.5–44.5)	9.4 (4.7–18.6)	<0.001	31	24.4 (24.7–45.2)	9.5 (5.6–16.1)	<0.001	30	29.1 (20.6–38.9)	7.2 (4.3–12.1)	<0.001
	No	25	4.6 (3.0–6.7)	1		43	5.3 (3.8–7.0)	1		48	5.4 (4.0–7.1)	1	
MRSA (n=4,361)	Yes	33	21.4 (15.2–28.2)	0.8 (0.6–1.2)	0.393	101	40.9 (34.7–47.3)	2.0 (1.5–2.5)	<0.001	108	41.2 (35.2–47.4)	2.0 (1.5–2.6)	<0.001
	No	1,028	24.4 (23.1–25.8)	1		1,824	26.1 (25.1–27.2)	1		1,852	26.1 (25.1–27.1)	1	
ESBL–E (n=4,124)	Yes	93	45.1 (38.2–52.2)	1.1 (0.8–1.5)	0.467	254	49.3 (44.9–53.7)	1.4 (1.1–1.6)	0.001	307	47.2 (43.3–51.1)	1.4 (1.2–1.7)	<0.001
	No	1,668	42.6 (41.0–44.1)	1		2,525	41.9 (40.6–43.1)	1		2565	38.6 (37.4–39.8)	1	

Pathogens	ICU	2017				2018				2019			
		Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*
CRAB (n=889)	Yes	86	32.2 (26.6–38.2)	6.1 (4.2–8.9)	<0.001	84	40.0 (34.2–48.0)	7.7 (5.3–11.2)	<0.001	33	24.4 (17.5–32.6)	4.4 (2.7–7.3)	<0.001
	No	55	7.2 (5.5–9.3)	1		64	8.3 (6.4–10.5)	1		45	6.8 (5.0–9.0)	1	
CRE (n=6,278)	Yes	56	5.3 (4.0–6.8)	2.8 (2.1–3.8)	<0.001	41	4.9 (3.5–6.5)	2.7 (1.9–3.8)	<0.001	38	4.7 (3.3–6.4)	2.5 (1.8–3.6)	<0.001
	No	189	1.9 (1.7–2.2)	1		174	1.8 (1.6–2.1)	1		170	1.9 (1.6–2.2)	1	
CRPA (n=604)	Yes	26	23.9 (16.2–33.0)	5.8 (3.4–9.8)	<0.001	39	33.1 (24.7–42.3)	5.6 (3.6–8.7)	<0.001	36	33.3 (24.6–43.1)	4.6 (2.9–7.3)	<0.001
	No	46	5.1 (3.8–6.8)	1		88	8.1 (6.5–9.9)	1		77	9.8 (7.8–12.1)	1	
MRSA (n=4,361)	Yes	83	29.0 (23.8–34.7)	1.0 (0.8–1.3)	0.883	123	41.4 (35.5–46.9)	1.7 (1.4–2.2)	<0.001	102	34.3 (29.0–40.0)	1.4 (1.1–1.8)	0.005
	No	2,058	28.6 (27.6–29.7)	1		2,238	28.8 (27.7–29.8)	1		2,118	27.0 (26.0–28.0)	1	
ESBL–E (n=4,124)	Yes	411	52.8 (49.2–56.3)	1.7 (1.4–1.9)	<0.001	320	53.8 (49.7–57.8)	1.9 (1.6–2.2)	<0.001	258	43.4 (39.4–47.5)	1.2 (1.0–1.4)	0.034
	No	2,630	40.0 (38.8–41.2)	1		2,464	38.0 (36.8–39.2)	1		2,263	39.0 (37.7–40.2)	1	

Abbreviations: CRAB=carbapenem-resistant *Acinetobacter baumannii*; CRE=carbapenem-resistant Enterobacteriaceae; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; MRSA=methicillin-resistant *Staphylococcus aureus*; ESBL-E=extended-spectrum β-lactamase-producing Enterobacteriaceae.

2019.

The prevalence and risk analysis of CRAB, CRE, CRPA, MRSA, and ESBL-E in ICU and non-ICU groups were described in Table 1. The prevalence and odds ratio (OR) in ICU group were significantly higher than that in non-ICU group. For CRAB, CRE, and CRPA, the prevalence and OR of ICU group were significantly higher than that in non-ICU group (P<0.001). For MRSA, the prevalence was close in ICU and non-ICU groups in 2014 and 2017, and the OR was not statistically significant in these years. For the remaining year, high prevalence and OR of MRSA in ICU group were observed (P<0.05). For ESBL-E, the prevalence in both the non-ICU group and the ICU group showed a high level, 38.0% to 42.6%, respectively. The OR in ICU group was slightly higher than that in non-ICU group.

Prevalence and risk levels of CRAB, CRE, CRPA, MRSA, and ESBL-E in different age groups were shown in Table 2. For CRAB, the age group with the lowest risk was 1 to 5 years old, and the highest risk age group was 15 to 17 years old. For CRE, the lowest risk age group in 2014 was found to be among children less than 1 year old; all the other age groups exhibited significantly higher risk (P=0.014, <0.05). The prevalence of CRPA in different age groups varied like that of CRAB during the study period, with the lowest risk age group being 1 to 5 years old, and the highest risk age group being 15 to 17 years old. For MRSA, the age group <1 year exhibited the highest risk. The age group <1 year also exhibited the highest risk of ESBL-E infection from 2014 onwards, and other age groups showed similar risk level.

Regarding antimicrobial resistance (AMR) in bloodstream infection (BSI) (Table 3), CRAB exhibited no significant difference between BSI and non-BSI consistently for six years. The risk level of CRE in BSI was significantly higher than non-blood samples (except for in 2014 and in 2018, P>0.05). For CRPA, no significant risk was found, but the prevalence decreased from 12.5% (95% CI 1.6%–38.3%) in 2014 to 3.0% (95% CI 0.1%–15.8%) in 2019. The prevalence of MRSA remained stable throughout, and the risk level in blood samples was only significantly higher than that of non-blood samples in 2015 (OR=1.4, 95% CI 1.0–2.1, P=0.037, <0.05). The prevalence of ESBL-E decreased since 2014 and there was no significant change in the risk of ESBL-E in BSI from 2015 to 2019.

CONCLUSIONS

The overall prevalences of the five key pathogens were lower than that recorded in the China Antimicrobial Resistance Surveillance System (CARSS) and Infectious Diseases Surveillance of Pediatrics (ISPED). Comparison of results from ISPED 2017–2019 (*4–6*) indicated that the prevalence of CRE not only remained at a low level (2.0% to 2.7% from our data *vs.* 8.2% to 10.8% from ISPED), but also exhibited a decreasing trend since 2016 (P=0.004, <0.05). The only exception is carbapenem-resistant *Klebsiella pneumonia*, being an upward trend observable in ISPED (*6*). Though the prevalence of CRPA was lower than the data from ISPED (*5*), the prevalence has risen continuously since 2017. ESBL-E decreased since 2014 but the prevalence remained at a high level. The decrease was also observed in CRAB since 2015 and the prevalence recorded each year was lower than that of CARSS (*2*). The prevalence of MRSA kept increasing in the first few years (24.3% in 2014 to 29.2% in 2018) but then fell in 2019 (27.2%). The trend and prevalence of MRSA was in general agreement with the report of CARSS (27.5%–29.5%) (*2*). These data suggested that the prevalence of MRSA and CRPA should be prioritized due to their high prevalence and increasing trends.

Investigating the pattern of pathogens in the ICU environment, especially for MDR organisms, will help develop specific prevention and control strategies. A recent study in a tertiary teaching hospital in western China reported that *Acinetobacter baumannii* was the leading cause of infection in almost every ICU (*7*). In this study, ESBL-E was the most prevalent pathogen in ICU non-adult patients in Zhejiang Province (43.4% to 53.8%). High prevalences of CRAB, CRPA, and MRSA were also reported, suggesting a complex ICU environment. Risk analysis identified ICU admission as a risk factor for MDR infection, especially those due to CRAB (OR ranged from 4.4 to 12.0) and CRPA (OR ranged from 4.6 to 9.5). This finding is consistent with previous studies (*8–9*). Therefore, monitoring the pathogens exposure and incident infections in ICU environment is critical.

Bloodstream infections (BSIs) represent a major cause of mortality and morbidity worldwide. In addition, antimicrobial-resistant organisms, most notably MRSA and ESBL-E, have emerged as the important etiological agents of community-acquired BSI (*10*). In our study, the prevalence of ESBL-E was the most common pathogen of bloodstream infections,

TABLE 2. Prevalence and risk analysis of critical pathogen in different age groups of non-adult patients — Zhejiang Province, 2014–2019.

Pathogens	Age group, years	2014				2015				2016			
		Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*
CRAB (n=889)	<1	23	14.9 (9.7–21.6)	1.9 (1.1–3.3)	<0.001	113	28.8 (24.4–33.6)	3.0 (2.2–4.3)	<0.001	71	23.1 (18.5–28.3)	5.7 (3.5–9.2)	<0.001
	1–5	39	8.6 (6.2–11.5)	1		61	11.8 (9.1–14.8)	1		25	5.0 (3.3–7.3)	1	
	6–14	26	12.0 (8.0–17.1)	1.5 (0.9–2.5)		37	14.5 (10.4–19.4)	1.3 (0.8–2.0)		41	17.6 (12.9–23.1)	4.0 (2.4–6.8)	
	15–17	22	34.9 (23.3–48.0)	5.7 (3.1–10.6)		32	50.8 (37.9–63.6)	7.8 (4.4–13.6)		24	44.4 (30.9–58.6)	15.2 (7.8–29.7)	
CRE (n=6,278)	<1	16	1.0 (0.6–1.7)	1	0.014	82	2.8 (2.2–3.4)	1	<0.001	94	3.0 (2.4–3.6)	1	<0.001
	1–5	66	2.3 (1.8–3.0)	1.3 (1.3–4.0)		96	2.4 (1.9–2.9)	0.9 (0.6–1.2)		92	2.2 (1.8–2.7)	0.7 (0.5–1.0)	
	6–14	31	2.1 (1.4–2.9)	2.0 (1.1–3.7)		54	2.2 (1.6–2.8)	0.8 (0.5–1.1)		71	2.5 (2.2–3.2)	0.9 (0.6–1.2)	
	15–17	11	2.8 (1.4–5.0)	2.8 (1.3–6.0)		32	6.3 (4.4–8.8)	2.4 (1.6–3.6)		36	6.3 (4.4–8.5)	2.2 (1.5–3.2)	
CRPA (n=604)	<1	8	8.5 (3.7–16.1)	2.9 (1.0–7.9)	0.014	20	11.0 (6.9–16.5)	2.1 (1.1–4.1)	0.009	27	15.7 (10.6–22.0)	3.4 (1.9–6.2)	<0.001
	1–5	8	3.1 (1.4–6.1)	1		20	5.5 (3.4–8.3)	1		21	5.2 (3.3–7.9)	1	
	6–14	13	6.4 (3.5–10.7)	2.1 (0.9–5.2)		23	7.8 (5.0–11.5)	1.5 (0.8–2.7)		24	7.2 (4.7–10.5)	1.4 (0.8–2.6)	
	15–17	14	26.9 (15.6–41.0)	11.4 (4.5–28.9)		11	16.4 (8.5–27.5)	3.4 (1.5–7.5)		6	7.1 (2.7–14.9)	1.4 (0.5–3.6)	
MRSA (n=4,361)	<1	330	36.8 (33.6–40.0)	3.5 (2.3–5.2)	<0.001	497	30.9 (28.6–33.2)	1.3 (1.0–1.6)	<0.001	531	27.8 (25.8–29.9)	1.1 (0.8–1.4)	0.308
	1–5	465	22.6 (20.8–24.5)	1.7 (1.2–2.6)		924	26.0 (24.6–27.5)	1.0 (0.8–1.3)		890	26.8 (25.3–28.4)	1.1 (0.8–1.3)	
	6–14	236	19.7 (17.5–22.1)	1.5 (1.0–2.2)		418	24.0 (22.0–26.1)	0.9 (0.7–1.2)		456	25.1 (23.2–27.2)	0.9 (0.7–1.2)	
	15–17	30	14.4 (9.9–19.9)	1		86	26.2 (21.5–31.3)	1		83	26.2 (21.4–31.4)	1	
ESBL–E (n=4,124)	<1	556	53.0 (49.9–56.1)	2.0 (1.5–2.7)	<0.001	1,002	52.1 (49.8–54.4)	2.0 (1.6–2.6)	<0.001	1025	44.8 (42.8–46.9)	1.6 (1.2–2.0)	<0.001
	1–5	738	40.2 (38.0–42.5)	1.2 (0.9–1.6)		1,004	39.4 (37.5–41.3)	1.2 (0.9–1.5)		970	36.7 (34.9–38.6)	1.1 (0.9–1.4)	
	6–14	383	38.0 (35.0–41.1)	1.1 (0.8–1.5)		665	37.6 (35.4–39.9)	1.1 (0.9–1.4)		762	37.4 (35.3–39.6)	1.2 (0.9–1.5)	
	15–17	84	35.9 (29.8–42.4)	1		108	35.2 (29.8–40.8)	1		115	33.9 (28.9–39.2)	1	

TABLE 2. (Continued)

Pathogens	Age group, years	2017				2018				2019			
		Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*
CRAB (n=889)	<1	41	14.6 (10.7–19.3)	1.8 (1.1–2.9)	<0.001	27	11.9 (8.0–16.8)	1.4 (0.8–3.2)	<0.001	16	8.2 (4.8–13.0)	0.9 (0.5–1.7)	<0.001
	1–5	35	8.8 (6.2–12.0)	1		39	8.9 (6.4–11.9)	1		31	9.0 (6.2–12.5)	1	
	6–14	38	14.1 (10.2–18.9)	1.7 (1.0–2.8)		42	18.4 (13.6–24.1)	2.3 (1.4–3.7)		19	8.8 (5.4–13.3)	1.0 (0.5–1.8)	
	15–17	27	33.8 (23.6–45.2)	5.3 (3.0–9.4)		40	48.2 (37.1–59.4)	9.5 (5.6–16.4)		12	28.6 (15.7–44.6)	4.0 (1.9–8.7)	
CRE (n=6,278)	<1	83	2.7 (2.1–3.3)	1	0.002	74	2.2 (1.8–2.8)	1	<0.001	75	2.4 (1.9–3.0)	1	0.014
	1–5	70	1.8 (1.4–2.2)	0.7 (0.5–0.9)		55	1.5 (1.2–2.0)	0.7 (0.5–1.0)		59	1.8 (1.4–2.3)	0.7 (0.5–1.1)	
	6–14	68	2.1 (1.7–2.7)	0.8 (0.6–1.1)		59	2.1 (1.6–2.7)	0.9 (0.7–1.3)		53	1.9 (1.4–2.5)	0.8 (0.5–1.1)	
	15–17	24	4.0 (2.6–5.9)	1.5 (1.0–2.4)		27	4.6 (3.0–6.6)	2.1 (1.3–3.3)		21	3.8 (2.3–5.7)	1.6 (1.0–2.6)	
CRPA (n=604)	<1	14	7.9 (4.4–12.8)	1.8 (0.8–3.6)	0.007	24	10.6 (6.9–15.2)	1.5 (0.8–2.5)	<0.001	14	8.4 (4.7–13.7)	0.9 (0.5–1.7)	0.001
	1–5	18	4.7 (2.8–7.3)	1		33	7.5 (5.2–10.4)	1		33	9.4 (6.6–13.0)	1	
	6–14	28	7.8 (5.2–11.0)	1.7 (0.9–3.2)		38	8.9 (6.4–12.1)	1.2 (0.7–2.0)		50	16.4 (12.5–21.1)	1.9 (1.2–3.0)	
	15–17	12	15.6 (8.3–25.6)	3.8 (1.7–8.2)		32	28.1 (20.1–37.3)	4.8 (2.8–8.3)		16	22.2 (13.3–33.6)	2.7 (1.4–5.3)	
MRSA (n=4,361)	<1	638	32.1 (30.1–34.2)	1.3 (1.0–1.7)	0.001	709	31.5 (29.6–33.5)	1.1 (0.9–1.4)	0.041	597	29.5 (27.5–27.5)	1.1 (0.9–1.4)	0.074
	1–5	890	27.4 (25.9–29.0)	1.1 (0.8–1.4)		939	28.4 (26.9–30.0)	1.0 (0.8–1.2)		933	26.4 (25.0–27.9)	1.0 (0.8–1.2)	
	6–14	534	27.5 (25.5–29.5)	1.1 (0.8–1.4)		599	28.0 (26.1–29.9)	0.9 (0.7–1.2)		586	26.4 (24.6–28.3)	1.0 (0.7–1.2)	
	15–17	79	26.3 (21.4–31.7)	1		114	29.5 (25.0–34.3)	1		104	27.3 (22.9–32.1)	1	
ESBL–E (n=4,124)	<1	1030	47.7 (25.5–49.8)	1.5 (1.2–1.9)	<0.001	969	42.4 (40.4–44.5)	1.5 (1.2–1.9)	<0.001	891	42.8 (40.7–45.0)	1.5 (1.2–1.9)	<0.001
	1–5	968	39.1 (37.2–41.1)	1.1 (0.9–1.3)		935	39.8 (37.8–41.8)	1.4 (1.1–1.7)		718	38.0 (35.8–40.2)	1.2 (1.0–1.6)	
	6–14	899	38.6 (36.6–40.6)	1.1 (0.8–1.3)		759	36.5 (34.4–38.6)	1.2 (0.9–1.5)		789	38.4 (36.2–40.5)	1.3 (1.0–1.6)	
	15–17	144	37.3 (32.5–42.3)	1		121	32.6 (27.9–37.6)	1		123	33.2 (28.4–38.2)	1	

Abbreviations: CRAB=carbapenem-resistant *Acinetobacter baumannii*; CRE=carbapenem-resistant Enterobacteriaceae; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; MRSA=methicillin-resistant *Staphylococcus aureus*; ESBL-E=extended-spectrum β-lactamase-producing Enterobacteriaceae.

TABLE 3. Prevalence and risk analysis of critical pathogen in BSI non-adult patients — Zhejiang Province, 2014–2019.

BSI		2014				2015				2016			
		Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*
CRAB (n=889)	Yes	5	23.8 (8.2–47.2)	2.3 (0.8–6.3)	0.202	6	20.0 (7.7–38.6)	1.0 (0.4–2.5)	0.973	5	20.0 (6.8–40.7)	1.5 (0.5–4.0)	0.641
	No	105	12.1 (10.0–14.5)	1		237	19.8 (17.5–22.1)	1		156	14.6 (12.5–16.9)	1	
CRE (n=6,278)	Yes	6	2.3 (0.8–4.8)	1.2 (0.5–2.6)	0.737	23	4.8 (3.1–7.1)	1.9 (1.2–3.0)	0.003	23	4.3 (2.8–6.5)	1.7 (1.1–2.6)	0.018
	No	118	2.0 (1.6–2.3)	1		241	2.5 (2.2–2.9)	1		270	2.6 (2.3–3.0)	1	
CRPA (n=604)	Yes	2	12.5 (1.6–38.3)	1.9 (0.4–8.7)	0.722	7	14.9 (6.2–28.3)	2.1 (0.9–4.8)	0.145	3	13.0 (2.8–33.6)	1.8 (0.5–6.2)	0.587
	No	41	7.0 (5.0–9.3)	1		67	7.8 (6.1–9.8)	1		75	7.7 (6.1–9.6)	1	
MRSA (n=4,361)	Yes	25	29.1 (19.8–39.9)	1.3 (0.8–2.1)	0.301	49	34.3 (26.5–42.7)	1.4 (1.0–2.1)	0.037	56	31.5 (24.7–38.8)	1.3 (0.9–1.8)	0.141
	No	1,036	24.2 (23.0–25.5)	1		1876	26.5 (25.5–27.5)	1		1904	26.5 (25.5–27.6)	1	
ESBL–E (n=4,124)	Yes	91	53.8 (46.0–61.5)	1.6 (1.2–2.2)	0.003	102	37.9 (32.1–44.0)	0.8 (0.6–1.1)	0.125	143	41.6 (36.3–47.0)	1.1 (0.9–1.4)	0.386
	No	1,670	42.2 (40.7–43.8)	1		2,677	42.6 (41.4–43.9)	1		2,729	39.2 (38.1–40.4)	1	

BSI		2017				2018				2019			
		Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*	Positive	Prevalence (%) (95% CI)	Odds ratio (95% CI)	*P*
CRAB (n=889)	Yes	7	26.9 (11.6–47.8)	2.4 (1.0–5.8)	0.091	9	33.3 (16.5–54.0)	2.9 (1.3–6.6)	0.016	3	16.7 (3.6–41.4)	1.9 (0.5–6.6)	0.554
	No	134	13.4 (11.3–15.7)	1		139	14.6 (12.4–17.0)	1		75	9.6 (7.6–11.9)	1	
CRE (n=6,278)	Yes	29	5.9 (4.0–8.4)	2.9 (2.0–4.4)	<0.001	14	3.0 (1.6–4.9)	1.5 (0.8–2.5)	0.174	18	4.3 (2.6–6.8)	2.2 (1.3–3.6)	0.002
	No	216	2.1 (1.8–2.4)	1		201	2.1 (1.8–2.4)	1		190	2.0 (1.8–2.4)	1	
CRPA (n=604)	Yes	3	13.6 (2.9–34.9)	2.1 (0.6–7.2)	0.442	3	9.4 (2.0–25.0)	0.9 (0.3–2.9)	1	1	3.0 (0.1–15.8)	0.2 (0.0–1.5)	0.153
	No	69	7.0 (5.5–8.8)	1		124	10.6 (8.9–12.5)	1		112	13.0 (10.9–15.5)	1	
MRSA (n=4,361)	Yes	33	25.8 (18.5–34.3)	0.9 (0.6–1.3)	0.471	52	34.9 (27.3–43.1)	1.3 (0.9–1.8)	0.123	41	29.3 (21.9–37.6)	1.1 (0.8–1.6)	0.581
	No	2,108	28.7 (27.7–29.7)	1		2,309	29.1 (28.1–30.1)	1		2179	27.2 (26.2–28.2)	1	
ESBL–E (n=4,124)	Yes	145	43.4 (38.0–48.9)	1.1 (0.9–1.4)	0.44	134	41.6 (36.2–47.2)	1.1 (0.9–1.4)	0.385	117	41.2 (35.4–47.2)	1.1 (0.8–1.4)	0.522
	No	2,896	41.3 (40.1–42.4)	1		2,650	39.2 (38.0–40.4)	1		2,404	39.3 (38.1–40.5)	1	

Abbreviations: BSI=blood stream infection; CRAB=carbapenem-resistant *Acinetobacter baumannii*; CRE=carbapenem-resistant Enterobacteriaceae; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; MRSA=methicillin-resistant *Staphylococcus aureus*; ESBL-E=extended-spectrum β-lactamase-producing Enterobacteriaceae.

followed by MRSA. The results agreed with the observations from a population-based and large multicenter cohort study in the US and Europe (*11*). The high prevalence of ESBL-E may be related to inappropriate antibiotic use. One study showed that clinical isolation of ESBL-producing *E. coli* or ESBL-producing *Klebsiella* spp. was closely linked to the third-generation cephalosporin treatment (*12*).

In China, third-generation cephalosporin is the most common antibiotics to treat infections in neonates and older children and therefore may be overused in hospitals (*13*). MRSA is another critical pathogen associated with significant clinical morbidity and mortality. The prevalence of MRSA in adults is stable in Zhejiang Province and is similar to that in children (from 33.0% in 2014 to 29.8% in 2017) according to the China Antimicrobial Surveillance Network (*14*). In addition, the MDR pathogens responsible for BSI vary significantly in different regions in China. The predominant pathogen of BSI in our study is ESBL-E, whereas MRSA was the predominant BSI pathogen in Hubei Province (*15*). Risk analysis indicated that BSI had been a risk factor for CRE infection for many years, but a significant difference was not observed among other bacterial groups.

Surveillance carried out in Zhejiang Province indicated that great attention should be paid to MDR organisms, especially for CRPA and MRSA. Some measures should be taken to alleviate the threat of AMR. On the one hand, for hospital-acquired infections, it is necessary to monitor the ICU environment, where broad-spectrum antibiotic use and the presence of MDR bacteria are common. On the other hand, antimicrobial stewardship programs should be advocated, especially for antibiotic prescription in the community since, in accordance with China Health Care Policy, pediatric patients were referred to community hospitals first, where the misuse and overuse of antibiotics occur frequently. Encouragingly, the government of China has started explorations of AMR. In 2016, National Action Plan for Containing Antibacterial Resistance (2016–2020) was published, aiming at reducing antimicrobial resistance through the synergy between national, regional, and local levels. Surveillance of MDR pathogens in clinical patients is necessary for monitoring AMR.

There were some limitations in this surveillance study. First, due to the differences in medical conditions, data collected from hospitals in rural areas might be lower than the actual value. Second, symptomatic patients were more likely to visit medical institutions compared with asymptomatic ones, which may lead to selection bias. Finally, the lack of available data on antibiotic prescription in the community may influence the analysis of community-sourced infection.

In conclusion, conducting surveillance of multidrug-resistant bacterial infections in non-adult patients to depict the prevalence and variation trends will support better diagnosis and clinical treatment.

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SUPPLEMENTARY TABLE S1. Statistical summary of patient recruitment data collected during the study period of 2014–2019, Zhejiang Province.

Item	All years (n=125), No. (%)	2014 (n=42), No. (%)	2015 (n=79), No. (%)	2016 (n=88), No. (%)	2017 (n=84), No. (%)	2018 (n=84), No. (%)	2019 (n=94), No. (%)
Age							
<1 year	53,809 (25.4)	4,754 (21.0)	8,735 (24.7)	9,576 (22.8)	10,001 (25.8)	11,081 (30.0)	9,662 (26.3)
1–5 year	95,639 (45.1)	11,212 (49.4)	16,420 (46.5)	20,701 (49.1)	16,570 (42.8)	15,054 (40.8)	15,682 (42.7)
6–14 year	52,815 (24.9)	5,437 (24.0)	8,516 (24.1)	9,786 (23.3)	10,361 (26.8)	9,060 (24.6)	9,655 (26.3)
15–17 year	9,989 (4.7)	1,286 (5.7)	1,658 (4.7)	1,865 (4.4)	1,762 (4.6)	1,702 (4.6)	1,716 (4.7)
Outpatient/inpatient							
Outpatient	24,185 (11.4)	3,556 (15.7)	4,385 (12.4)	4,265 (10.2)	4,230 (10.9)	3,093 (8.4)	4,656 (12.7)
Inpatient	188,067 (88.6)	19,133 (84.3)	30,944 (87.6)	37,663 (89.8)	34,464 (89.1)	33,804 (91.6)	32,059 (87.3)
No. of hospital beds							
<800	26,322 (12.4)	1,314 (5.8)	4,416 (12.5)	4,918 (11.7)	5,219 (13.7)	4,225 (11.5)	6,158 (16.8)
≥800	185,930 (87.6)	21,375 (94.5)	30,913 (87.5)	37,010 (88.3)	33,403 (86.3)	32,672 (88.5)	30,557 (83.2)
Hospital rank							
Tertiary-A hospital	156,016 (73.5)	17,635 (77.7)	26,093 (73.9)	27,505 (65.6)	29,127 (75.3)	28,410 (77.0)	27.246 (74.2)
Tertiary-B hospital	42,189 (19.9)	5,054 (22.3)	7,138 (20.2)	11,400 (27.2)	6,990 (18.1)	6,079 (16.5)	5,528 (15.1)
Secondary-A hospital	13,207 (6.2)	0	1,968 (5.6)	2,898 (6.9)	2,328 (6.2)	2,188 (5.9)	3,771 (10.3)
Secondary-B hospital	840 (0.4)	0	130 (0.4)	125 (0.3)	195 (0.5)	220 (0.5)	170 (0.5)
Location							
Northern plain	107,262 (50.5)	10,680 (47.1)	19,092 (54.0)	22,730 (54.2)	19,801 (51.2)	17,734 (48.1)	17,225 (46.9)
Coastal area	77,764 (36.3)	9,229 (40.7)	11,990 (33.9)	13,689 (32.6)	13,591 (35.1)	14,759 (40.0)	14,506 (39.5)
Inland area	27,226 (12.8)	2,780 (12.3)	4,247 (12.0)	5,509 (13.1)	5,302 (13.7)	4,404 (11.9)	4,984 (13.6)
City							
Hangzhou	57,054 (26.9)	2,839 (12.5)	10,477 (29.7)	10,346 (24.7)	12,219 (31.6)	11,090 (30.1)	10,083 (27.5)
Jiaxing	30,029 (14.1)	5,427 (23.9)	5.766 (16.3)	5,105 (12.2)	5,163 (13.3)	4,107 (11.1)	4,461 (12.2)
Huzhou	3,946 (1.9)	955 (4.2)	882 (2.5)	832 (2.0)	291 (0.8)	215 (0.6)	771 (2.1)
Shaoxing	16,233 (7.6)	1,459 (6.4)	1,967 (5.6)	6,447 (15.3)	2,128 (5.5)	2,322 (6.3)	1,910 (5.2)
Ningbo	17,265 (8.1)	689 (3.0)	3,134 (8.9)	3,325 (7.9)	3,101 (8.0)	3,470 (9.4)	3,546 (9.7)
Taizhou	18,172 (8.6)	2,031 (9.0)	1,549 (4.4)	3,462 (8.3)	3,072 (7.9)	4,169 (11.3)	3,889 (10.6)
Wenzhou	39,903 (18.8)	6,076 (26.8)	6,943 (19.7)	6,473 (15.4)	7,056 (18.2)	6,690 (18.1)	6,665 (18.2)
Zhoushan	2,424 (1.1)	433 (1.9)	364 (1.0)	429 (1.0)	362 (0.9)	430 (1.2)	406 (1.1)
Jinhua	13,874 (6.5)	1,701 (7.5)	2,330 (6.6)	3,259 (7.8)	3,157 (8.2)	1,768 (4.8)	1,659 (4.5)
Lishui	8,476 (4.0)	516 (2.3)	1,436 (4.1)	1,291 (3.1)	1,232 (3.2)	1,619 (4.4)	2,182 (6.5)
Quzhou	4,876 (2.3)	563 (2.5)	481 (1.4)	595 (2.3)	913 (2.4)	1,017 (2.8)	943 (2.6)