Journal of Microbiology, Immunology and Infection 56 (2023) 84—92

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Original Article

Clinical characteristics and outcomes of carbapenem-resistant *Enterobacterales* bacteremia in pediatric patients

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Received 30 April 2022; received in revised form 28 September 2022; accepted 30 September 2022
Available online 2 November 2022

KEYWORDS
Bacteremia;
Carbapenem-resistant *Enterobacterales*;
Children;
Taiwan

Abstracts *Background/purpose:* Clinical data on carbapenem-resistant *Enterobacterales* (CRE) bacteremia in the pediatric population are limited. This study investigated the clinical characteristics and outcomes of pediatric CRE bacteremia.
Methods: Clinical data on bacteremia caused by carbapenem-susceptible and carbapenem-resistant *Enterobacterales*, including *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Serratia marcescens*, *Proteus mirabilis*, *Citrobacter* spp., and *Morganella* spp., in pediatric patients from a children's hospital in Taiwan were retrospectively retrieved and analyzed.
Results: From January 2013 to December 2021, 471 clinical isolates of *Enterobacterales* bacteremia were identified in 451 episodes from 379 pediatric patients. Among all the isolates, the predominant species were *E. coli* (199/471, 42.2%), *Klebsiella* spp. (168/471, 35.6%), and *Enterobacter* spp. (59/471, 12.5%), with carbapenem-resistance rates of 1.5%, 11.9%, and 25.0%, respectively. Overall, 40 (8.4%) showed a carbapenem resistance phenotype. Patients' all-cause mortality rate at 14 days was significantly higher in CRE bacteremia episodes than non-CRE ones (12.5% vs. 3.6%, $p < 0.05$). The predicting factor of a CRE bacteremia episode was the causative agent of *Enterobacter* spp. (adjusted OR of 2.551, CI 1.073—6.066, $p < 0.05$) and ESBL-producing phenotype (adjusted OR 14.268, CI 5.120—39.762, $p < 0.001$).

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https://doi.org/10.1016/j.jmii.2022.09.010

Conclusion: Bloodstream infections caused by CRE are associated with a higher mortality rate in the pediatric population. Attention must be paid to preventing and managing pediatric patients with CRE infections.

Introduction

Gram-negative bacteria (GNB) are common causes of bloodstream infection in children.[1—3] Gram-negative bacteremia can be especially severe in neonates,[4] pediatric oncology patients,[5,6] and patients requiring intensive care. *Enterobacterales*, including *Escherichia coli, Klebsiella pneumoniae, Enterobacter* spp., and non-lactose-fermenting bacteria such as *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, and *Acinetobacter* spp., are the primary pathogens causing gram-negative bacteremia.[4—6]

Resistance to antimicrobial agents is a growing public health threat. In the World Health Organization (WHO) antibiotic-resistant priority pathogen list declared in 2017, resistant GNB, including carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *P. aeruginosa* (CRPA), extended-spectrum β-lactamase (ESBL)-producing *Enterobacterales,* and carbapenem-resistant *Enterobacterales* (CRE), are the most critical groups.[7] Infections with resistant strains of GNB are associated with delayed appropriate antibiotic treatment, prolonged hospitalization, and poor outcome in children.[4,5,8,9] Pediatric CRE infection has been increasing in the United States and has shown to be associated with a worse prognosis in children in Italy and Turkey.[10—13] However, data on CRE infections in infants and children in Taiwan are relatively limited.

This study investigated the clinical presentation, treatment, outcomes, and microbiological features of CRE bacteremia in children of Taiwan.

Methods

Setting

This retrospective study was conducted at the National Taiwan University Children's Hospital (NTUCH), a pediatric medical center in Northern Taiwan with 370 beds, 13 specialty departments of pediatrics and pediatric surgery with general wards and pediatric, infant, and neonate intensive units.

Patients and study design

This study aimed to illustrate the clinical features and impact of carbapenem resistance on invasive GNB infections in children of Taiwan. We focused on bloodstream infections caused by pathogenic *Enterobacterales*, including *E. coli, Klebsiella* spp., *Enterobacter* spp., *Serratia marcescens, Proteus mirabilis, Citrobacter* spp., and *Morganella* spp. The genus Salmonella was not included because carbapenem resistance in Salmonella is rarely seen.[14] Episodes of *Enterobacterales* bacteremia were identified by retrospective searches of positive blood culture results of *Enterobacterales* from the database in the microbiology laboratory of NTUCH. Data on patient demographics, characteristics, and outcomes were compared between CRE and non-CRE episodes. The primary outcome of mortality rate on the 14th day of the episode was used to evaluate bacteremia-related death,[15] and secondary outcomes such as in-hospital mortality were used to assess the long-term prognosis of the patients. The predictive factors for acquisition and outcome of CRE bacteremia were investigated (Fig. 1).

Data collection

All data were retrospectively collected from electronic medical records and reviewed by the investigators. Demographic data included patients' age, sex, and underlying diagnoses categorized by organ systems. Patients were stratified by age <1, 1—6, 7—12, and 13—18 years old because infants accounted for most pediatric GNB bacteremia cases and tended to be more fragile than older children.[16] Clinical data on sources of bacteremia, ward setting during this bacteremia episode, intensive care unit (ICU) admission in the past 6 months, patients' ward setting, and antibiotics usage were recorded. ICU admission during this episode was used as an indirect index of severity. Patient survival status and time were also collected for outcome assessment.

Microbiology

Microbiological tests were performed, and reports were issued by the Microbiology Lab of the Division of Laboratory Medicine, National Taiwan University Hospital (NTUH). Bacterial cultures of blood samples from pediatric patients were performed using an automated microbial detection system (VersaTREK™). Bacterial species were identified using a MALDI-TOF MS system (Bruker MALDI Biotyper). The susceptibility and minimum inhibitory concentration (MIC) of clinical isolates were determined using an automated system for antimicrobial susceptibility testing (VITEK-2™). Susceptibility was determined using the VITEK-2™ system according to the susceptibility breakpoint of the MIC proclaimed by the National Committee for Clinical Laboratory Standards Institute (CLSI M100 23rd to 30th edition) during the study period. MIC breakpoints of resistance for ertapenem, imipenem, and meropenem were 2, 4, and 4 μg/

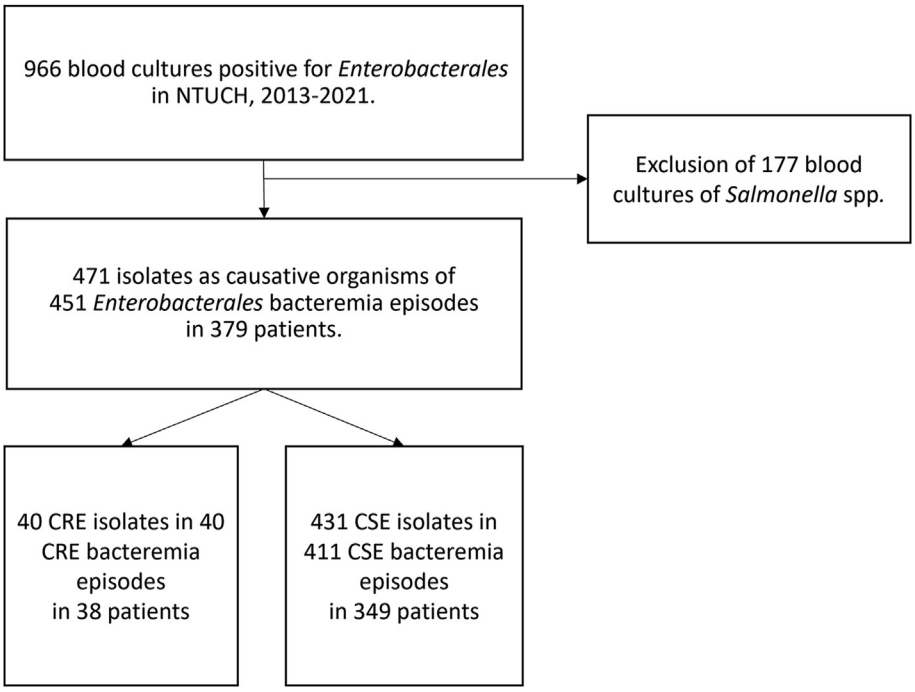

Figure 1. Flow chart of enrollment of cases of pediatric *Enterobacterales* bacteremia in NTUCH, 2013—2021. CRE, carbapenem-resistant *Enterobacterales*; CSE, carbapenem-susceptible *Enterobacterales*.

mL, respectively; breakpoints of intermediate resistance were 1, 2, and 2 μg/mL, respectively. Data on the species, susceptibility, and MIC of the CRE isolates were aggregated and analyzed. Carbapenem resistance rates was also calculated. The laboratory modified the taxonomy of *Enterobacter aerogenes* in 2018, which was replaced by *Klebsiella aerogenes*. This change was also observed in the present study.

Definitions

Children and infants were defined as those aged 18 years or less and under one year of age, respectively. Bacteremia episodes were identified based on positive blood culture records. Multiple sets of positive blood cultures over a time interval of longer than 14 days were regarded as different episodes. Isolates of the same species identified in a single bacteremia episode were regarded as single. Episodes with more than one species isolated were defined as polymicrobial episodes; episodes with any one isolate with a carbapenem-resistant (CR) phenotype were considered CRE episodes.

Carbapenem resistance was defined as non-susceptibility to at least one carbapenem in drug sensitivity testing (DST) for *Enterobacterales* isolates other than *Proteus* spp. and *Morganella* spp., for which the CRE definition was based on ertapenem or meropenem because they are often intrinsically non-susceptible to imipenem.[17,18] Clinical isolates resistant to the 3rd or 4th generation cephalosporins were recognized as ESBL-producing. Bacteremia was considered catheter-related if the diagnostic criteria of the guidelines for catheter-related bloodstream infection (CRBSI) issued by the Infectious Disease Society of America (IDSA) were met. The urinary tract, skin, soft tissue, or lower respiratory tract were considered sources of bacteremia if isolates of blood culture of the same resistance phenotype were also recovered in concomitant urine cultures, skin pus cultures, or sputum cultures in a company by focal infection evidence. Prominent intra-abdominal infection without other infection foci was regarded as the source of bacteremia. Episodes with paired central and peripheral blood cultures that failed to meet the CRBSI criteria of the IDSA guidelines or with peripheral blood culture reports only were classified as isolated bacteremia. In the analysis of antibiotic usage in CRE episodes, appropriate initial antibiotic treatment was defined as the use of a susceptible agent before the DST report was available; targeted antibiotic was defined as effective antibiotic agents according to the DST; treatment failure was defined as mortality on the 14th day of the episode.

Statistical analysis

Numerical variables are shown as mean plus standard deviation or median plus interquartile range (IQR), ordinal variables are shown as median plus IQR, and categorical variables are shown as absolute numbers and percentages in contingency tables. For comparison of numerical variables, Student's t-test, Mann—Whitney U test, or Kruskal—Wallis test was applied. The chi-square test or Fisher's exact test was used to compare independence between categorical variables. Comparisons of the variables between groups were considered statistically significant at a p-value of less than 0.05. To investigate the factors of acquisition of CRE and outcomes of CRE

bacteremia, univariate and stepwise multivariate logistic regression analyses were performed. Factors with a p value < 0.05 in univariate analysis were subjected to stepwise multiple logistic regression analysis, in which a p value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 23.0.

Ethics

The National Taiwan University Hospital Research Ethics Committee approved this study (Institutional Review Board approval No: 202011039RINA). The requirement for informed consent was waived because of the retrospective nature of the study, and the analysis used anonymous clinical data.

Results

Microbiology

From January 2013 to December 2021, 966 blood cultures were positive for *Enterobacterales* in patients aged 18 years or less in the NTUCH. After excluding 177 *Salmonella* spp. and repeated culture results in a given episode, we identified 451 episodes of *Enterobacterales* bacteremia with 471 isolates of causative organisms in 379 patients (Fig. 1). Nine episodes (1.9%) were polymicrobial. *E. coli* (42.2%), *Klebsiella* spp. (35.6%), and *Enterobacter* spp. (12.5%) were the major species in all age groups and throughout the study period (Figs. 2 and 3).

CR strains accounted for 8.4% (40/471), 11.9% (20/168), 25% (15/59), and 1.5% (3/199) of all species, *Klebsiella* spp., *Enterobacter* spp., and *E. coli*, respectively. *Klebsiella* spp. (50%) and *Enterobacter* spp. (37.5%) accounted for most of CR isolates (Table 1). *Enterobacter* spp. harbored the highest carbapenem resistance rate in most years, except for 2017 and 2021 (Fig. 3). The susceptibility of these CRE isolates to carbapenems was divergent, as noted by the wide ranges of MIC, except for that of CR-*Enterobacter* spp. for meropenem. Overall, amikacin showed the highest susceptible rate (38/40, 95%), followed by meropenem (35/40, 87.5%) (Table S2).

Study population and demographics

Of 451 episodes, 248 (55%) episodes occurred in infants younger than one year old and 257 (57%) occurred in male patients. For those having underlying diagnoses (358/451, 79.3%), cardiovascular diseases (100/358, 27.9%, almost congenital heart diseases), hematologic/oncologic diseases (106/251, 29.6%), and gastrointestinal diseases (93/358, 25.9%) were most common categories. Frequently encountered infection sources were isolated bacteremia (200/451, 44.3%), infected catheters (108/203, 43.2%), urinary tract infections (71/251, 28.2%), and intra-abdominal infections (48/251, 19.1%) (Table 2). The proportion of infectious sources in different age groups changed dramatically. Almost all *Enterobacterales* bacteremia episodes in patients aged >7 years were designated as either catheter-related or isolated bacteremia (Fig. 4).

Clinical features, outcomes, and associated factors

CRE episodes vs. non-CRE episodes

Among 451 episodes of *Enterobacterales* bacteremia, 8.8% (40/451) were classified as CRE and 91.1% (411/451) as non-

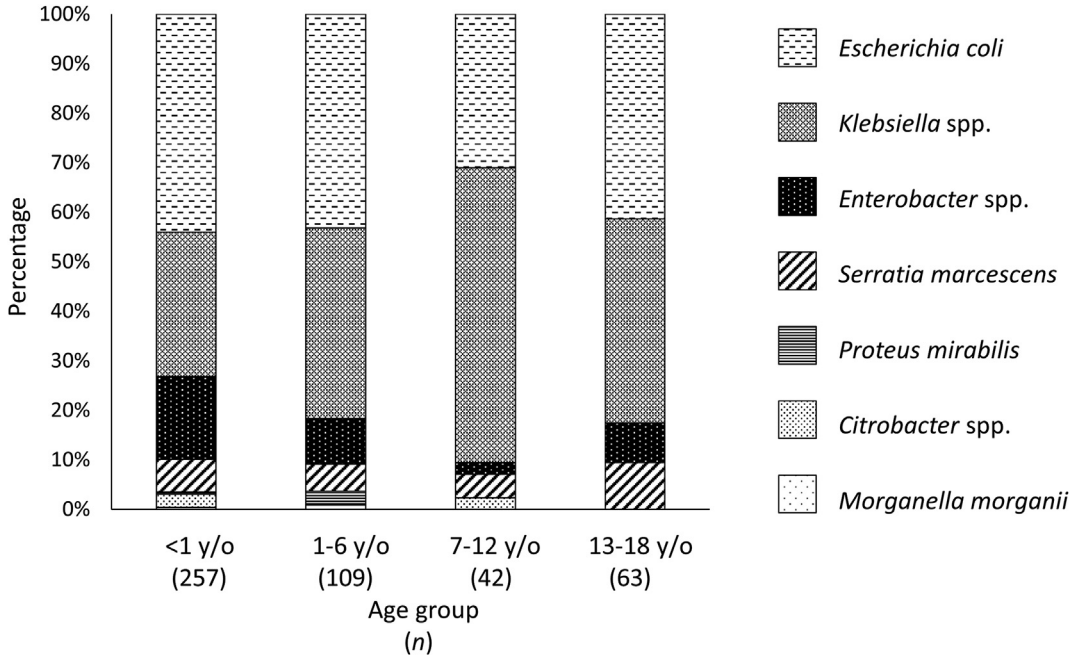

Figure 2. Proportions of causative organisms of *Enterobacterales* bacteremia in groups of age <1, 1–6, 7–12, 13–18 years old, from 2013 to 2021. Proportions of *Klebsiella* spp. and *Enterobacter* spp. between age groups were significantly different, but not for *Escherichia coli* (Data not shown).

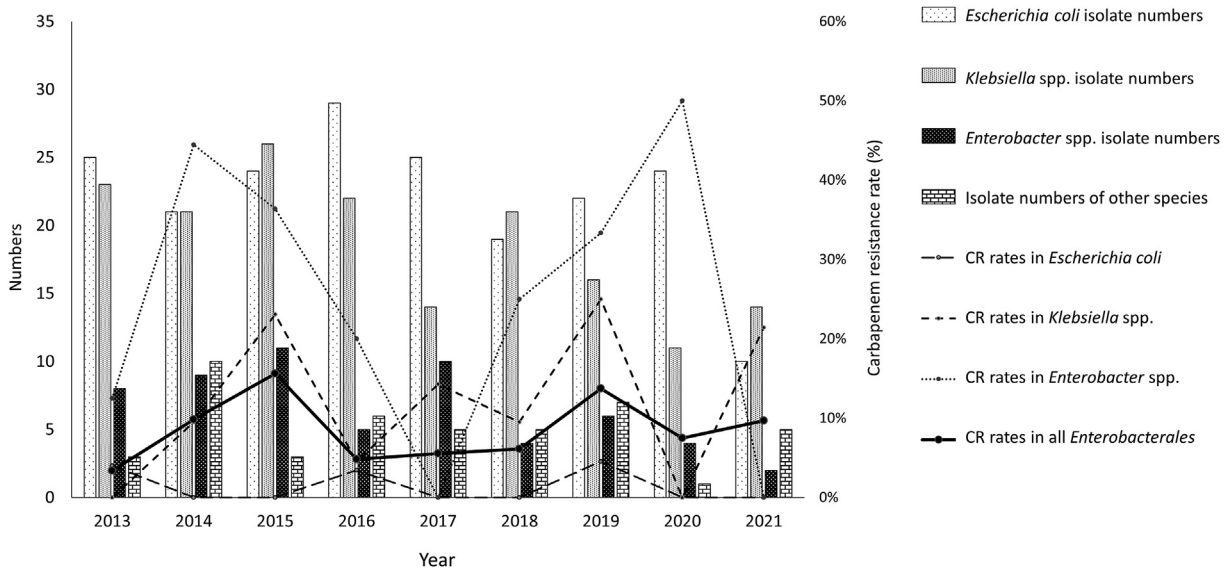

Figure 3. Yearly data from 2013 to 2021 including isolate numbers of *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., and the group of other species including *Serratia* spp., *Citrobacter* spp., *Proteus mirabilis, and Morganella* spp., and carbapenem resistance rates of isolates of *E. coli*, *Klebsiella* spp., and *Enterobacter* spp. respectively and in all *Enterobacterales*. CR, carbapenem resistance.

CRE episodes. Most CRE episodes (27/40, 67.5%) occurred in infants. Patients with CRE episodes had significantly higher rates of ICU admission in the past six months, ICU admission during this episode, and underlying cardiovascular diseases. The CRE group also had a higher proportion of causative agents for *Enterobacter* spp., *Klebsiella* spp., and pathogens with ESBL-producing phenotypes. In multivariate analysis, the predictive factor of a CRE episode was the causative agent of *Enterobacter* spp. (adjusted OR of 2.551, CI 1.073—6.066, $p < 0.05$) and causative agents with ESBL-producing phenotype (adjusted OR of 14.268, CI 5.120—39.762, $p < 0.001$) (Table 2).

The CRE group had worse primary and secondary outcomes, as shown by the significantly higher all-cause 14-day mortality rate (CRE vs. non-CRE, 12.5% vs. 3.6%, $p < 0.05$) and all-cause in-hospital mortality rate (CRE vs. non-CRE, 25% vs. 10%, $p < 0.01$). In the subgroup analysis, infants in the CRE group had worse primary and secondary outcomes

Table 1 Species, numbers, and proportions of carbapenem resistant strains of 471 clinical isolates as causative agents for 451 episodes of *Enterobacterales* bacteremia in pediatric patients during 2013—2021.

Species	Total ($n = 471$)	CR isolates ($n = 40$)	CS isolates ($n = 431$)
Escherichia coli, *n* (%)	199 (42.2)	3 (7.5)	196 (45.5)
Klebsiella spp., *n* (%)	168 (35.6)	20 (50.0)	148 (34.3)
Klebsiella pneumoniae	151	19	18
Klebsiella oxytoca	12	1	11
Klebsiella variicola	4	0	4
Klebsiella aerogenes	1	0	1
Enterobacter spp., *n* (%)	59 (12.5)	15 (37.5)	44 (10.2)
Enterobacter cloacae complex	48	13	35
Enterobacter aerogenes	8	2	6
Enterobacter cloacae	2	0	2
Enterobacter kobei	1	0	1
Serratia marcescens, *n* (%)	31 (6.5)	2 (5.0)	29 (6.7)
Citrobacter spp., *n* (%)	8 (1.7)	0	8 (1.8)
Citrobacter freundii complex	3	0	0
Citrobacter koseri	5	0	0
Proteus mirabilis, *n* (%)	4 (0.8)	0	4 (0.9)
Morganella spp., *n* (%)	2 (0.4)	0	2 (0.4)

Data of categorical variables are shown as number alone or number (percentage).
Abbreviations: CR, carbapenem-resistant; CS, carbapenem-susceptible.

Table 2 Comparison of characteristics between carbapenem-resistant *Enterobacterales* (CRE) episodes and non-CRE episodes, and factors predicting a carbapenem-resistance in *Enterobacterales* bacteremia in children.

Variables, *n* (%)	Total ($n = 451$)	CRE episodes ($n = 40$)	Non-CRE episodes ($n = 411$)	*p*-value	Adjusted OR (95% CI)[b]	*p*-value
Age groups[a]						
<1 y/o	248 (55)	27 (67.5)	221 (53.8)	0.096		
1–6 y/o	102 (22.6)	7 (17.5)	95 (23.1)			
7–12 y/o	40 (8.9)	5 (12.5)	35 (8.5)			
13–18 y/o	61 (13.5)	1 (2.5)	60 (14.6)			
Gender (male)	257 (57.0)	20 (50.0)	237 (57.7)	0.350		
Underlying diagnoses						
Without underlying diagnoses	93 (20.6)	3 (7.5)	90 (21.9)	<0.05	0.776 (0.183–3.290)	0.730
Cardiovascular diseases	100 (22.2)	22 (55.0)	78 (19.0)	<0.05	1.697 (0.640–4.498)	0.288
Immunologic/rheumatologic diseases	13 (2.9)	3 (7.5)	10 (2.4)	0.099		
Gastrointestinal diseases	93 (20.7)	6 (15.0)	87 (21.2)	0.354		
Pulmonary diseases	7 (1.6)	1 (2.5)	6 (1.5)	0.480		
Kidney diseases	14 (3.1)	3 (7.5)	11 (2.7)	0.118		
Hematologic/oncologic diseases	106 (23.5)	2 (5.0)	104 (25.3)	<0.05	0.248 (0.049–1.254)	0.092
Neurological diseases	31 (6.9)	4 (10.0)	27 (6.6)	0.342		
Prematurity	32 (7.1)	2 (5.0)	30 (7.3)	>0.99		
Genetic diseases/congenital anomalies	42 (9.3)	6 (15.0)	36 (8.8)	0.195		
ICU admission in 6 months	167 (37.0)	26 (65.0)	141 (34.3)	<0.05	0.775 (0.141–4.249)	0.769
ICU admission during this episode	164 (36.4)	25 (62.5)	139 (33.8)	<0.05	0.751 (0.138–4.073)	0.739
Etiology						
ESBL-producing phenotype	160 (35.5)	35 (87.5)	125 (30.4)	<0.05	14.268 (5.120–39.762)	<0.05
Escherichia coli	197 (43.7)	3 (7.5)	194 (47.2)	<0.05	0.116 (0.031–0.435)	<0.05
Klebsiella spp.	163 (36.1)	20 (50.0)	143 (34.8)	0.056		
Enterobacter spp.	57 (12.6)	15 (37.5)	42 (10.2)	<0.05	2.551 (1.073–6.066)	<0.05
Outcomes (mortality)						
At 14_{th} days	21 (4.7)	5 (12.5)	15 (3.9)	<0.05	NA	
In hospital	51 (11.3)	10 (25.0)	41 (10.0)	<0.05	NA	

[a] For comparison of the categorized age factors, Fisher's exact test was used, and only one p-value was obtained. Statistical significance was set at $p < 0.05$.

[b] Factors with p value < 0.05 in univariate analysis proceeded to stepwise multivariate logistic regression analysis. A p value of <0.05 was considered significant in multivariate analysis. Cox and Snell R-square = 0.128.

Data of categorical variables are shown as number (percentage).

Abbreviations: CRE, carbapenem-resistant *Enterobacterales*; ESBL, extended-spectrum β-lactamase. ICU, intensive care unit.

Chi-square test or 2-tailed Fisher's exact test was used to compare categorical variables. Statistical significance was set at $p < 0.05$.

(Table S2). In multivariate analysis, only male sex significantly predicted all-cause 14-day mortality (adjusted OR 3.282, CI 1.040–10.357, p < 0.05) (Table S2).

Antibiotic usage in CRE episodes

Only half (20/40, 50%) of patients with CRE episodes were given appropriate initial antibiotic treatment. The inappropriateness of initial antibiotics was significantly associated with penicillin/β-lactamase inhibitor combinations and 3rd generation cephalosporins. Of the 39 patients receiving appropriate antibiotic treatment, 25.6% were administered a combination regimen (80% had a meropenem-based regimen). Meropenem was the most frequently appropriate antibiotic (25/39, 64.1%) among all antibiotics. Combination therapy showed no statiscally significant difference in survival rate with monotherapy (Table S4).

Discussion

To our knowledge, this is one of the first studies on the clinical and microbiological features and outcomes of children with CRE bacteremia in Taiwan. Our data demonstrated that most CREs were *Klebsiella* spp. (50%) followed by *Enterobacter* spp. (37.5%). *Enterobacter* spp. harbored the highest carbapenem resistance rate, similar to findings of a previous multicenter *Enterobacterales* antimicrobial susceptibilities surveillance study in Taiwan.[19] The ranges of carbapenem MIC of these isolates were wide, except for the low MIC of meropenem in CR-*Enterobacter* spp. Variations in MIC values suggest that the resistance mechanisms of these CRE isolates are divergent. Most CRE that are resistant exclusively to ertapenem are caused by ESBL carriage plus porin loss instead of carbapenemase

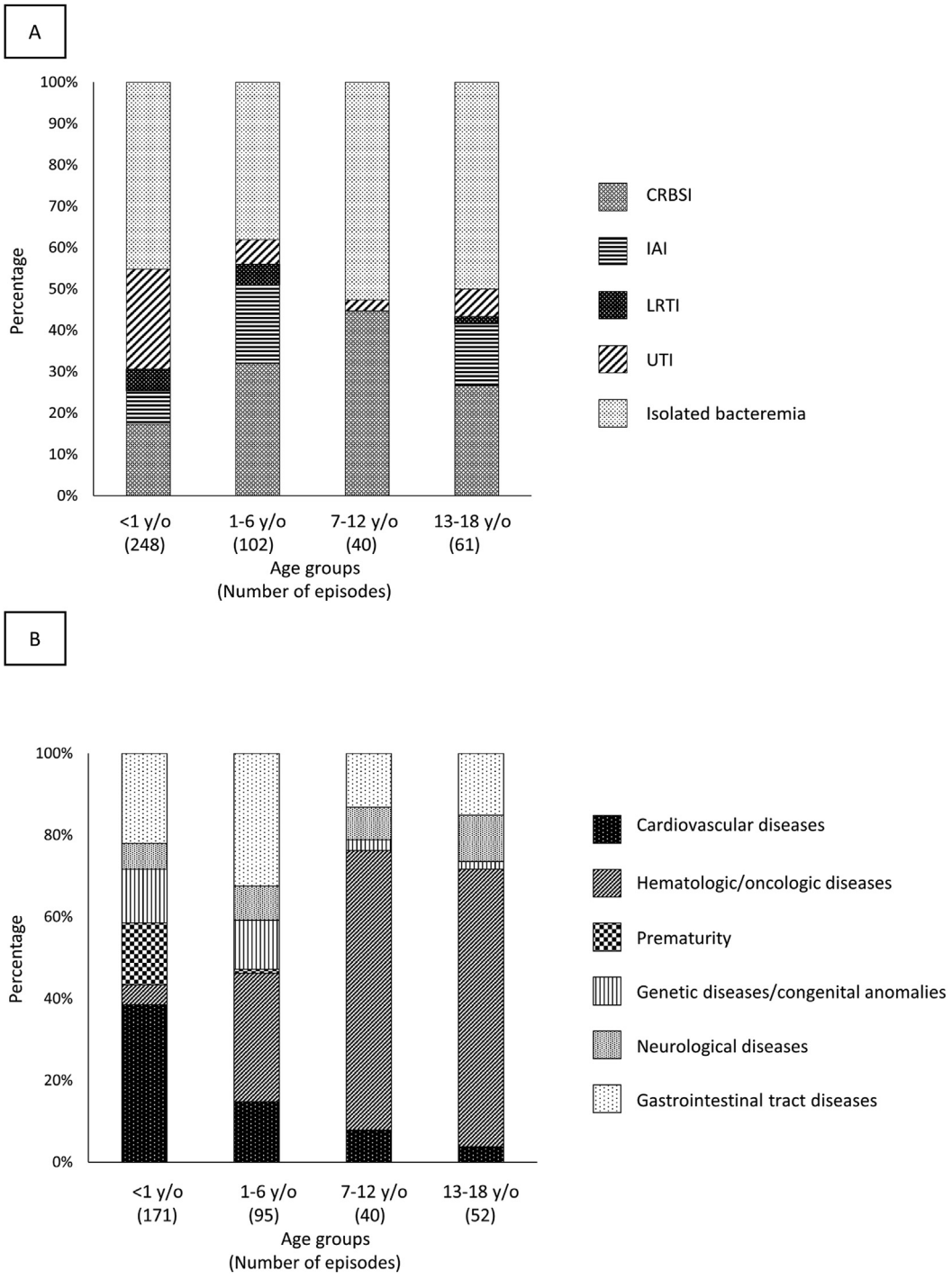

Figure 4. A. Proportions of infectious sources of *Enterobacterales* bacteremia episodes in different age groups, from 2013 to 2021. CRBSI, catheter-related blood stream infection; IAI, intra-abdominal infections; LRTI, lower respiratory tract infections; UTI, urinary tract infections. B. Proportions of patients with underlying diagnoses in different age groups.

production.[20,21] However, even for carbapenemase-producing CRE (CP-CRE), different carbapenemases confer different resistance levels.[22,23] KPC-2-producing *K. pneumoniae* and IMP-8-producing *Enterobacter cloacae* were the most prevalent carbapenemase genotypes in Taiwan, with the latter showing lower carbapenem resistance. In another cohort study, including 113 clinical isolates of carbapenem-nonsusceptible *Enterobacterales* bacteremia in Taiwan, none of the 13 isolates of *Enterobacter* spp. produced carbapenemase.[24] These results may explain the low MIC of meropenem observed in CR-*Enterobacter* spp. isolates.

On the other hand, CP-CRE invasive infection is associated with worse outcomes than those that do not.[15] The IDSA released treatment guidelines for CRE in 2021.[25] It begins with the differentiation of carbapenemase production. New agents targeting carbapenemases such as

ceftazidime-avibactam and meropenem-vaborbactam are recommended for infections outside the urinary tract.[23] Ceftazidime-avibactam has not been approved for use in Taiwanese children until the end of our study period (01, June 2020). Commercialized products for detecting carbapenemase in CRE, such as NG-Test® CARBA 5®, are becoming available in Taiwan. This may enable more rapid implementation of targeted antibiotic use for future CRE infections in children in Taiwan.

A previous study demonstrated that combination antibiotic therapy leads to better outcomes than monotherapy for CR-*K. pneumoniae* bacteremia in adults.[26] Our results were inadequate in concluding this due to the retrospective nature of design, limited case numbers, and heterogeneous antibiotic usage. Since CRE in our cohort had good susceptibility to amikacin, adding amikacin to the empirical regimen might offer extra benefit for critical CRE infections in Taiwanese children.

In our study, patients' mortality rates at one month in this cohort were 6.2% for total episodes and 12.5% for CRE episodes. Reported CR GNB bacteremia mortality rates at one month ranged from 14.8% to 35.5% in children,[11,12] 27.4% (all CRE included) to 66.7% (CR-*K. pneumoniae* only) in adult patients.[15,27] Although these results from different study settings cannot be compared directly, pediatric patients seem to have better outcomes than adult patients. Our study also showed that, despite the lower proportion of adequate initial antibiotics in the CRE group (Table 2), it was not a predictive factor for 14-day mortality (Table S2). One possible explanation is that most of the CRE isolates in our study cohort retained susceptibility to at least one carbapenem (Table S1, susceptible rate 43.6% for imipenem and 87.5% for meropenem). Targeted antibiotic treatment with carbapenems remains effective. As in our study, although half of the patients with CRE episodes initially received inappropriate antibiotics, most were treated successfully with meropenem (Table S4). The lower the level of antibiotic resistance, the more chances the patient receives an appropriate regimen, and more likely they are to survive. This notion is supported by some studies of CRE bacteremia in adult patients that meropenem and imipenem MIC levels of patient isolates are significantly associated with survival.[17,27]

In current and earlier studies, 1-year-old children have contributed the most to pediatric gram-negative bacteremia.[16,28] Our analysis also showed that most pediatric CRE bacteremia episodes occur in infants (Table 2), and carbapenem resistance is significantly associated with a higher mortality rate in such patients (Table S2). The clinical features of gram-negative bacteremia in infants differ significantly from those of older children. In our cohort, congenital heart diseases were the most frequently encountered underlying diseases in the infants (Fig. 4). This reflects disease prevalence in children of different age groups. The incidence of sepsis in infants with congenital heart disease in this special population was high in a previous study.[29] Such infants usually received intensive surgical intervention heralding post-surgery intensive care in the ICU. GNB are the primary cause of bloodstream infection in children during ICU stay after cardiac surgery.[30] Mechanical ventilation and placement of arterial or central venous catheters might also increase the risk of MDR pathogens infection.[4] It should be noted that prolonged antibiotic use is not uncommon in such patients during their stay at the surgical ICU, which might also result in the selection of resistant strains. Therefore, antibiotic stewardship is crucial for patients with high risk of *Enterobacterales* bacteremia to avoid the development of carbapenem resistance.

Our study has some limitations. The sample size of CRE isolates in a single center for nine years was still small due to the relatively low prevalence rate of CRE. Severity scoring systems for children with sepsis were not widely used in the early years of the study. Clinical data were incomplete, and scoring severity was difficult. The alternative method was to use ICU admission during this episode as an indirect index of a patient's overall disease severity. Carbapenem resistance was defined based on in vitro DST. Further phenotypic tests, such as the modified Hodge test, modified carbapenem inactivation method, or even molecular genotyping of carbapenemase genes, might be needed for a deeper understanding of the effect of carbapenemase production on the clinical outcome of CRE bacteremia in a local pediatric population.

In conclusion, our study showed that carbapenem resistance rate was 8.4% among *Enterobacterales*, excluding *Salmonella* spp., higher in *Enterobacter* spp. (25.4%), and lower in *E. coli* (1.5%) in pediatric patients in Taiwan. CRE bacteremia was associated with a higher 14-day mortality rate. CRE bacteremia is associated with specific patient populations that warrant particular concern.

Funding/support

No funding or support was received for this study.

Declaration of competing interest

All the authors have no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2022.09.010.