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ORIGINAL RESEARCH

Intestinal Colonization and Subsequent Nosocomial Infection with Carbapenem-Resistant Organisms in a PICU: Risk Factors and Molecular Homology Analysis

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Background: Rates of carbapenem-resistant organism (CRO) colonization and infection are rising in pediatric intensive care units (PICUs), mainly due to underlying comorbidities, frequent invasive procedures, prolonged hospitalization, and extensive use of broad-spectrum antibiotics. Colonized patients can act as reservoirs for nosocomial transmission of drug-resistant bacteria, posing a serious threat to other children and healthcare workers. Prevention and control of CRO are therefore of urgent clinical importance.

Methods: Based on active screening measures, we analyzed risk factors for intestinal CRO colonization and subsequent nosocomial infection in critically ill children. Pulsed-field gel electrophoresis (PFGE) was used to determine molecular homology between colonizing and infecting strains isolated from the same patient.

Results: A total of 1069 children were admitted to our PICU between January 2021 and September 2022. Seventy-seven cases of intestinal CRO colonization were detected, with a colonization rate of 7.2%. Of these colonized children, 15 developed subsequent CRO infection, and PFGE confirmed that the infecting strains were homologous to the colonizing ones. Independent risk factors for CRO colonization included underlying neuromuscular disease (OR 7.048, 95% CI 3.003–16.545, P<0.001) and longer hospital stay (OR 1.063, 95% CI 1.034–1.092, P<0.001). Among colonized children, independent risk factors for subsequent nosocomial infection were carbapenem exposure (OR 4.041, 95% CI 1.310–12.470, P=0.014), absence of contact isolation (OR 0.033, 95% CI 0.002–0.496, P=0.010), and longer hospital stay (OR 1.083, 95% CI 1.002–1.170, P=0.045).

Conclusion: Intestinal CRO colonization significantly increases the risk of subsequent homologous nosocomial infection in PICU children. Rational carbapenem use,aprompt contact isolation following colonization and shorten hospitalization time are crucial strategies to reduce CRO-related nosocomial infections.

Keywords: carbapenem-resistant organisms, intestinal colonization, active screening, homology analysis, nosocomial infections

Introduction

Since the first identification of carbapenem-resistant Enterobacteriaceae (CRE) in 1996, these pathogens have evolved into a formidable global public health threat, entrenched in healthcare settings worldwide due to their extraordinary capacity for transmission and persistence.[1] Carbapenem-resistant organisms (CROs) stand as the leading cause of nosocomial infections, conferring prohibitively high mortality rates, prolonged hospital stays, and substantial economic burdens, primarily owing to the dwindling armamentarium of effective therapeutic agents.[2–5] Central to the clinical

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challenge is the observation that CRO colonization—whereby bacteria persist asymptomatically within the host, most commonly the intestinal tract—represents a critical, reversible precursor to subsequent invasive infection.[6–8] This process is governed by complex biological interplay: while the intestinal microbiota provides a physical barrier to colonization, dysbiosis induced by broad-spectrum antibiotics, combined with immune compromise, creates an ecological niche enabling CRO expansion, translocation across the mucosal barrier, and the development of clinical disease.[9,10]

Epidemiologically, the global landscape of CRO is marked by disturbing trends. The widespread and often empiric use of carbapenems has driven a continuous upward trend in CRO prevalence.[11] In China, national surveillance data highlights *Escherichia coli* and *Klebsiella pneumoniae* as the predominant CRE species, with reported carbapenem resistance rates of 1.5% and 10.1%, respectively.[12] More alarmingly, pediatric populations, particularly critically ill children in intensive care units (ICUs), face disproportionately high risks. Their immature immune systems, frequent exposure to invasive procedures, and higher antibiotic exposure frequency render them a vulnerable high-risk group for both colonization and subsequent nosocomial transmission.[13]

Despite this, a critical research gap persists. While the clinical consequences of CRO are well-documented, fundamental questions regarding the biological drivers of colonization-to-infection transition in the pediatric ICU (PICU) context remain underexplored. Specifically, the specific ecological and immunological factors that tip the balance from asymptomatic carriage to active disease in this unique population are poorly defined. Furthermore, although active CRO screening and isolation precautions have been gradually implemented in adult tertiary hospitals, such strategies are still in their infancy in most pediatric institutions.[14] Currently, only a handful of pediatric tertiary care centers conduct routine CRO screening in neonatal ICUs (NICUs) or hematology/oncology wards, and large-scale, prospective studies systematically linking CRO intestinal colonization to subsequent nosocomial infection in PICUs are exceedingly rare.[13] This dearth of high-quality epidemiological evidence hinders the development of targeted, evidence-based prevention and control strategies for Chinese children.

To address this gap, our study employed a multifaceted approach. First, we conducted active CRO screening via rectal swabs in a large cohort of PICU patients, leveraging the well-established high sensitivity of this method for CRE detection (49.3%).[9,11] Second, we utilized pulsed-field gel electrophoresis (PFGE), a gold-standard molecular typing technique, to perform a rigorous homology analysis of colonizing and subsequent infecting CRO strains isolated from individual patients. This allowed us to definitively establish the clonal relationship between colonization and infection, a key step in confirming the causal link. Finally, we employed rigorous univariate and multivariate regression analyses to systematically identify independent risk factors for both CRO acquisition and the progression from colonization to clinical infection. By integrating these epidemiological, molecular, and clinical dimensions, our study aims to provide in-depth biological insights, fill critical knowledge gaps, and generate actionable evidence to guide the prevention and control of CRO in the PICU.

Materials and Methods

Study Design and Definitions

This was a single-center, cross-sectional, prospective study performed at the pediatric intensive care unit (PICU) of the Children's Hospital of Fudan University. CRO intestinal colonization screening and CRO surveillance were conducted in all patients who were admitted to the PICU from January 1, 2021, to September 30, 2022. The inclusion criteria included: 1) age between 29 days and 18 years; 2) admitted to PICU with acute onset in one week. The exclusion criteria included: 1) admitted to PICU after surgical operations and was transferred to a general ward; 2) died, discharged, or transferred to a general ward within 48 hours after admission; 3) correction of preterm infants with gestational age less than 38 weeks.

To analyze the risk factors of CRO colonization, we compared the groups of patients with CRO colonization to those whose screening results were negative during the whole time during admission. We determined the candidate range for the non-colonization group based on age, gender, and weight as matching conditions, and randomly selected 77 patients with negative CRO screening results during hospitalization as the non-colonization group using the RANDBEATWEEN function in Microsoft Excel 2018.

To analyze the risk factors of subsequent nosocomial CRO infection, we compared the group of patients with clinical infections to those whose screening results were positive but developed no infection after the CRO colonization. Furthermore, we ran a homological analysis to confirm whether the CRO colonization was the reservoir of the subsequent CRO infection.

CRO Surveillance

Intestinal CRO colonization was screened within 48 hours of admission and monitored weekly throughout hospitalization. For patients with clinical signs of infection, appropriate clinical specimens were collected for bacterial culture and antimicrobial susceptibility testing.Bacterial identification was performed using a Bruker MALDI Biotyper Sirius system (Bruker Daltonics, Bremen, Germany) with the MALDI Biotyper 4.0 software platform. Antimicrobial susceptibility testing (AST) was performed using the bioMérieux VITEK 2 Compact automated system. Interpretation of susceptibility results was performed according to the breakpoints recommended by the CLSI M100-S27 documents (2017 and 2018 editions). All clinical and laboratory data of CRO-positive patients were extracted from electronic medical records by the study authors.

Pulsed-Field Gel Electrophoresis (PFGE)

The concentration of the bacterial suspension was controlled with a bioMérieux DENSIMAT turbidimeter to ensure that its turbidity did not exceed 3.8–4.2. Gel blocks were made by adding 1% Seakem Gold:1% SDS gel to achieve homogeneity. The pellet was digested by cell lysis buffer (CLB) containing proteinase K for 2 h, and then washed twice with purified water to avoid residue of lysate, and washed four times with TE (10 mmol/L Tris:1 mmol/L EDTA, pH 8.0). The lysate was digested by XbaI endonuclease and incubated at 37°C for 4 h. The standard strain H9812 was digested by XbaI. The standard strain H9812 was digested with XbaI. Pulsed-field gel electrophoresis was performed in a CHEF-DRIII (BioRad, CA, USA) electrophoresis apparatus. At the end of electrophoresis, staining was performed with GelRed nucleic acid dye. Gel was imaged in a gel reader and converted to TIFF image format for storage. PFGE images of Salmonella H9812 were processed in BioNumerics (Version 8.1, Applied Maths, Belgium) software and calibrated using a molecular weight standard. Similarity coefficients between each image were calculated using the Dice coefficient, and clustering was performed using the unweighted pair group method with arithmetic mean (UPGMA) to construct a clustering tree. The SD value reflects the degree of similarity between PFGE images of different strains and ranges between 0 and 1, with 0 representing completely different and 1 representing completely the same. Different band patterns were recognized as different types.

Data Collection

The clinical information collected as possible risk factors for CRO intestinal colonization were age, weight, type of primary disease, criticality score, hormone/immunosuppressant use, Carbapenem antibiotic administration, invasive procedures (surgery, catheterization, tracheoscopy, etc), ventilation, duration of hospital stay.

Statistical Methods

Univariable analysis of risk factors was done using $\chi 2$/Fisher and unpaired Student's *t*-test to identify the risk factors for CRO colonization and subsequent nosocomial infection. Statistically significant risk factors for CRO colonization and infection were considered where $P < 0.05$. Multivariable logistic regression analysis was performed on statistically significant risk factors for CRO intestinal colonization and infection to identify independent risk factors.

Risk of Bias Assessment

This study adopted a prospective observational nested case-control design, so randomization and blinding of participants or treating clinicians were not applicable. To minimize detection bias, laboratory technicians performing bacterial identification, AST, and PFGE were blinded to patients' clinical status and group assignment (colonized vs. non-colonized, infection vs. non-infection). Selection bias was reduced by frequency matching of controls to cases by age,

gender, and weight, and information bias was minimized by standardized data extraction from electronic medical records by independent investigators.

Results

CRO Intestinal Colonization Incidence

A total of 1069 children were admitted to our PICU between January 1, 2021, and September 30, 2022. Seventy-seven cases of CRO intestinal colonization were identified, with a colonization rate of 7.2%. The isolated strains comprised 38 *Escherichia coli*, 25 *Klebsiella pneumoniae*, 10 *Acinetobacter baumannii*, 2 *Stenotrophomonas maltophilia*, 1 *Pseudomonas aeruginosa*, and 1 *Enterobacter aerogenes*. Of the CRO-colonized patients, 70.1% first tested positive within two weeks after admission, and 77.9% tested positive by the third week. Enrollment flowchart (Figure 1).

CRO Subsequent Nosocomial Infection Incidence

Of the children with CRO intestinal colonization, 19 developed subsequent clinical infections caused by the same CRO category. PFGE was used to analyze colonization and infection strains from the same patients. Homology analysis confirmed that 15 pairs were of the same strain origin, corresponding to a subsequent nosocomial infection rate of 19.5% (Figures 2 and 3).

In the infection group, 9 cases were *Acinetobacter baumannii* (Appendix Table 1), 4 were *Klebsiella pneumoniae* (Appendix Table 2), and 2 were *Escherichia coli* (Appendix Table 3).

Among these patients, 60.0% first tested positive within two weeks of admission, and 80.0% tested positive by the third week.

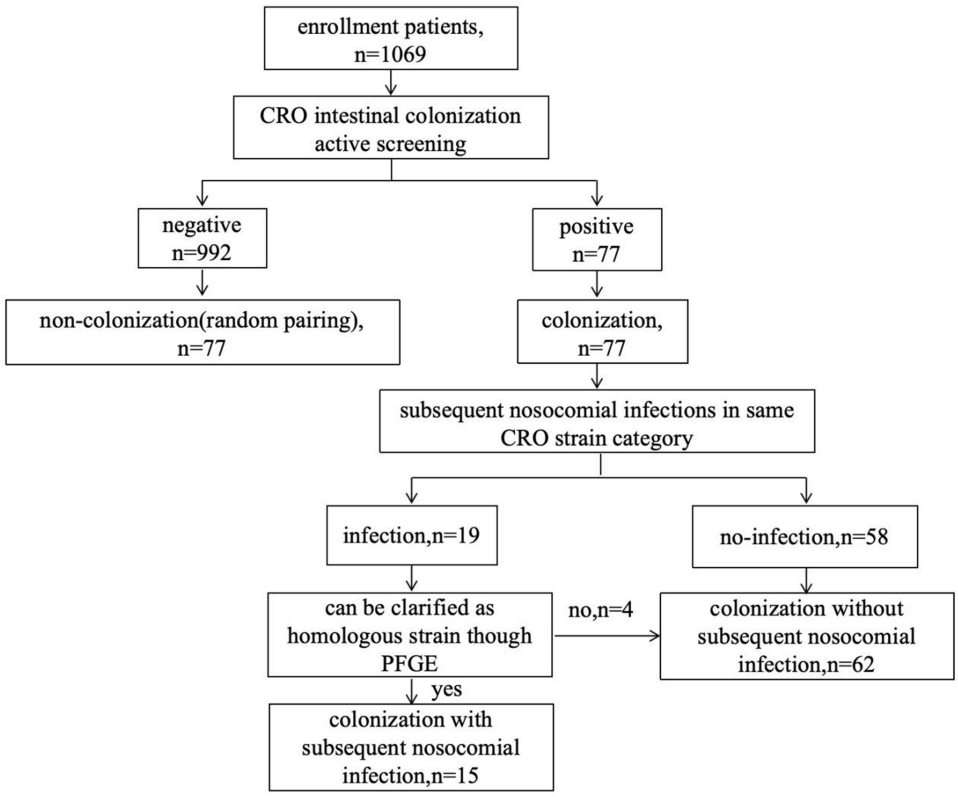

Figure 1 Enrollment Flowchart.

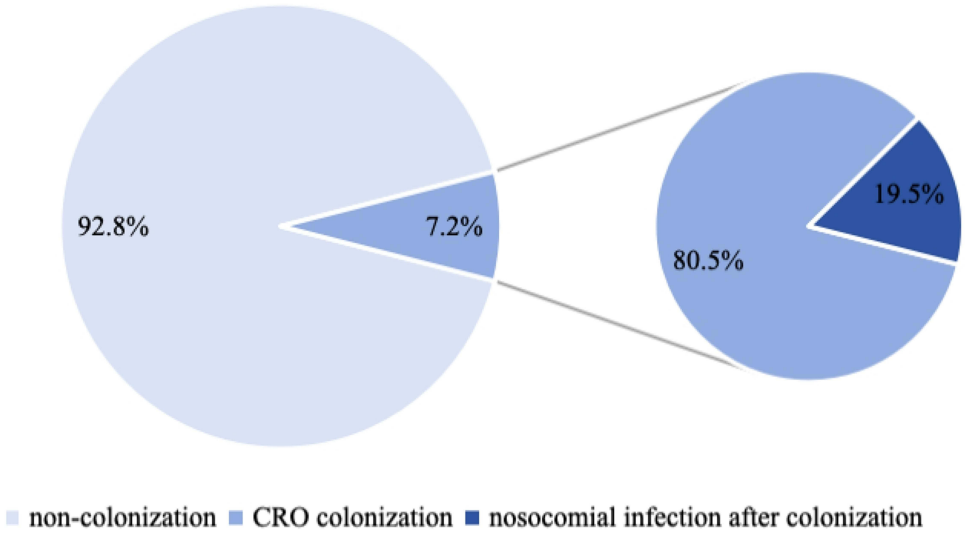

Figure 2 Proportion of CRO Intestinal Colonization and Post-colonization Infections Among Children in PICU.

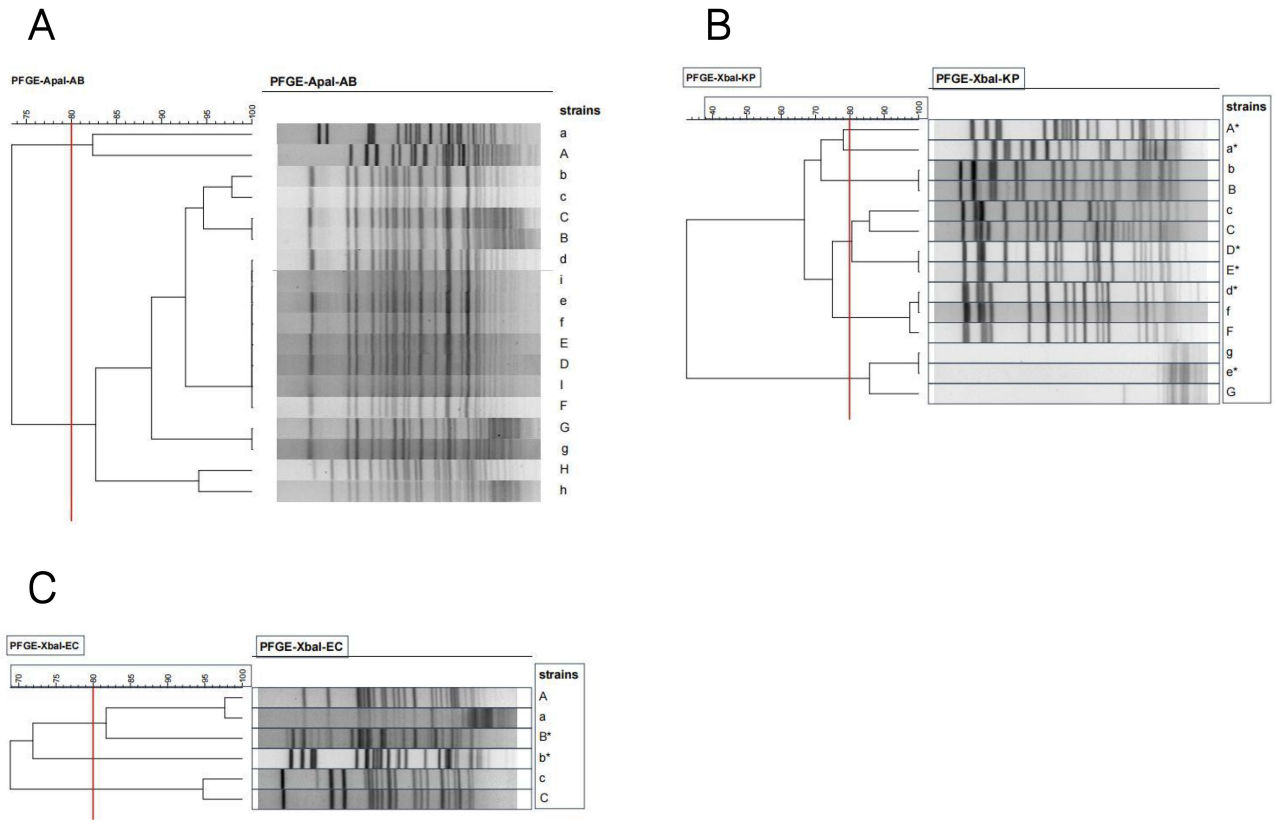

Figure 3 PFGE Analysis of Colonization and Infection Strains Isolated from The Same Patients. The upper case letter indicates the intestinal colonizing bacteria, and the lower case letter indicates the CRO strain isolated from the clinical specimen. The upper and lower case of the same letter indicates that both strains originate from the same patient, and the colonizing bacteria and the infecting pathogenic bacteria have a sequential time order, and "*" indicates that the colonizing bacteria from the same patient and the clinical pathogenic bacteria are confirmed to be different typed strains by homology analysis. (**A**) *Acinetobacter baumannii*. (**B**) *Klebsiella pneumonia*. (**C**) *Escherichia coli*.

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Risk Factors of CRO Intestinal Colonization and Subsequent Nosocomial Infection

Clinical data were compared between colonized and non-colonized children. Univariate analysis showed that neuromuscular underlying diseases, surgery, puncture procedures (including lumbar puncture, thoracentesis, paracentesis, bone marrow aspiration, pericardiocentesis, etc)., invasive procedures such as indwelling catheters or drainage tubes, length of hospital stay, and duration of mechanical ventilation were potential risk factors for CRO intestinal colonization in PICU children (Table 1).

Among children with CRO intestinal colonization, use of steroids or immunosuppressive agents, use of carbapenem antibiotics, absence of contact isolation following colonization, age at first CRO screening, length of hospital stay, duration of mechanical ventilation, and concurrent respiratory failure, circulatory failure, or digestive failure were potential risk factors for subsequent CRO infection (Table 2).

Multivariate analysis identified neuromuscular underlying disease and length of hospital stay as independent risk factors for CRO intestinal colonization. In colonized children, use of carbapenem antibiotics, absence of contact isolation after colonization, and length of hospital stay were independent risk factors for subsequent CRO infection (Table 3 and Table 4).

Discussion

Effect of Length of Hospitalization on Intestinal Colonization and Subsequent Nosocomial Infection in CRO

In this study, we observed that the proportion of children with CRO intestinal colonization and infection detected increased significantly with the duration of hospitalization. In addition, 70.1% of all children with CRO intestinal colonization were detected for the first time within 2 weeks of hospitalization, making it important to initiate proactive

Table 1 Results of Single-Factor Analysis of CRO Intestinal Colonization

Variables	Colonization, n=77	Non-colonization, n=77	p-value
Age, years	4.1±3.4	3.9±4.0	0.140
Gender, male	48	40	0.193
Weight, kg	17.3±12.7	14.9±10.8	0.405
Length of hospitalization, days	48.6±33.7	19.4±18.7	0.001
Underlying diseases involved			
Infectious diseases	30(39.0%)	36(46.8%)	0.329
Rheumatologic diseases	14(18.2%)	12(15.6%)	0.667
Metabolic disease	4(5.2%)	6(7.8%)	0.746
Oncological disease	19(24.7%)	16(20.8%)	0.564
Neuromuscular diseases	50(64.9%)	16(20.8%)	<0.001
Traumatic injuries/drowning	3(3.9%)	5(6.5%)	0.719
Others	14(18.2%)	24(28.6%)	0.182
Subsequent nosocomial infections	19(24.7%)	19(24.7%)	1.000
Survive	68	66	0.632
Use of steroids/immunosuppressive	41(53.2%)	33(42.9%)	0.197
Use of carbapenem antibiotics	29(37.7%)	29(37.7%)	1.000
Invasive procedures (n,%)			
Arteriovenous catheter	61(79.2%)	58(75.3%)	0.564
Other catheters (catheterization, drainage, etc.)	74(96.1%)	65(84.4%)	0.014
Surgery	36(46.8%)	17(22.1%)	0.001
Puncture (lumbar puncture, chest puncture, etc.)	42(54.5%)	29(37.7%)	0.036
Endotracheal intubation	54(70.1%)	58.4(58.4%)	0.130
Tracheoscopy	19(24.7%)	30(39.0%)	0.057
ECMO/CBP/TPE	9(11.7%)	16(20.8%)	0.126
Biopsy	1(1.3%)	3(3.9%)	0.620
Others	3(3.9%)	5(6.5%)	0.719
Length of mechanical ventilation (days)	21.2±30.0	9.2±13.9	<0.001

Table 2 Results of Single-Factor Analysis of Indicators Related to Nosocomial Infection After CRO Colonization

Variables	Infection Group after Colonization, n=15	Noninfected Group after Colonization, n=62	p-value
Age, years	5.6±4.1	3.7±3.1	0.597
Gender, male	10/5	38/24	0.700
Weight, kg	20.9±17.0	16.4±11.4	0.210
Critical illness score	86.3±10.6	89.0±8.8	0.439
Length of hospitalization at the time of colonization (days)	32.2±29.8	10.6±13.6	<0.001
Length of hospitalization, days	83.7±49.2	40.1±22.0	<0.001
Underlying diseases involved			
Infectious diseases	7(46.7%)	23(37.1%)	0.495
Rheumatologic diseases	5(33.3%)	9(14.5%)	0.132
Metabolic disease	2(13.3%)	2(3.2%)	0.113
Oncological disease	3(20.0%)	16(25.8%)	0.750
Neuromuscular diseases	10(66.7%)	40(64.5%)	0.876
Traumatic injuries/drowning	0(0.0%)	3(4.8%)	0.385
Others	2(13.3%)	12(19.4%)	0.725
Prognosis, death	12/3	56/6	0.366
Treatment (n, %)			
Use of steroids/immunosuppressive	13(86.7%)	35(45.2%)	0.004
Use of carbapenem antibiotics	12(80.0%)	17(27.4%)	<0.001
Lack of contact isolation after colonization	15(80.0%)	61(98.4%)	0.022
Invasive procedures (n,%)			
Arteriovenous catheter	14(93.3%)	47(75.8%)	0.173
Other catheters (catheterization, drainage, etc.)	14(93.3%)	60(96.8%)	0.483
Surgery	6(40.0%)	30(48.4%)	0.559
Puncture (lumbar puncture, chest puncture, etc.)	11(73.7%)	31(50.0%)	0.103
Endotracheal intubation	11(73.7%)	43(69.4%)	1000
Tracheoscopy	4(26.7%)	15(24.2%)	1000
ECMO/CBP/TPE	4(26.7%)	5(8.1%)	0.066
Biopsy	1(6.7%)	0(0.0%)	0.195
Length of mechanical ventilation (days)	42.8±52.0	16.2±20.0	<0.001
Organ/system failure (n,%)			
Respiratory system	14(93.3%)	40(64.5%)	0.031
Circulatory system	9(60.0%)	15(24.2%)	0.012
Blood system	4(26.7%)	7(11.3%)	0.210
Digestive system	7(46.7%)	10(16.1%)	0.017
Kidney	3(20.0%)	10(16.1%)	0.710
Central Nervous System	6(40.0%)	25(40.3%)	0.982

screening within 2 weeks of admission for children at high risk of CRO colonization and infection. In addition, 80.0% of children with CRO intestinal colonization developed subsequent infections within 3 weeks of the first detection of colonized bacteria, so it is important to strengthen the monitoring and management of clinical infections in children with CRO intestinal colonization within 3 weeks.

In the univariate analysis, the differences in length of stay between the colonized and non-colonized groups and between the post-colonization infected and non-infected groups were statistically significant, suggesting that the colonized and infected CRO strains may have originated in the inpatient setting. Children are often treated with different types of broad-spectrum antimicrobials from the time they are admitted to the PICU ward, so the colonized strains in the gut are susceptible to pan-resistance, while CRO strains are more likely to spread epidemically in the ward as the length of stay increases. Irregular disinfection of clinical operations by medical staff and incomplete disinfection of the ward environment are among the causes of CRO colonization and dissemination in the in-hospital environment, and some

Table 3 Results of Multifactorial Analysis of CRO Intestinal Colonization

Risk Factors	β value	SE	Wald value	OR value	95% CI	P value
Neuromuscular disease	1.953	0.451	18.785	7.048	3.003–16.545	<0.001
Length of hospitalization	0.061	0.014	19.536	1.063	1.034–1.092	<0.001
Puncture	0.561	0.472	1.412	1.752	0.689–4.455	0.235
Catheterization	−0.561	0.787	0.509	0.571	0.118–2.758	0.476
Length of mechanical ventilation	−0.662	0.474	1.952	0.516	0.196–1.358	0.162
Surgery	−0.561	0.787	0.509	0.571	0.118–2.758	0.476

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 4 Results of Multifactorial Analysis of Indicators Related to Nosocomial Infection After CRO Colonization

Risk Factors	β value	SE	Wald value	OR value	95% CI	P value
Length of admission for the first screening for CRO intestinal colonization	−0.009	0.034	0.074	0.991	0.926–1.061	0.786
Length of hospitalization	0.08	0.04	4.002	1.083	1.002–1.170	0.045
Length of mechanical ventilation	−0.004	0.03	0.018	0.996	0.939–1.056	0.892
Use of steroids/immunosuppressive	1.043	0.637	2.684	2.838	0.812–9.920	0.101
Use of carbapenem antibiotics	1.396	0.569	6.013	4.041	1.310–12.470	0.014
Lack of contact isolation after colonization	−3.408	1.327	6.592	0.033	0.002–0.496	0.010
Respiratory failure	0.995	1.959	0.258	2.704	0.047–156.296	0.612
Circulatory failure	0.653	1.323	0.244	1.921	0.135–27.297	0.621
Digestive failure	1.773	1.429	1.539	5.889	0.387–89.573	0.215

Abbreviations: CI, confidence interval; OR, odds ratio.

studies have shown that the incidence of CRO infections in ICU wards can be effectively reduced by strengthening hand hygiene education of medical staff and environmental disinfection measures.[15–17] In addition, as the length of stay increases, children receive more invasive operations in the PICU, which may also contribute to the increase in the rate of CRO colonization and infection. In this study, univariate analysis showed that the length of mechanical ventilation was one of the risk factors for increased risk of CRO colonization and infection. Previous literature has reported that risk factors for CRO infections include invasive procedures, but few studies have pointed out the specific effects of different invasive procedures on increasing the risk of CRO infections. Invasive procedures commonly performed in PICU include surgery, tracheal intubation, bronchoscopy, arteriovenous placement, various types of punctures, indwelling catheters or drainage tubes, etc. Most of these invasive procedures involve the reuse of medical devices, such as bronchoscopy, ventilators, etc. Even if this part of the reused equipment is cleaned and disinfected, the disinfection efficacy can be substantially reduced by the formation of bacterial biofilm and will be easily contaminated by various types of bacteria.[18–20] In addition, the skin and intestinal barriers of children are less developed than those of adults, so repeated invasive operations or prolonged mechanically assisted ventilation will cause varying degrees of damage to the child, thus increasing the risk of CRO colonization and infection.[21,22]

Effect of Neuromuscular Diseases on CRO Intestinal Colonization and Subsequent Hospital Infections

Neuromuscular disease was significantly associated with an increased risk of intestinal colonization by carbapenem-resistant organisms (CRO) and subsequent nosocomial infection. Patients with neuromuscular disorders frequently present with impaired swallowing, weakened cough reflex, recurrent aspiration, and impaired gastrointestinal motility, all of which disrupt the normal intestinal flora and compromise intestinal mucosal barrier function. These pathophysiological changes provide favorable conditions for CRO to colonize the intestinal tract. In addition, such patients often require prolonged hospital stays, frequent invasive procedures, including mechanical ventilation, tracheal intubation, and

indwelling catheters, as well as long-term use of broad-spectrum antibiotics, especially carbapenems. These factors further promote the selection and overgrowth of resistant strains, increase the risk of exogenous transmission, and facilitate the transition from intestinal colonization to clinical infection. Therefore, neuromuscular disease can be regarded as an important risk factor for CRO intestinal colonization and subsequent nosocomial infection, and patients with such conditions should be prioritized for active screening and enhanced infection control measures.

Impact of Carbapenem Antibiotic Use on Subsequent Nosocomial Infections in CRO

Carbapenem antibiotics have a broad antibacterial spectrum and are outstanding in antibacterial and bactericidal performance, mainly because of their ability to block bacterial cell wall mucopeptide synthase. Drugs such as imipenem, meropenem, and ertapenem, all belong to this type. In the multifactorial analysis of this study, the presence of children with CRO colonization, followed by secondary homologous infection and non-infected children showed a statistically significant difference in the rate of carbapenem antibiotic use between the two groups, suggesting that carbapenem antibiotics induce secondary infectious events in children with CRO intestinal colonization, without the involvement of other factors throughout the process. Previous literature has shown that carbapenem antibiotics increase the resistance rate of pathogenic bacteria and make it easier to develop CRO intestinal invasion when the original intestinal flora balance is disrupted, making a history of carbapenem antibiotic use a high-risk factor for CRO infection.[23–25]

Timing of Active Screening for CRO Intestinal Colonization

There is no international consensus on the optimal timing and frequency of active screening, and it is common for healthcare institutions to initiate active screening for CRO within 24 hours of new admission and to follow up with those at high risk of infection with regular testing (eg., weekly) during subsequent hospitalization.[13,26,27] It is evident that 77.9% of children had their first detection of CRO intestinal colonization within three weeks of admission, and the proportion of CRO intestinal colonization detected by active screening continued to increase with the duration of hospitalization. Therefore, active screening for CRO intestinal colonization within the first 3 weeks of admission is essential for all children admitted to the PICU, and regular screening throughout the hospital stay thereafter is still necessary, but the frequency of screening can be reduced according to the economic conditions of the ward.

Conclusion

Intestinal colonization with CRO may be associated with an increased risk of subsequent CRO-related nosocomial infection in the PICU. Carbapenem antibiotic use, lack of contact isolation following colonization, and longer length of hospitalization were significantly associated with the development of subsequent nosocomial CRO infection. However, given the small number of confirmed homologous infection cases (only 15 cases) and the resulting wide confidence intervals indicating unstable odds ratio estimates, as well as the correlational observational design and potential confounding factors including underlying disease severity, these findings should be interpreted with considerable caution, and further large-scale prospective studies are warranted to verify these relationships.

Ethics Approval

The study protocol was approved by the Ethics Committee of the Children's Hospital of Fudan University [(2021) 111]. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all parents or legal guardians of the enrolled patients. Assent was obtained from older children where applicable according to institutional guidelines. Attending physicians were informed of the patients' screening and test results to guide appropriate clinical management and treatment.

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 report no conflicts of interest in this work.

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