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Asymptomatic gastrointestinal carriage of multidrug-resistant carbapenemase-producing Enterobacteriaceae among children under five years in a Kenyan hospital

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ABSTRACT

Objectives: Asymptomatic gastrointestinal carriage of carbapenem-resistant Enterobacteriaceae (CRE) is a threat to global health in developing countries with inadequate safe drinking water, poor hygiene, and weak antimicrobial stewardship; however, epidemiological data to guide CRE infection prevention and control is limited in these settings. We assessed asymptomatic CRE and carbapenem-producing Enterobacteriaceae (CPE) fecal carriage rates and associated risk factors among hospitalized children aged under 5 years.

Methods: We adopted a cross-sectional study at Mama Lucy Kibaki Hospital in Nairobi-City County, Kenya, between June and September 2022. We collected demographic and clinical characteristics using a structured questionnaire and clinical reports and analyzed stool/rectal swab samples by standard and automated bacteriological methods.

Results: Asymptomatic CRE and CPE fecal carriage rate was 2.25% (6/267), with six isolates recovered, predominated by *Escherichia coli* (33.33%) and *Enterobacter cloacae subsp dissolvens* (33.33%). Third-generation cephalosporin and ciprofloxacin resistance were highest in *Citrobacter farmer* and *E. cloacae subsp cloacae*. All CRE and CPE were multidrug-resistant, and except *E. cloacae subsp cloacae*, were 100% colistin-resistant.

Conclusions: Asymptomatic gastrointestinal carriage of multidrug-resistant-CRE among hospitalized children under 5 years, presents a substantial public health threat. This calls for continuous surveillance including molecular characterization of isolates, to inform infection prevention and antimicrobial stewardship adherence in line with local and global plans on AMR.

Background

Antimicrobial resistance (AMR) is a growing public health challenge globally [1]. In the United States alone, drug-resistant bacteria are responsible for more than 2 million infections and about 25,000 deaths yearly [2]. In East Africa, AMR prevalence is higher, reaching up to 35%, because of the limited resources for infection prevention and control [3]. Increased use of carbapenem antibiotics as the priority drugs for multidrug-resistant infections caused by extended-spectrum beta-lactamase (ESBL)- and AmpC β-lactamase-producing bacteria has also resulted in a dramatic rise in carbapenem-resistant Enterobacteriaceae (CRE), including *Klebsiella pneumoniae, Escherichia coli, Aeromonas hydrophila, Serratia marsenscens*, and *Enterobacter cloacae* [4].

Though structurally similar to penicillin, carbapenems possess an additional ring, the carbapenem group, which protects them from some bacterial degrading enzymes [5]. Bacteria have, however, evolved several carbapenem resistance mechanisms, including enzymatic inactivation, target site mutation, and efflux pumps, with carbapenemase enzyme production being the most common mechanism [6]. Globally, the emergence and spread of carbapenemase-producing (CP) bacteria are rising due to inappropriate antibiotic prescription and uncontrolled public access in settings where antibiotic stewardship programs and hospital infection prevention and control measures are inadequate [7]. The carbapenem-producing organisms present a critical public threat because they carry resistance genes transferable among clinical bacterial isolates and cause difficult-to-control outbreaks associated with increased infections, about 33-50% mortality, and healthcare expenditure in hospitalized patients [8]. As per the World Health Organization (WHO), CRE are critical global priority pathogens for the development of newer antimicrobial agents.

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The available treatment options for infections by carbapenem-resistant (CR) bacteria, the triple combination of polymyxin, carbapenem, and rifampin or tigecycline, are faced with efficacy uncertainty due to emerging resistance [5]. The other options, ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, imipenem-cilastatin-sulbactam, plazomicin, eravacycline, and cefiderocol, are limited due to inadequate high-quality clinical data, delayed approval for susceptibility testing methods, the complexity of antibacterial spectra, and high purchase costs [9]. WHO states that in line with the global action plan on AMR, it is critical to control the emergence and spread of CR bacterial strains among the clinical isolates through structured research, surveillance and controlled use of antibiotics in clinical, and agricultural settings.

Recent epidemiological study findings show that the prevalence of CRE has escalated in hospitals from low and middle-income countries [2]. The spread of these infections is associated with inadequate infection control measures, a lack of surveillance programs to identify asymptomatic carriage, and weak antibiotic stewardship [2].

Fecal carriage plays a crucial role in the epidemiology of drug-resistant bacteria. Enterobacteriaceae are known gastrointestinal microflora, and asymptomatic fecal carriage of carbapenem-resistant strains, CRE, presents a grievous challenge to hospital infection prevention and control programmes [10]. The human gut can serve as a rich reservoir for bacteria harboring antibiotic-resistance genes, allowing horizontal exchange among the colonizing bacteria populations. Information on the fecal carriage is paramount to guide interventions to control the cross-transmission of CRE among patients, healthcare workers, and the environment within hospital settings [11]. However, there is limited information on the epidemiology of CRE gastrointestinal carriage in Kenya, as in many other developing countries. This study aimed to determine the asymptomatic gastrointestinal carriage of CRE and CP Enterobacteriaceae (CPE) among children under 5 years in a Kenyan hospital setting.

Materials and methods

Study setting, population, design, and sample collection

The study was done at Mama Lucy Kibaki Hospital (MLKH), Nairobi-City County, Kenya, a level 4 facility in Nairobi City's most populous Embakasi constituency. It is located precisely between Umoja II and Komarock estates, 11 km east of the city center and at the junction of Kangundo Road and Kayole Spine Road. The area is mainly a residential estate surrounded by numerous informal settlements. MLKH serves both inpatients and outpatients, and children have a separate outpatient department with admissions to the pediatric ward.

The study population was children aged 5 years and below, with ≥72 hours of hospital stay in a pediatric ward, excluding those presenting with diarrhea. We adopted a hospital-based cross-sectional study design and recruited 267 study participants through a systematic random sampling technique.

Data on factors associated with CRE carriage were collected using a structured questionnaire administered and clinical forms. The study collected stool samples in dry, clean, and leak-proof sterile containers, and for children unable to pass stool, rectal swabs were considered and collected in Cary-Blair media. All the samples were transported to the laboratory department in a cool box and processed within 4-6 hours of collection.

Laboratory analysis

Screening for asymptomatic CRE fecal carriage

The study screened for CRE gastrointestinal carriage following the protocol published by [12] emulsifying samples in sterile normal saline (0.9 w/v: 9 g/1l), and inoculating 10-1 dilutions into MacConkey broth (HiMedia, India) supplemented with meropenem drug (0.5 mg/l) and incubated at 37°C for 18 to 24 hours. Subsequently, 10 µl of the resultant cultures were streaked on MacConkey agar (HiMedia, India) plates containing meropenem (1 mg/l) and incubated at 37°C for 18 to 24 hours. We identified the putative CRE by Vitek 2® automated platform (bioMèrieux, Marcy l'.Etoile, France), following the manufacturer's instructions, with *Escherichia coli* (American type culture collection [ATCC] 25922) and *K. pneumonia* (ATCC 1705) as negative and positive control organisms, respectively.

Screening CRE isolates for carbapenemase production

We screened CRE isolates for carbapenemase production using the modified carbapenem inactivation method (mCIM) [13], where each identified isolate was inoculated in 2 ml of Trypticase Soy Broth (TSB) (HiMedia, India) containing meropenem (10 µg) and incubated at 30-35°C for 4 hours. Subsequently, we prepared *E. coli* (ATCC 25922) strain suspension equivalent to 0.5 McFarland standard in sterile saline, plated on Mueller–Hinton agar (MHA), and meropenem disk retrieved from the test organism TSB culture added, and incubated for 18-24 hours at 35°C. We interpreted a 6-15 mm and ≥19 mm inhibition zone diameter as positive and negative results, respectively, as per Clinical and Laboratory Standards Institute (CLSI) guidelines. *E. coli* (ATCC 25922) and *K. pneumonia* (ATCC 1705) were used as negative and positive, respectively, control organisms.

Antimicrobial susceptibility testing

Vitek 2® automated platform (bioMèrieux, Marcy l'.Etoile, France) was used for antimicrobial susceptibility testing (AST), using an XN05 AST card and following the manufacturer's instructions. The study based the choice of antibiotic tested and interpretation of AST data on CLSI (2021) guidelines. The antibiotics tested were: amoxicillin/clavulanic acid, piperacillin/tazobactam, cefazolin, cefuroxime, cefuroxime axetile, cefoxitin, cefotaxime, ceftazidime, ceftriaxone, cefipime, aztreonam, amikacin, gentamicin, ciprofloxacin, nitrofurantoin, and cotrimoxazole.

Colistin susceptibility testing

We performed colistin susceptibility testing following a simple disk diffusion method [14], whereby the test bacteria inoculum, equivalent to 0.5 McFarland standard, was streaked on modified MHA (Oxoid, United Kingdom) plate, colistin disk (10 µg) (Oxoid, United Kingdom) placed on the surface, and the plates incubated for 16-24 hours at 30-35°C in 5% CO^2. We compared the resultant inhibition zones with broth microdilution's minimum inhibitory concentrations as per CLSI guidelines, with *E. coli* (ATCC 25922) and *P. seudomonas aeruginosa* (ATCC 27853) as the quality control organisms.

Data analysis

We analyzed the study data by SPSS version 24 for Windows (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA), with descriptive statistics, including frequency and percentages used to describe the demographic and clinical characteristics. We defined multidrug-resistant (MDR) organisms as non-susceptible to ≥1 agent in ≥3 antimicrobial categories [15]. The study used bivariate analysis using logistic regression to calculate the crude odds ratio (OR) and variables with *P*-value ≤0.2 subjected to a multivariate analysis to calculate the adjusted OR. *P*-value ≤0.05 with a corresponding 95% confidence interval was considered for statistical significance. We presented the study data using tables and figures.

Ethical considerations and research approval

We obtained ethical approval and a research permit from the Kenyatta University Ethical Review Board and the National Commission of Science, Technology and Innovation (NACOSTI), respectively. The study sought permission to collect the study samples from Mama Lucky

Table 1
Sociodemographic and clinical characteristics of the study participants.

Variable	Category	Frequency (F)	Percentage (%) (%) (%)
Gender	Male	190	71.16
	Female	77	28.84
Age group	≤24 months	205	76.78
	>24 months	62	23.22
Caregiver	Parent	235	88.01
	Guardian	32	11.99
Caregiver's education status	No education	151	56.55
	Primary	59	22.10
	Secondary or higher	57	21.35
Caregiver's marital status	Single	140	52.43
	Married	127	47.57
Caregiver's occupation	Employed	221	82.77
	Unemployed	46	17.23
Travel history in the last 3 months	Yes	16	5.99
	No	251	94.01
Type of facility where healthcare services are sought	Private	57	21.35
	Public	210	78.65
Drink treated water	Yes	183	68.54
	No	84	31.46
Type of toilet used	Pit	163	61.05
	Flush	104	38.95
Children on ABS	Yes	150	56.18
	No	117	43.82
History of ABS dose completion	Yes	166	62.17
	No	101	37.83
Relationship to the child	Guardian	235	88.01
	Caretaker	32	11.99
Presence of invasive device	Yes	30	11.24
	No	237	88.76

ABS, antibiotics.

Kibaki Hospital management. We obtained informed written consent from guardians/parents of children before enlisting and assigned unique identification numbers to participants' samples to ensure confidentiality. This study did not deny participants medical services for declining to give study consent.

Results

Sociodemographic and clinical characteristics of the study population

This study sampled 267 hospitalized children below 5 years. Of these, the majority were male (71.16%), below 24 months (76.78%), on antibiotics (56.18%), had a history of completing antibiotic doses (62.17%), used treated domestic water (68.57%), used pit latrines (61.05%), had no invasive devices (88.76) fitted and no history of travel in the last 3 months (94.01%). The majority of the children's parents/guardians were employed (82.77%), single (52.43%) and had no formal education (56.55%). Most of these parents/guardians preferred public health facilities (78.65%) for medical services of their children, Table 1.

Asymptomatic CRE and CPE gastrointestinal carriage and spectrum

In this study, the asymptomatic gastrointestinal carriage rate of CRE was 2.25% (6/267), with all the CRE isolates identified from different patients, Figure 1. We recovered six CRE isolates, predominated by *E. coli* (33.33%) and *Enterobacter cloacae* subsp *dissolvens* (33.33%). All the CRE isolates were carbapenemase producers, Figure 1.

CRE and CPE antimicrobial susceptibility profiles

In the current study, CPE and CPE isolates, except *Citrobacter farmeri*, were 100% resistant to β-lactam inhibitors (BLI) tested (amoxicillin/clavulanic acid and piperacillin/tazobactam). Additionally, all isolates were 100% resistant to cefazolin, cefuroxime, cefuroxime axetil, and aztreonam, Figure 2.

We observed a high CRE and CPE resistance to the third-generation cephalosporin (3GCs, ceftazidime, cefotaxime, and ceftriaxone) and fluoroquinolones (ciprofloxacin), ranging from 50-100%, being highest in *C. farmer* and *E. cloacae* subsp *cloacae. E. cloacae* subsp. *dissolvens* and *E. coli 3*GCs resistance ranged from 75-100% and 50-100%, respectively. CRE and CPE aminoglycosides (amikacin and gentamicin) resistance was 50%.

All isolates, except *E. cloacae* subsp *cloacae*, were 100% resistant to colistin. We observed the lowest (50%) drug resistance for all CRE and CPE isolates in amikacin, gentamicin, and nitrofurantoin, Figure 2.

CRE and CPE MDR phenotypes

All CRE/CPE were MDR, Table 3. All MDR phenotypes involved colistin resistance, except in *E. cloacae* subsp *cloacae. C. farmer* showed the highest multidrug resistance, exhibiting resistance to seven antibiotic classes tested. The multiple antibiotic resistance index (MARI) ranged from 0.69-0.81 and was highest in *E. cloacae* subsp. *cloacae C. farmeri*, Table 3.

Factors associated with asymptomatic CRE/CPE gastrointestinal carriage among the study population

There was no statistically significant association between the variables investigated and CRE /CPE gastrointestinal carriage among the study population as shown in Table 2.

Discussion

CRE, especially the CP strains, is an imminent threat to global health security in developing countries with inadequate safe drinking water, poor sanitation and hygiene, and weak antimicrobial stewardship programs such as East Africa, where pooled diarrhea prevalence among under 5 years children is estimated at 14.28% [16], there are limited epidemiological data to inform CPE infection prevention and control programs (IPCs).

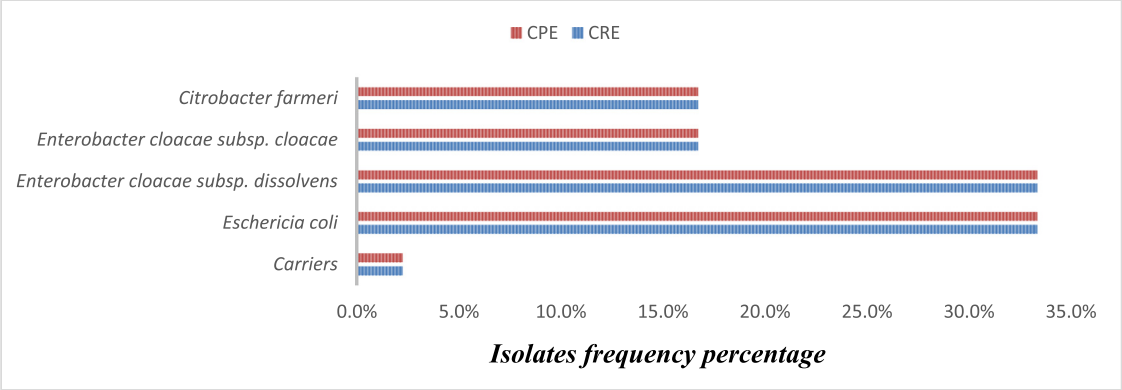

Figure 1. Asymptomatic CRE and CPE gastrointestinal carriage and spectrum.
CPE, carbapenemase-producing Enterobacteriaceae; CRE, carbapenem-resistance Enterobacteriaceae.

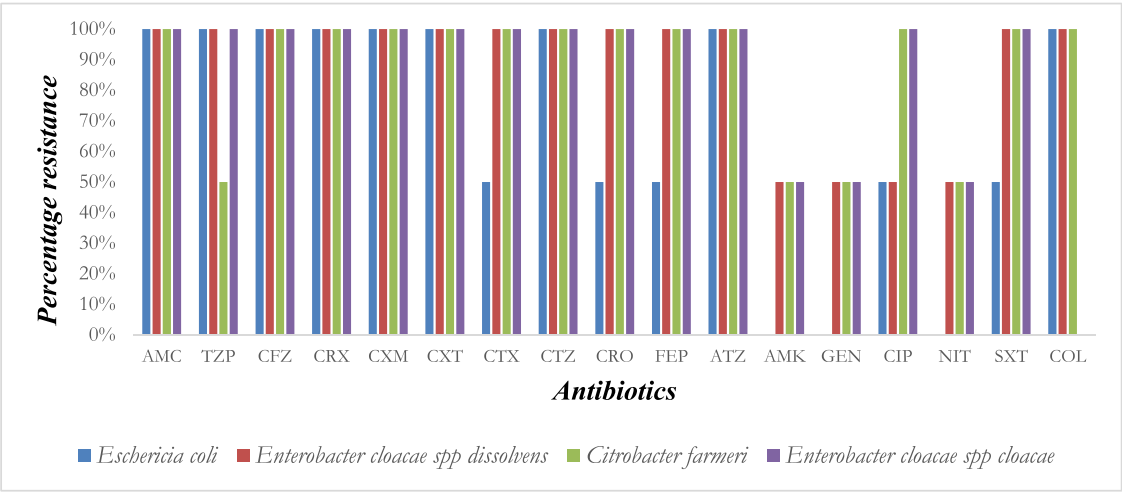

Figure 2. CRE and CPE Antimicrobial susceptibility profiles.
AMC, amoxicillin/clavulanic acid, AMK, amikacin; ATZ, aztreonam; CFZ, cefazolin; CIP, ciprofloxacin; COL, colistin; CRO, ceftriaxone; CRX, cefuroxime; CTX, cefotaxime; CTZ, ceftazidime; CXM, cefuroxime axetil; CXT, cefoxitin; FEP, cefepime; GEN, gentamicin; NIT, nitrofurantoin; SXT, trimethoprim/sulfamethoxazole; TZP, piperacillin/tazobactam.

In this study, the asymptomatic CPE intestinal carriage rate was 2.25%, with all the isolates identified from different patients. To our knowledge, this is the first report on CPE intestinal carriage in Kenya. Data on CPE fecal carriage in hospitalized children is scarce. Cunha et al. reported CPE and CRE carriage rates of 0.4% and 1.4%, respectively, from nursing home residents admitted at acute care hospitals [17], lower than that reported in this study. Our study finding agrees with those documented by Desta *et al.* [18] on CRE carriage (2%, 5/267) among hospitalized children aged between 1 month and 12 years in Ethiopia. However, CRE intestinal carriage rate in the current study was lower than reported in China by Pan et al. [10] (3.6%) among outpatient children (≤18 years) and Xu et al. [8] (8.6%) in a pediatric hospital. The observed variation in CRE fecal carriage might be due to differences in the study population characteristics, screening methods, and carbapenem drug exposure variations.

Intestinal CPE carriage may precede infection, with carriers serving as potential hotspots for dissemination among patients and healthcare staff, and clonal and plasmid-mediated resistance traits spread in hospital settings with weak IPCs. The CPE strains pose a substantial public health threat since carbapenems are considered the mainstay drugs for MDR infections, especially those caused by ESBL-E. CPE therapeutic options are limited because the mobile plasmids encoding carbapenemase enzymes coexist with multiple resistance traits that mediate resistance to other drug classes, such as aminoglycosides and fluoroquinolones. The CPE are, therefore, difficult-to-treat and result in adverse patient outcomes and high healthcare costs. By 2050, drug-resistant bacteria will cause a predicted 10 million deaths and 100 trillion US dollars in expenditure yearly [19].

We recovered 6 CRE isolates, all (100%) being CPE and predominated by *E. coli* (33.33%) and *E. cloacae* subsp *dissolvens* (33.33%). The CPE spectrum was similar to that reported on CRE in India [20,21] and China [8,10,22]. In study reports by Liu et al. [22] and Xu et al. [23] in China, 91% and 92% of CRE isolates were carbapenemase producers, respectively. Cunha et al. [17] documented a comparatively low CRE carriage rate in Miriam Hospital and Rhode Island Hospital, USA. The predominant CRE or CPE in fecal carriage varies across the published literature. *E. coli* was shown to be the most common bacterium in CRE gastrointestinal carriage reports from India [21], China [10,20,22,23], and Uganda [24], whereas *K. pneumonia* was the leading CPE reported in Ethiopia [15]. These variations might be due to differences in local adherence to antibiotic stewardship programs, infection control programs in different health facilities, and geographical distribution of bacterial isolates.

The predominant CPE and CRE isolates were *E. coli* (33.33%) and *E. cloacae* subsp *dissolvens* (33.33%) in the current study. Study reports have revealed diverse MDR *E. cloacae* clones, including several potential epidemic lineages and the bacterium intrinsic β-lactam resistance and a unique ability to acquire genes encoding resistance to multiple

Table 2
Risk factors for asymptomatic CRE/CPE gastrointestinal carriage among the study population.

Factors	CRE/CPE carriage		Crudes OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
	Yes, n (%)	No, n (%)				
Age						
≤24 months	3(50)	202(77.4)	0.29(0.06 - 1.49)	0.140	0.29(0.06 - 1.51)	0.141
>24 months	3(50)	59(22.6)	Ref		Ref	
Gender						
Male	5(83.3)	185(70.9)	2.05(0.24 - 17.88)	0.176	2.60(0.28 - 24.11)	0.411
Female	1(16.7)	76(29.1)	Ref		Ref	
Marital status						
Single	4(66.7)	136(52.1)	1.84(0.33 - 10.21)	0.686		
Married	2(33.3)	125(47.9)	Ref			
Education						
No education	3(50)	148(56.7)	Ref			
Primary	2(33.3)	57(21.8)	0.88(0.09 - 8.65)	0.913		
Secondary or higher	1(16.7)	56(21.5)	0.51(0.05 - 5.77)	0.586		
Occupation						
Employed	5(83.3)	216(82.8)	1.04(0.12 - 9.13)	0.724		
Unemployed	1(16.7)	45(17.2)	Ref			
Travel history						
Yes	0	16(6.1)	n/a			
No	6(100)	245(93.9)	n/a			
Relationship with child						
Guardian	4(66.7)	231(88.5)	0.26(0.05 - 1.48)	0.154	0.22(0.04 - 1.34)	0.100
Caretaker	2(33.3)	30(11.5)	Ref			
Child on antibiotics						
Yes	4(66.7)	146(55.9)	1.58(0.28 - 1.48)	0.231		
No	2(33.3)	115(44.1)	Ref			
Presence of invasive device						
Yes	0	30(11.5)	n/a			
No	6(100)	231(88.5)	n/a			
Dosage completion						
Yes	6(100)	160 (61.3)	n/a			
No	0	101(38.7)	n/a			
Treat drinking water						
Yes	3(50)	180(69)	0.45(0.09 - 2.28)	0.383		
No	3(50)	81(31)	Ref			
Type of facility						
Public facility	4(66.7)	206(78.9)	0.53(0.10 - 3.00)	0.611		
Private facility	2(33.3)	55(21.1)	Ref			
Type of toilet						
Pit latrine	6(100)	157(60.2)	n/a			
Flush toilet	0	104(29.8)	n/a			

CI, confidence interval; CRE, carbapenem-resistant Enterobacteriaceae; CPE, carbapenem-producing Enterobacteriaceae; n/a, not applicable; OR, odds ratio; Ref, reference.

Table 3
Carbapenem-resistant Enterobacteriaceae and carbapenem-producing Enterobacteriaceae multidrug-resistant phenotypes.

Isolates	Antibiotics resisted	Frequency n (%)	Antibiotics classes resisted	Multiple antibiotic resistance indexing
Escherichia coli (2)	*AMC,TZPCFZ,CRX,CXM,CXT,CTZ,ATZ,COL*	1(50)	4	0.72
	AMC-TZP,CFZ,CRX,CXM,CXT,CTX,CTZ,CRO,FEP,ATZ,SXT,COL	1(50)	5	0.78
Enterobacter cloacae ssp dissolvens (2)	*AMC-TZP,CFZ,CRX,CXM,CXT,CTX,CTZ,CRO-FEP,ATZ,SXT,COL*	1(50)	5	0.75
	AMC,TZP,CFZ,CRX,CXM,CXT,CTX,CRO,FEP,ATZ,SXT,COL	1(50)	5	0.69
E. cloacae ssp cloacae (1)	*AMC-TZP,CFZ,CRX,CXM,CXT,CTX,CTZ,CRO,FEP,ATZ,CIP,SXT*	1(100)	5	0.81
C. farmeri (1)	*AMC,CFZ,CRX,CXM,CXT,CTX,CTZ,CRO,FEP,ATZ,CIP,NIT,SXT,COL*	1(100)	7	0.81

AMC, amoxicillin/clavulanic acid; AMK, amikacin; ATZ, aztreonam; CFZ, cefazolin; CIP, ciprofloxacin; COL, colistin; CRO, ceftriaxone; CRX, cefuroxime; CTX, cefotaxime; CTZ, ceftazidime; CXM, cefuroxime axetil; CXT, cefoxitin; FEP, cefepime; GEN, gentamicin; NIT, nitrofurantoin; SXT, trimethoprim/sulfamethoxazole; TZP, piperacillin/tazobactam.

classes of antibiotics, including a variety of carbapenemase genes. *Enterobacter* species are the second most common CRE in the United States, contributing to the spread of carbapenem-resistant infections [25].

In the current study, CPE isolates, except *C. farmeri*, were 100% resistant to BLI tested (amoxicillin/clavulanic acid and piperacillin/tazobactam). Similar findings have been documented [15]. The three classical BLI (e.g., clavulanic acid, tazobactam, and sulbactam) combined with β-lactam antibiotics are the mainstay of antibiotic therapy against Gram-negative bacterial infections. However, bacteria have evolved the mechanisms of resistance to overcome the inhibitory effects of these inactivators since these inhibitors share a β-lactam core structure. The resistance occurs due to mutations of β-lactamase, particularly the amino acids at the active site, leading to ineffective binding and reduced inhibition [26].

We observed a high CPE and CRE resistance to the 3GCs (ceftazidime, cefotaxime, and ceftriaxone) and fluoroquinolones (ciprofloxacin), ranging from 50-100%, being highest in *C. farmer* and *E. cloacae* subsp *cloacae*. *E. cloacae* subsp. *dissolvens* and *E. coli* 3GCs resistance ranged from 75-100% and 50-100%, respectively. CPE and CRE aminoglycosides (amikacin and gentamicin) resistance was 50%. Liu et al. [22] iso-

lated *E. coli* exhibiting 100% 3GC-R (ceftazidime and ceftriaxone) in China, whereas in a study by Okoche et al. [24] in Uganda, *Enterobacter* sp. susceptible to 3GCs (ceftriaxone, cefotaxime) from CRE clinical isolates. Cephalosporin resistance is mediated mainly by plasmid-borne β-lactamase enzymes, categorized under the Ambler classification system as class C enzymes [27]. Despite the spirited multifaceted efforts to reduce and control the global AMR burden, epidemiological data on 3GC-resistant pathogens, classified as WHO global priority pathogens, remains inadequate in many SSA countries [28].

In the current study, all CPE and CRE isolates, except *E. cloacae* subsp *cloacae,* were 100% colistin-resistant. Ngbede et al. [29] reported strains of *E. coli* and *Citribacter* sp. co-resistant to colistin and carbapenem in Nigeria from human and animal sources. Colistin is a narrow-spectrum antimicrobial agent that has significant activity against most members of Enterobacteriaceae; however, in the last few decades, the emergence of colistin-resistant isolates has been frequently reported probably due to increased inappropriate use [30]. Colistin resistance involves overexpression of chromosomally mediated two-component system genes (PmrAB and PhoPQ), the mutation in lipid A biosynthesis genes, and plasmid-borne genes (*mcr*-1 to *mcr*-10).

All the CRE and CPE were multidrug-resistant (MDR), defined as nonsusceptible to ≥1 agent in ≥3 antimicrobial categories [15]. MDR rates vary widely in the published literature [15]. Misuse and overuse of antimicrobials are the main drivers in the emergence of MDR organisms, with inadequate clean water, sanitation, and infection prevention and control promoting the spread, a problem facing most developing countries. In the current study, the MARI ranged from 0.69-0.81 and was highest in *E. cloacae* subsp. *cloacae* and *C. farmeri.*

This study has several limitations. It was a monocentric study, suggesting that the findings may not inform the health situation in the entire country. Also, the study was unable to establish factors associated with the CRE and CPE carriage and to elucidate the molecular mechanisms of resistance due to financial constraints. We did not exclude participants on antibiotics, which could have affected the laboratory recovery of target bacteria.

Conclusion

Our findings highlight a substantial public health threat from the asymptomatic gastrointestinal carriage of CPE isolates that are MDR involving BLI, 3GC, and fluoroquinolones among children under 5 years hospitalized with conditions other than diarrhea. The study findings call for continuous and systematic surveillance of gastrointestinal carriage of CPE, including molecular characterization of isolates, to inform infection prevention interventions and strict adherence to antimicrobial stewardship policies in line with local and global action plans on AMR.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethics approval and consent to participate

Ethical approval was sought from Kenyatta University Ethical Review Board and written consent sought from all the study participants. Unique personal identification number (PIN) was assigned to all samples collected and remained confidential. There was no monetary gain for the participant and no penalties for those who declined to participate in the study. Approval to carry out the study was given by National Commission for Science, Technology and Innovation (NACOSTI) and hospital management.

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Author contributions

CKM, JM and AMM conceived and designed the study, analyze and interpreted the data. CKM and AKM collected the data directed by AMM and JN. CKM wrote the draft manuscript. AMM and JM reviewed the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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