

Systematic review

Molecular epidemiological exploration of carbapenem-resistant *Enterobacteriaceae* in Africa from One Health perspective: a systematic review

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Abstract

Carbapenem-resistant *Enterobacteriaceae* (CRE) are associated with high morbidity and mortality in humans due to very limited therapeutic options. This systematic review examines the prevalence and geographic distribution of CRE, as well as the associated genetic factors at the human-animal-environment interface in Africa. To extract information for this study, the Medical Subject Headings (MeSH) technique was used to identify studies that employed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines, with a focus on original research articles. Additionally, this systematic review employed the CoCoPop (conditions, context, and population) framework to identify relevant articles. Search engines used to retrieve articles included Web of Science, Google Scholar, Scopus, ResearchGate, and PubMed. By August 2025, only eight articles from Africa met the search criteria and were included in the analysis. The observed prevalence of CRE across the heterogeneous studies was 18.58%. The animal domain exhibited the highest CRE prevalence (9.89%), followed by the human (6.06%) and environmental (2.63%) domains. *Escherichia coli* (58.35%) and *Klebsiella pneumoniae* (28.28%) were the predominant spp. among the reported CRE isolates. The highest gene prevalence was observed for *bla*OXA-48 (42%), followed by *bla*KPC (33%) and *bla*OXA-66 (9.78%). Geographically, North Africa had the highest prevalence (55.78%), followed by Eastern Africa (29.82%), whereas Southern Africa had the lowest prevalence (3.08%). Our study emphasizes the significant burden of CRE infections and genes, as well as their spread across human, animal, and environmental sectors in Africa. The simultaneous presence of CRE in these areas indicates potential interfaces, but current evidence does not permit a definitive assignment of specific transmission routes. Surveillance programs, research, infection prevention, and control measures from a One Health perspective should be implemented to inform interventions.

Keywords: Africa, Antimicrobial resistance, Carbapenem-resistant *Enterobacteriaceae*, Critical priority bacteria, One Health

Introduction

Antimicrobial resistance (AMR) occurs when microorganisms develop resistance to antimicrobial agents. AMR is driven by anthropogenic activities, including the misuse and overuse of antimicrobials in humans and animals, which can lead to treatment failures. This phenomenon has been associated with rising morbidity and mortality, as well as significant impacts on public and animal health and the economy [1, 2]. AMR is a silent pandemic and one of the 10 leading 21st century global health threats, and it does not respect geographical borders [3, 4]. Globally, AMR is responsible for approximately 700,000 deaths annually, and this number is projected to rise to 10 million by 2050, with Africa accounting for 4.5 million [5, 6]. AMR-associated deaths were highest in Africa, with an estimated 27.3–114.8 deaths per 100,000 population in 2019, higher than those observed in East Asia, Western Europe, and Central Latin America [7, 8]. AMR is a complex epidemiological phenomenon, as antimicrobial-resistant bacteria can emerge under selective pressure and be transmitted across the human-animal-environment interface [9]. The

emergence of antimicrobial-resistant bacteria in animals of clinical importance to humans has raised global health security concerns about certain uses of antimicrobials in veterinary medicine [10].

The emergence of carbapenem-resistant *Enterobacteriaceae* (CRE) is concerning primarily because the genes involved are often located on plasmids, mobile genetic elements (MGEs) that rapidly transfer between bacteria and facilitate the spread of resistance [11, 12]. CRE can also arise through co-resistance with other commonly administered antimicrobials [13]. Despite the global prohibition on the use of carbapenems in food-producing animals, CRE have emerged in livestock, companion animals, and wildlife over the past decade [11, 14]. This emergence raises concerns about potential spillover into the livestock population, which could serve as a transmission route to humans via consumption of CRE-contaminated meat and milk, contact, and aerosol inhalation [12]. The 2024 World Health Organization (WHO) bacterial priority pathogens list (BPPL) is an essential tool for combating AMR worldwide. The updated classification categorizes

pathogens into critical, high, and medium priorities to inform research, development, and prevention strategies [15]. The critical group comprises CRE, which were designated priority pathogens by the WHO in 2024 [15].

Enterobacteriaceae is a family within Enterobacterales, a large order of Gram-negative bacteria. The most critical CRE include carbapenem-resistant *Klebsiella* (*K.*) *pneumoniae*, *Escherichia* (*E.*) *coli*, *Enterobacter* spp., *Serratia* spp., and *Proteus* spp. These organisms are particularly concerning due to their high mortality during infections and their ability to disseminate carbapenem resistance via MGEs [16, 17]. The epidemiology of CRE infections is driven by carbapenem resistance, mediated by hydrolytic enzymes called carbapenemases, which constitute a major global health challenge due to their widespread dissemination across human, animal, and environmental reservoirs [18, 19]. CRE is increasingly detected in humans, livestock, and ecosystems [20, 21, 22].

Many regions worldwide have implemented measures to reduce the use of critical antimicrobials in food-producing animals [23]; however, little is known about these efforts in Africa. CRE are increasingly reported in humans, and limited information from animals and ecosystems in Africa suggests that these settings serve as reservoirs for these critical priority bacteria [24, 25]. Given the rising prevalence of carbapenem resistance and the lack of integrated surveillance systems in Africa, an overview of the epidemiology of CRE infections at the human-animal-environment interface is paramount, as these infections pose risks to global health security [17, 23]. Consequently, understanding the mechanisms of CRE emergence and transmission dynamics, along with the associated genes, would inform data-driven strategies for interventions, surveillance, and research using the One Health concept, thereby helping to bridge the epidemiological knowledge gap [26, 27].

This systematic review examines the molecular epidemiology of CRE in Africa from a One Health perspective. The study objectives were to: (i) explore the emergence, dissemination, and prevalence of CRE and associated genes at the human-animal-environment interface in Africa; and (ii) highlight the importance of applying a One Health approach to interventions. CRE were defined by phenotypic carbapenem resistance, whereas carbapenemase-producing *Enterobacteriaceae* (CPE) are isolates harboring genes encoding carbapenemase. Accordingly, some included studies reported phenotypic carbapenem resistance in the absence of detectable carbapenemase genes, indicating alternative resistance mechanisms.

Materials and methods

Literature search and strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to conduct the systematic review. The PRISMA checklist was used to ensure that all eligible studies were included in the review. A literature search was performed through August 2025 using the following databases: Web of Science, Google Scholar, Scopus, ResearchGate, and PubMed. Information was extracted using the Medical Subject Headings (MeSH) technique, and research papers were retrieved using keywords such as “carbapenem-resistant Enterobacterales/*Enterobacteriaceae* (CRE)”, “carbapenemase”, “carbapenemase-producing Enterobacterales/*Enterobacteriaceae* (CPE)”, “Gram-negative”, “carbapenem resistance genes”, “occurrence”, “emergence”, “transmission dynamics”, “dissemination”, “carbapenem-resistant Enterobacterales/*Enterobacteriaceae* at human-animal-environment interface”, “carbapenem-resistant Enterobacterales/*Enterobacteriaceae* at human-animal interface”, “carbapenem-resistant Enterobacterales/*Enterobacteriaceae* at human-environment interface”, “carbapenem-resistant Enterobacterales/*Enterobacteriaceae* at animal-environment interface”, “One Health”, and “Africa”. The keywords were used alone and with Boolean operators (AND, OR, and NOT) to narrow the results. In addition, the CoCoPop framework (conditions, context, and population) was employed to identify relevant articles. The condition was carbapenem-resistant *Enterobacteriaceae* (Co), the context was Africa (Co), and the populations were humans, animals, and the environment (Pop).

Original articles were prioritized over reviews. Systematic or literature reviews that provided insights into the epidemiology of CRE in Africa were considered. The reference lists of all included articles were used to conduct supplementary literature searches. Furthermore, only English-language articles were retrieved and assessed for potential relevance. After the initial screening of titles and abstracts for relevance to the study objectives, the authors independently screened and evaluated the full texts of the articles. A consensus was reached through discussions of each article to resolve disagreements and inconsistencies among the authors.

Inclusion and exclusion criteria

The authors independently assessed articles against the predefined eligibility criteria. Inclusion and exclusion criteria were defined based on the relevance of the articles to the research questions. The inclusion criteria were used to confirm the eligibility of the papers identified in the search, defined as peer-reviewed original research papers that present reports and data on CRE and the occurrence of such bacteria at the human-animal-environment interface and/or at the level of two domains in Africa. The

exclusion criteria included research articles that investigated other Gram-negative bacilli, focused on carbapenem susceptibility, or did not include data on CRE and/or CPE. In addition, papers from outside African countries and articles not written in English were excluded. Zotero version 6.0.27 was used to manage references.

Synthesis of data

A quantitative synthesis of the data was conducted using descriptive statistics at a 95% confidence level. The various potential resistance mechanisms were recorded, and the relevant evidence supporting each reported mechanism was assessed as described above.

Results

Data analysis

Following PRISMA guidelines (Figure 1), the search and systematic review identified eight studies from Africa (Table 1). The published works reported findings from investigations conducted in African countries at the human-animal-environment interface, using primarily samples from human-animal, human-environment, animal-environment, and human-animal-environment interfaces, among others [28, 29, 30, 31, 32, 33, 34, 35]. Several *Enterobacteriaceae* have been reported to harbor antimicrobial resistance genes (ARGs) and MGEs, as shown in Table 1.

A descriptive statistical analysis was conducted at the 95% confidence level across the eight included original research articles. The prevalence of CRE among bacterial isolates was 18.58% (CI: 16.95-20.29; 389/2,094) (Table 2). The predominant CRE isolates were *E. coli* (58.35%; 95% CI: 53.40-63.18; 227/389), followed by *K.*

pneumoniae (28.28%; 95% CI: 23.97-32.91; 110/389), while other bacterial species accounted for only 13.37% (95% CI: 10.25-17.03; 52/389). Therefore, CRE prevalence was highest among *E. coli* isolates (Table 3). The animal domain had the highest CRE prevalence at 9.89% (95% CI: 8.66-11.22; 207/2,094), followed by the human domain at 6.06% (95% CI: 5.10-7.15; 127/2,094), and the environmental domain at 2.63% (96% CI: 2.00-3.38; 55/2,094) (Table 4).

Among *Enterobacteriaceae* isolates, 624 carbapenem resistance genes were identified across the studies. *E. coli* had the highest gene prevalence at 50.16% (95% CI: 46.24–54.08; 313/624), followed by *K. pneumoniae* at 21.47% (95% CI: 18.39–24.83; 134/624), and other bacterial species at 28.37% (95% CI: 24.93–32.00; 177/624). The most frequently occurring gene was *blaOXA-48* at 42% (95% CI: 38.16–45.89; 262/624), followed by *blaKPC* at 33.01% (95% CI: 29.40–36.78; 206/624), and *blaOXA-66* at 9.78% (95% CI: 7.63–12.30; 61/624). Less common genes included *blaNDM-1* at 3.21% (95% CI: 2.024–4.82; 20/624), *blaOXA-23* at 1.12% (95% CI: 0.49–2.21; 7/624), *blaOXA-9* at 0.64% (95% CI: 0.20–1.54; 4/624), and *blaOXA-69* at 0.16% (95% CI: 0.01-0.79; 1/624). The highly prevalent *blaOXA-48* gene was found in CRE isolates from all sources. Figure 2 summarizes the types and numbers of resistance-associated genes detected across the studies. Regarding regional distribution, North Africa had the highest CRE prevalence at 55.78% (95% CI: 50.81–60.67; 217/389), followed by East Africa at 29.82% (95% CI: 25.43-34.51; 116/389), while South Africa had the lowest prevalence at 3.08% (95% CI: 1.68-5.19; 12/389). No readily available data were reported from Central Africa (Table 5).

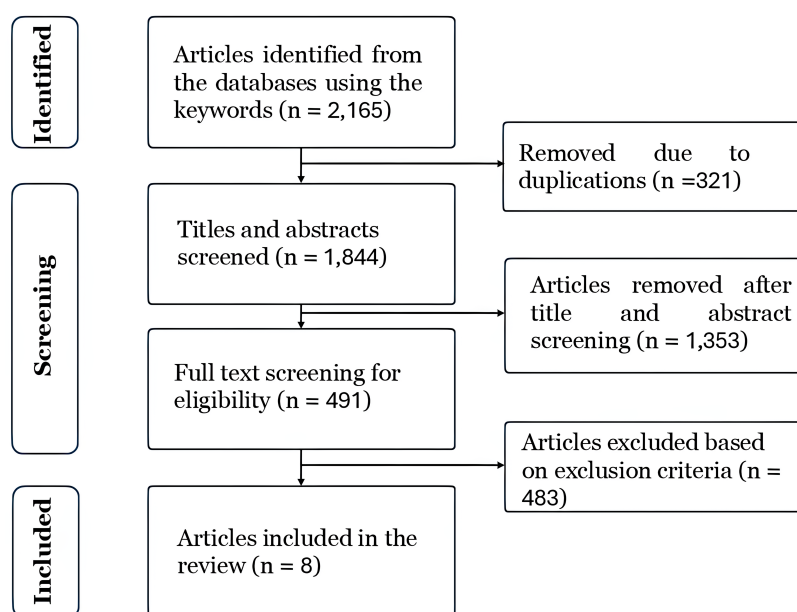


Figure 1: Flowchart of the study selection process for the data included in the review.

Table 1: General characteristics of studies investigating carbapenem-resistant *Enterobacteriaceae* (CRE) in Africa, arranged from recent to old.

No.	Country (African region)	Species involved in the interface	Samples	Identification methods	Bacterial species	Carbapenem resistance genes and other genes involved	MGE carrying carbapenemase-encoding genes	Study information and references
1	Djibouti (East Africa)	Humans and fish	Faeces and fillet	WGS	<i>K. pneumoniae</i>	<i>bla</i> NDM-1, <i>bla</i> NDM-5 and <i>bla</i> OXA-48	NA	Galal et al., 2024 [33]
2	Djibouti (East Africa)	Humans, animals (livestock, fish), and the environment (water)	Urine, faeces, fillets, and water	Illumina and Nanopore WGS	<i>E. coli</i> , <i>K. pneumoniae</i> , <i>P. mirabilis</i>	<i>E. coli</i> (<i>bla</i> NDM-1 and <i>bla</i> OXA-181), <i>K. pneumoniae</i> (<i>bla</i> NDM-1, <i>bla</i> NDM-5 and <i>bla</i> OXA-48), <i>P. mirabilis</i> (<i>bla</i> NDM-1)	ColKP3- <i>IncX3</i> hybrid plasmid, MDR <i>IncFIB</i> and <i>IncHI1B</i>	Mohamed et al., 2023 [28]
3	Uganda (East Africa)	Humans and livestock (cattle, goats, swine, and chickens)	Faeces	PCR	<i>E. coli</i>	<i>bla</i> KPC	NA	Tuhamize et al., 2023 [30]
4	South Africa (South Africa)	Humans and the environment (water)	Faeces and water	VITEK 2 automated platform and WGS	<i>K. pneumoniae</i> , <i>E. hormaechei</i> , <i>K. quasipneumoniae</i> , <i>C. freundii</i> , <i>S. marcescens</i>	<i>K. pneumoniae</i> (<i>bla</i> OXA-181, <i>bla</i> OXA-48, <i>bla</i> OXA-484, <i>bla</i> NDM-1, and <i>bla</i> GES-5) genes	Col440I, ol440I, <i>IncFIB</i> (K), <i>IncHI2</i> , <i>IncHI2A</i> , <i>IncN</i> , <i>IncQ1</i> , <i>ncL/M</i> (pMU407) and <i>IncL/M</i> (pOXA48)	Ramsamy et al., 2022 [29]
5	Nigeria (West Africa)	Humans, animals (cattle, camel, pigs, dogs, poultry), and the environment	Faeces, urine, liver, and hospital environment	WGS, PlasmidFinder, and MGEFinder	<i>K. pneumoniae</i> , <i>E. coli</i>	No carbapenemase gene detected. <i>E. coli</i> (<i>ompC</i>), <i>K. Pneumoniae</i> (<i>ompK36</i> , <i>ompK37</i>), <i>E. coli</i> , and <i>K. Pneumoniae</i> (<i>mcr-1</i> to <i>mcr-8</i>)	<i>IncFIB</i> , <i>ncFIB</i> (K), <i>IncFII</i> and <i>IncFIA</i> , <i>IncFII</i> (K) and <i>IncR</i>	Ngbede et al., 2021 [32]
6	Egypt (North Africa)	Humans, fish, water, and the environment	Fillet, pond, and tap water	PCR	<i>E. coli</i> , <i>K. pneumoniae</i> , <i>E. cloacae</i> complex	<i>bla</i> KPC, <i>bla</i> OXA-48, <i>bla</i> NDM	Incompatible (<i>Inc.</i>) plasmids like <i>ncF</i> and <i>IncHI</i> groups of plasmids, <i>IncX</i> , <i>IncI</i> , <i>IncA/C</i> , <i>IncP</i> , <i>IncW</i> , <i>IncN</i> , <i>IncN2</i> , <i>IncR</i> , <i>IncU</i> , and <i>IncT</i>	Hamza et al., 2020 [35]
7	Egypt (North Africa)	Humans, dogs, and the environment	Urine, faeces, swabs from water troughs, feed containers, walls, and floors	Illumina MiSeq WGS	<i>E. coli</i>	<i>E. coli</i> (<i>bla</i> NDM-5, <i>bla</i> NDM-1 and <i>bla</i> OXA-181)	<i>IncX3</i> -type plasmids and <i>IncColKP3</i>	Ramadan et al., 2020 [31]
8	Algeria (North Africa)	Farm animals, wild animals, pets, and environment (water)	Faeces and water	PCR -based replicon typing and WGS	<i>K. pneumoniae</i> , <i>R. ornithinolytica</i> , <i>E. cloacae</i> , <i>C. amalonaticus</i> , <i>R. planticola</i> , <i>C. werkmanii</i> , <i>P. gergoviae</i>	<i>bla</i> OXA-48	<i>IncL</i> group plasmid and <i>pOXA-48a</i> plasmids	Mairi et al., 2019 [34]

NA = Not available; MGE = mobile genetic elements; WGS = Whole-genome sequencing; PCR = Polymerase chain reaction; *K. pneumoniae* = *Klebsiella pneumoniae*; *R. ornithinolytica* = *Raoultella ornithinolytica*; *E. cloacae* = *Enterobacter cloacae*; *C. amalonaticus* = *Citrobacter amalonaticus*; *S. marcescens* = *Serratia marcescens*; *R. planticola* = *Raoultella planticola*; *C. werkmanii* = *Citrobacter werkmanii*; *P. gergoviae* = *Pluralibacter gergoviae* (formerly *Enterobacter gergoviae*)

Table 2: Distribution of CRE among bacterial isolates at the human-animal-environment interface in Africa.

Year of the study and references	Samples numbers (Sample size)	Number of bacteria isolated	Number of CRE isolated	Proportion (%)
2024 [33]	1,650	32	4	12.5
2023 [28]	1,650	452	32	7.08
2023 [30]	192	192	80	41.67
2022 [29]	588	588	12	2.04
2021 [32]	583	583	44	7.55
2020 [35]	250	160	130	81.25
2020 [31]	647	9	9	100
2019 [34]	3,309	78	78	100
Total	8,869	2,094	389	18.58

Table 3: Distribution of CRE species isolates at the human-animal-environment interface in Africa.

Year of the study and references	Number of CRE isolates	<i>E. coli</i> , n (%)	<i>K. pneumoniae</i> , n (%)	Others (<i>Enterobacter</i> spp., etc.), n (%)
2024 [33]	4	NA	4 (100)	NA
2023 [28]	32	19 (59.38)	5 (15.62)	8 (25)
2023 [30]	80	80 (100)	NA	NA
2022 [29]	12	NA	5 (41.67)	7 (58.33)
2021 [32]	44	24 (54.55)	19 (43.18)	1 (2.27)
2020 [35]	130	88 (67.69)	18 (13.85)	24 (18.46)
2020 [31]	9	9 (100)	NA	NA
2019 [34]	78	7 (8.97)	59 (75.64)	12 (15.39)
Total	389	227 (58.35)	110 (28.27)	52 (13.38)

NA = Not available

Table 4: Distribution of CRE isolates from each domain at the human-animal-environment interface in Africa.

Year of the study and references	Number of bacterial isolates	CRE isolated from humans, n (%)	CRE isolated from animals, n (%)	CRE isolated from the environment, n (%)
2024 [33]	32	2 (6.25)	2 (6.25)	NA
2023 [28]	452	16 (3.54)	14 (3.1)	2 (0.44)
2023 [30]	192	49 (25.52)	46 (24)	NA
2022 [29]	588	15 (2.55)	NA	4 (0.68)
2021 [32]	583	33 (5.66)	74 (12.69)	3 (0.51)
2020 [35]	160	6 (3.75)	60 (37.5)	36 (22.5)
2020 [31]	9	2 (22.22)	7 (77.78)	NA
2019 [34]	78	4 (5.13)	4 (5.13)	10 (12.82)
Total	2,094	127 (6.06)	207 (9.89)	55 (2.63)

NA = Not available

Table 5: Distribution of CRE isolates from the regions at the human-animal-environment interface in Africa.

Region	<i>E. coli</i> , n (%)	<i>K. pneumoniae</i> , n (%)	Others, n (%)	Total
East Africa	99 (85.34)	9 (7.76)	8 (6.90)	116 (29.87)
North Africa	104 (47.93)	77 (35.38)	36 (16.59)	217 (55.78)
West Africa	24 (54.55)	19 (43.18)	1 (2.27)	44 (11.31)
South Africa	0 (0)	5 (41.67)	7 (58.33)	12 (3.08)
Central Africa	NA	NA	NA	NA

NA = No available

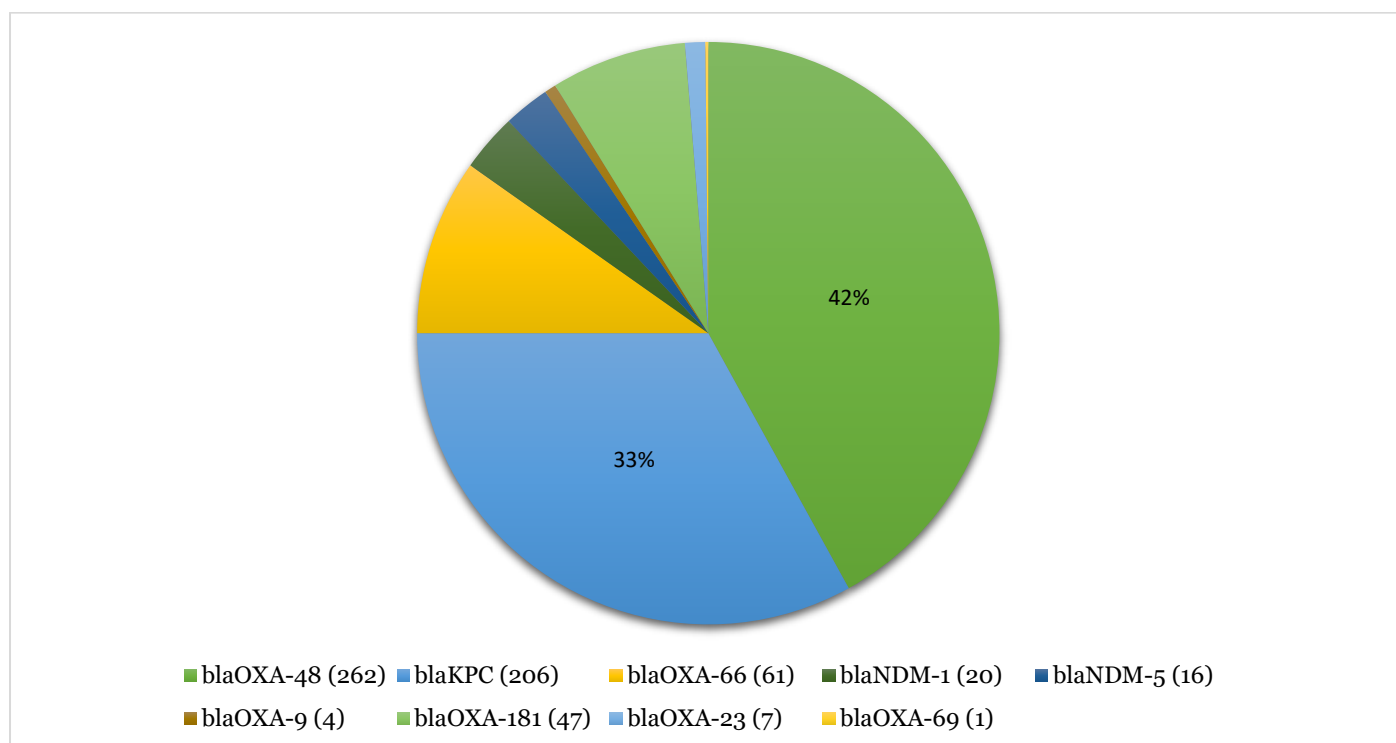


Figure 2: Types and number of genes associated with resistance detected in the analyzed studies.

Discussion

To the best of our knowledge, this is the first study to systematically investigate the burden and distribution of CRE within a One Health framework in Africa, offering crucial insights for global health security. It synthesizes evidence on the occurrence and spread of CRE at the human-animal-environment interface. CRE have been designated a WHO critical priority among antibiotic-resistant bacteria, necessitating extensive research and development of new antibiotics to address them [15]. These critical-priority One Health bacteria can cause a wide range of infections in humans and animals [36, 37]. Africa was selected because of limited multidisciplinary surveillance, low awareness of antimicrobial resistance, and weak biosecurity and infection-control mechanisms.

Based on the outcomes of this systematic review, which included eight relevant research articles, the prevalence of CRE infections across human, animal, and environmental domains in Africa was estimated at 18.58% (95% CI: 16.95–20.29). This distribution highlights the widespread and relatively consistent occurrence of CRE across humans, animals, and the environment in Africa [38]. This pattern likely reflects gaps in integrated One Health surveillance, limited antimicrobial stewardship, and inadequate infection prevention and control practices [39]. The paucity of research on these pathogens across the three regions, particularly in Central Africa, underscores the need for a collaborative, integrated surveillance system using a One Health approach, as a one-size-fits-all strategy is unlikely to be sufficient.

Carbapenems have recently been recognized as the last line of defense against serious multidrug-resistant Gram-negative infections in humans and animals [37]. CRE constitutes a significant threat that can only be effectively addressed through the implementation of informed One Health strategies [38]. Additionally, the findings of this review provide a basis for understanding the extent of the CRE burden across different domains and regions in Africa. This foundational baseline is crucial for the development of public health, animal, and environmental health policies; infection prevention and control strategies; and antimicrobial stewardship programs, which will mitigate the impacts of CRE. Nevertheless, international collaborations are also vital for sharing innovations and best practices to prevent further spread of CRE strains across the African continent and beyond.

Our analysis identified *E. coli* as the major contributor to CRE infections, with a notably high prevalence of carbapenemase resistance genes, followed by *K. pneumoniae*, underscoring the need to improve understanding of their infection epidemiology. The prevalence of these predominant species suggests that certain members of the *Enterobacteriaceae* harbor specific virulence factors or resistance mechanisms that facilitate their dissemination, making them critical priority bacteria for research at the human-animal-environment interface [15]. A major concern is the variable occurrence of CRE across humans, animals, and the environment, highlighting their dissemination through fecal contamination and gene transfer, which can

hinder AMR interventions [40, 41]. Therefore, future molecular research is needed to strengthen surveillance and elucidate the genetic mechanisms of CRE emergence, by enabling targeted One Health interventions.

Among the carbapenemase resistance genes identified, *bla*OXA-48 had the highest prevalence, followed by *bla*KPC, *bla*OXA-66, and *bla*OXA-181, while *bla*OXA-69 was the least prevalent. The diversity of carbapenemase genes highlights the complexity of antimicrobial resistance within the CRE group. Many authors have reported CRE in the environment, with a tendency to spread to humans and animals [21, 42, 43]. Notably, some bacterial species may not express resistance genes, while others rarely harbor them, resulting in very low frequencies with minimal epidemiological impact. Meanwhile, the distribution of *bla*OXA-48 and *bla*KPC genes in wastewater and effluents underscores the need to investigate CRE beyond clinical settings, including environmental reservoirs. Other environmental components, including air and surfaces from aquaculture, farms, zoos, and interfaces among the three domains, should also be surveyed. Further research across all domains and regions in Africa is imperative to identify the factors driving the burden of these species and genes and to provide supporting data to inform the development of targeted CRE interventions.

The *bla*OXA-48 gene has primarily been identified in *E. coli*, *K. pneumoniae*, and *Enterobacter* species in humans. Detection of this gene in animals and related environments indicates environmental contamination and identifies these settings as potential reservoirs and transmission routes. As the gene is plasmid-borne, the risk of dissemination is elevated [44]. Additionally, the *bla*OXA-48 gene has been reported in *Enterobacteriaceae* isolated from poultry and pig carcasses in Europe and Asia, as well as from drinking water systems in industrialized countries [45]. The predominance of *bla*OXA-48 and *bla*KPC genes, particularly in *E. coli* and *K. pneumoniae*, represents a significant concern due to their high prevalence and the associated threat to treatment outcomes [37]. The observed variation in the distribution of these genes among CRE species indicates that carbapenem resistance determinants are not uniformly distributed and may be influenced by selective pressures or facilitated by MGE such as plasmids and bacteriophages [46]. This genetic heterogeneity is consistent with previous research documenting variable carriage of resistance genes among *Enterobacteriaceae* species [47]. Importantly, *bla*OXA-48 and *bla*KPC are among the most prevalent carbapenemases in human clinical isolates from endemic regions and pose a major One Health concern, as they have also been detected in livestock isolates. Therefore, the identification and surveillance of specific carbapenemase genes, including *bla*OXA-48 and *bla*KPC, within CRE are critical for

elucidating the dissemination of resistance across human, animal, and environmental domains [37]. Surveillance efforts should also encompass species such as *Enterobacter* spp., which, despite lower prevalence, may serve as vectors for gene transmission across these domains.

These findings have important implications for the One Health framework, underscoring the need for ongoing research into the genetic determinants of carbapenem resistance and the anthropogenic and climatic factors that drive their dissemination across bacterial species and domains. Analysis of the distribution of resistance genes, such as *bla*OXA and *bla*KPC, provides insight into the escalating threats posed by CRE and informs the development of strategies to mitigate their impact on both public and animal health. The substantial burden of CRE infections, particularly those caused by *E. coli* and *K. pneumoniae*, underscores deficiencies in infection prevention and control measures in Africa, largely attributable to insufficient multisectoral collaboration.

Limitations of the study

This systematic review offers important insights into the molecular epidemiology of CRE in Africa; however, several limitations must be considered. The eight included studies varied in design, sampling strategies, target populations, and laboratory methodologies. Some focused exclusively on carbapenem-resistant isolates, while others examined broader bacterial populations. The analysis was also constrained by a limited number of recent studies, which may affect generalizability and introduce publication bias. These limitations underscore the need for integrated, multisectoral, and multidisciplinary CRE surveillance across Africa to generate comprehensive data. The absence of standardized study designs and harmonized sampling frameworks prevented direct comparisons and limited the ability to draw causal or temporal inferences regarding CRE emergence and dissemination at the human–animal–environment interface. Despite these challenges, using central tendency measures to summarize prevalence remains valuable, even in the presence of methodological imperfections. Sustained, adequately funded, and One Health-oriented research on CRE in Africa is crucial to address existing knowledge gaps.

Conclusion

This review revealed a high burden of CRE, particularly *E. coli* and *K. pneumoniae*, and their associated resistance genes at the human-animal-environment interface in Africa. These findings pose a serious concern for food safety and public health. Moreover, the results highlight the urgent need for integrated, One Health-based surveillance and research that connect human, animal, and environmental health to mitigate threats posed by CRE and other multidrug-resistant pathogens globally. To

enable effective interventions, further studies across all regions of Africa are required to elucidate the mechanisms driving the dominance and dissemination of critically important bacterial species and resistance genes across One Health domains.

Declarations and supplementary information

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References

- Liu CM, Stegger M, Aziz M, Johnson TJ, Waits K, Nordstrom L, et al. *Escherichia coli* ST131-H22 as a foodborne uropathogen. *mBio*. 2018;9(4). <https://doi.org/10.1128/mBio.00470-18>
- De Oliveira DMP, Forde BM, Kidd TJ, Harris PNA, Schembri MA, Beatson SA, et al. Antimicrobial resistance in ESKAPE pathogens. *Clin Microbiol Rev*. 2020;33(3). <https://doi.org/10.1128/cmr.00181-19>
- Tarakdjian J, Capello K, Pasqualin D, Santini A, Cunial G, Scollo A, et al. Antimicrobial use on Italian pig farms and its relationship with husbandry practices. *Animals*. 2020;10(3). <https://doi.org/10.3390/ani10030417>
- Ranjbar R, Alam M. Antimicrobial resistance collaborators (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *Evid Based Nurs*. 2023. <https://doi.org/10.1136/ebnurs-2022-103540>
- O'Neill J. Antimicrobial resistance: Tackling a crisis for the health and wealth of nations. Review on Antimicrobial Resistance. 2016. Available at: <https://iif.wellcomecollection.org/file/b28552179AMR%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations.pdf> Accessed 21 Aug 2024.
- Alhaji NB, Aliyu MB, Ghali-Mohammed I, Odetokun IA. Survey on antimicrobial usage in local dairy cows in North-central Nigeria: Drivers for misuse and public health threats. *PLoS One*. 2019;14(12):e0224949. <https://doi.org/10.1371/journal.pone.0224949>
- Elton L, Thomason MJ, Tembo J, Velavan TP, Pallerla SR, Arruda LB, et al. Antimicrobial resistance preparedness in sub-Saharan African countries. *Antimicrob Resist Infect Control*. 2020;9(1):145. <https://doi.org/10.1186/s13756-020-00800-y>
- Mouiche MMM, Mazra M, Moffo F, Mpouam SE, Ngoujigne AI, Feussom KJM, et al. Veterinary drugs market in Cameroon: Regulations, organization, and distribution channels. *Bull Anim Health Prod Afr*. 2018;66:591-605.
- WHO. Guidelines on use of medically important antimicrobials in food-producing animals: Web annex A: Evidence base. World Health Organization. (No. WHO/NMH/FOS/FZD/17.2). The World Health Organization, Geneva. 2017. Available at: <https://apps.who.int/iris/bitstream/handle/10665/259241/WHO-NMH-FOS-?sequence=1>. Accessed 21 Aug 2024.
- Collignon P, Aarestrup FM, Irwin R, McEwen S. Human deaths and third-generation cephalosporin use in poultry, Europe. *Emerg Infect Dis*. 2013;19(8):1339-40. <https://doi.org/10.3201/eid1908.120681>
- Anderson REV, Boerlin P. Carbapenemase-producing *Enterobacteriaceae* in animals and methodologies for their detection. *Can J Vet Res*. 2020;84(1):3-17. PMID: 31920216
- Irrgang A, Tausch SH, Pauly N, Grobbel M, Kaesbohrer A, Hammerl JA. First detection of GES-5-producing *Escherichia coli* from livestock-an increasing diversity of carbapenemases recognized from German pig production. *Microorganisms*. 2020;8(10); <https://doi.org/10.3390/microorganisms8101593>
- Levi G, Lurie-Weinberger M, Keren-Paz A, Andreumont AO, Schwartz D, Carmeli Y. Unraveling the diversity of co-colonization by CPE. *Microorganisms*. 2022;10(7). <https://doi.org/10.3390/microorganisms10071292>
- Köck R, Daniels-Haardt I, Becker K, Mellmann A, Friedrich AW, Mevius D, et al. Carbapenem-resistant *Enterobacteriaceae* in wildlife, food-producing, and companion animals: A systematic review. *Clin Microbiol Infect*. 2018;24(12):1241-50. <https://doi.org/10.1016/j.cmi.2018.04.004>
- WHO. World Health Organization (WHO) bacterial priority pathogens list, 2024: Bacterial pathogens of public health importance to guide research, development, and strategies, prevent and control antimicrobial resistance. 2024. Available at: <https://iris.who.int/bitstream/handle/10665/376776/9789240093461-eng.pdf?sequence=1&isAllowed=y>. Accessed 21 August 2024.
- Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant *Enterobacteriaceae*: Epidemiology and prevention. *Clin Infect Dis*. 2011;53(1):60-7. <https://doi.org/10.1093/cid/cir202>
- Ramírez-Castillo FY, Guerrero-Barrera AL, Avelar-González FJ. An overview of carbapenem-resistant organisms from food-producing animals, seafood, aquaculture, companion animals, and wildlife. *Front Vet Sci*. 2023;10:1158588. <https://doi.org/10.3389/fvets.2023.1158588>
- Taggar G, Attiq Rheman M, Boerlin P, Diarra MS. Molecular epidemiology of carbapenemases in Enterobacterales from humans, animals, food and the environment. *Antibiotics (Basel)*. 2020;9(10). <https://doi.org/10.3390/antibiotics9100693>
- Ma J, Song X, Li M, Yu Z, Cheng W, Yu Z, et al. Global spread of carbapenem-resistant *Enterobacteriaceae*: Epidemiological features, resistance mechanisms, detection and therapy. *Microbiol Res*. 2023;266:127249. <https://doi.org/10.1016/j.micres.2022.127249>
- Makharita RR, El-Kholy I, Hetta HF, Abdelaziz MH, Hagagy FI, Ahmed AA, Algammal AM. Antibigram and genetic characterization of carbapenem-resistant gram-negative pathogens incriminated in healthcare-associated infections. *Infect Drug Resist*. 2020;13:3991-4002. <https://doi.org/10.2147/idr.S276975>
- Feng J, Xiang Q, Ma J, Zhang P, Li K, Wu K, et al. Characterization of carbapenem-resistant *Enterobacteriaceae* cultured from retail meat products, patients, and porcine excrement in China. *Front Microbiol*. 2021;12:743468. <https://doi.org/10.3389/fmicb.2021.743468>
- Montezzi LF, Campana EH, Corrêa LL, Justo LH, Paschoal RP, da Silva IL, et al. Occurrence of carbapenemase-producing bacteria in coastal recreational waters. *Int J Antimicrob Agents*. 2015;45(2):174-7. <https://doi.org/10.1016/j.ijantimicag.2014.10.016>
- Vougat-Ngom R, Jajere SM, Ayissi GJ, Tanyienow A, Moffo F, Watsop HM, et al. Unveiling the landscape of resistance against high priority critically important antimicrobials in food-producing animals across Africa: A scoping review. *Prev Vet Med*.

- 2024;226:106173. <https://doi.org/10.1016/j.prevetmed.2024.106173>
24. Manenzhe RI, Zar HJ, Nicol MP, Kaba M. The spread of carbapenemase-producing bacteria in Africa: A systematic review. *J Antimicrob Chemother.* 2015;70(1):23–40. <https://doi.org/10.1093/jac/dku356>
25. Mitgang EA, Hartley DM, Malchione MD, Koch M, Goodman JL. Review and mapping of carbapenem-resistant *Enterobacteriaceae* in Africa: Using diverse data to inform surveillance gaps. *Int J Antimicrob Agents.* 2018;52(3):372–84. <https://doi.org/10.1016/j.ijantimicag.2018.05.019>
26. WHO. The One Health definition and principles developed by One Health high level expert panel. World Health Organization, updated on July 24, 2023. 9P. 2023 Available at: <https://www.who.int/publications/m/item/one-health-definitions-and-principles>. Accessed 21 August 2024.
27. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: One Health approach. *Vet World.* 2022;15(3):743–9. <https://doi.org/10.14202/vetworld.2022.743-749>
28. Mohamed HS, Galal L, Hayer J, Benavides JA, Bañuls AL, Dupont C, et al. Genomic epidemiology of carbapenemase-producing Gram-negative bacteria at the human-animal-environment interface in Djibouti city, Djibouti. *Sci Total Environ.* 2023;905:167160. <https://doi.org/10.1016/j.scitotenv.2023.167160>
29. Ramsamy Y, Mlisana KP, Amoako DG, Abia ALK, Ismail A, Allam M, et al. Mobile genetic elements-mediated Enterobacterales-associated carbapenemase antibiotic resistance genes propagation between the environment and humans: A One Health South African study. *Sci Total Environ.* 2022;806(3):150641. <https://doi.org/10.1016/j.scitotenv.2021.150641>
30. Tuhamize B, Asiimwe BB, Kasaza K, Sabiiti W, Holden M, Bazira J. *Klebsiella pneumoniae* carbapenemases in *Escherichia coli* isolated from humans and livestock in rural south-western Uganda. *PLoS One.* 2023;18(7):e0288243. <https://doi.org/10.1371/journal.pone.0288243>
31. Ramadan H, Gupta SK, Sharma P, Ahmed M, Hiott LM, Barrett JB, et al. Circulation of emerging NDM-5-producing *Escherichia coli* among humans and dogs in Egypt. *Zoonoses Public Health.* 2020;67(3):324–9. <https://doi.org/10.1111/zph.12676>
32. Ngbede EO, Adekanmbi F, Poudel A, Kalalah A, Kelly P, Yang Y, et al. Concurrent resistance to carbapenem and colistin among *Enterobacteriaceae* recovered from human and animal sources in Nigeria is associated with multiple genetic mechanisms. *Front Microbiol.* 2021;12:740348. <https://doi.org/10.3389/fmicb.2021.740348>
33. Galal L, Mohamed HS, Dupont C, Conquet G, Carriere C, Aboubaker MH, et al. Circulation of hypervirulent carbapenem-resistant *Klebsiella pneumoniae* in humans and fish in Djibouti. *J Antimicrob Chemother.* 2024;79(8):2068–71. <https://doi.org/10.1093/jac/dkae144>
34. Mairi A, Pantel A, Ousalem F, Sotto A, Touati A, Lavigne JP. OXA-48-producing Enterobacterales in different ecological niches in Algeria: Clonal expansion, plasmid characteristics, and virulence traits. *J Antimicrob Chemother.* 2019;74(7):1848–55. <https://doi.org/10.1093/jac/dkz146>
35. Hamza D, Dorgham S, Ismael E, El-Moez SIA, Elhariri M, Elhelw R, et al. Emergence of β -lactamase- and carbapenemase- producing *Enterobacteriaceae* at integrated fish farms. *Antimicrob Resist Infect Control.* 2020;9(1):67. <https://doi.org/10.1186/s13756-020-00736-3>
36. Soliman EA, Saad A, Abd El Tawab AA, Elhofy FI, Rizk AM, Elkhayat M, et al. Exploring AMR and virulence in *Klebsiella pneumoniae* isolated from humans and pet animals: A complement of phenotype by WGS-derived profiles in a One Health study in Egypt. *One Health.* 2024;19:100904. <https://doi.org/10.1016/j.onehlt.2024.100904>
37. Tuhamize B, Bazira J. Carbapenem-resistant *Enterobacteriaceae* in the livestock, humans, and environmental samples around the globe: A systematic review and meta-analysis. *Sci Rep.* 2024;14(1):16333. <https://doi.org/10.1038/s41598-024-64992-8>
38. Kelly AM, Mathema B, Larson EL. Carbapenem-resistant *Enterobacteriaceae* in the community: A scoping review. *Int J Antimicrob Agents.* 2017;50(2):127–34. <https://doi.org/10.1016/j.ijantimicag.2017.03.012>
39. van Loon K, Voor In 't Holt AF, Vos MC. A Systematic review and meta-analyses of the clinical epidemiology of carbapenem-resistant *Enterobacteriaceae*. *Antimicrob Agents Chemother.* 2018;62(1). <https://doi.org/10.1128/aac.01730-17>
40. Pavez M, Vieira C, de Araujo MR, Cerda A, de Almeida LM, Lincopan N, et al. Molecular mechanisms of membrane impermeability in clinical isolates of *Enterobacteriaceae* exposed to imipenem selective pressure. *Int J Antimicrob Agents.* 2016;48(1):78–85. <https://doi.org/10.1016/j.ijantimicag.2016.04.016>
41. Paschoal RP, Campana EH, de SCL, Picão RC. Predictors of carbapenemase-producing bacteria occurrence in polluted coastal waters. *Environ Pollut.* 2020;264:114776. <https://doi.org/10.1016/j.envpol.2020.114776>
42. Gong X, Zhang J, Su S, Fu Y, Bao M, Wang Y, et al. Molecular characterization and epidemiology of carbapenem non-susceptible *Enterobacteriaceae* isolated from the Eastern region of Heilongjiang Province, China. *BMC Infect Dis.* 2018;18(1):417. <https://doi.org/10.1186/s12879-018-3294-3>
43. Haller L, Chen H, Ng C, Le TH, Koh TH, Barkham T, et al. Occurrence and characteristics of extended-spectrum β -lactamase- and carbapenemase- producing bacteria from hospital effluents in Singapore. *Sci Total Environ.* 2018;615:1119–25. <https://doi.org/10.1016/j.scitotenv.2017.09.217>
44. Suay-García B, Pérez-Gracia MT. Present and future of carbapenem-resistant *Enterobacteriaceae* (CRE) infections. *Antibiotics (Basel).* 2019;8(3). <https://doi.org/10.3390/antibiotics8030122>
45. Nordmann P, Poirel L. The difficult-to-control spread of carbapenemase producers among *Enterobacteriaceae* worldwide. *Clin Microbiol Infect.* 2014;20(9):821–30. <https://doi.org/10.1111/1469-0691.12719>
46. Tilahun M, Kassa Y, Gedefie A, Ashagire M. Emerging carbapenem-resistant *Enterobacteriaceae* infection, its epidemiology and novel treatment options: A review. *Infect. Drug Resist.* 2021;14:4363–74. <https://doi.org/10.2147/idr.S337611>
47. Partridge SR. Resistance mechanisms in *Enterobacteriaceae*. *Pathology.* 2015;47(3):276–84. <https://doi.org/10.1097/pat.0000000000000237>