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REVIEW

Carbapenem resistance in West Africa: a systematic review

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ABSTRACT

OBJECTIVES: The World Health Organization (WHO) has reported carbapenem-resistant *Enterobacteriaceae* (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAb), and carbapenem-resistant *Pseudomonas aeruginosa* (CRPa) as critical priority pathogens for human health. Therefore, this study aimed to review clinical carbapenem resistance systematically and comprehensively in West Africa.

DATA SOURCES: A total of 102 research articles on carbapenem resistance from the sixteen countries forming the West African region were included in this review.

DATA SYNTHESIS: Carbapenem-resistant bacteria (CRB) were isolated mainly from urine 73/300 (24.3%) and pus/wounds of patients 69/300 (23%). The mean prevalence of CRB in West Africa was 4.6% (1902/41635), ranging from 1.6% to 18.6%. CRB identified were mainly *Escherichia* spp. (34/130; 26.1%), *Klebsiella* spp. (27/130, 20.8%), *Pseudomonas* spp. (26/130, 20%), and *Acinetobacter* spp. (25/130; 19.2%). Bacteria isolated in West African countries produced carbapenemases that belong to the four Ambler classes and include 13 types. The bla_{OXA}-type (34/104; 32.7%), bla_{NDM} (31/104; 29.8%), and bla_{VIM} (13/104; 12.5%) were the most common carbapenemase genes. These genes are carried by plasmids, composite transposons, and integrons. The Kirby-Bauer disc diffusion method (74/172; 43.0%), PCR (38/172; 22.1%), and whole genome sequencing (17/172; 9.9%) were the most common methods for carbapenem resistance detection. The most reported alternative antibiotics active against CRB were amikacin, colistin, and fosfomycin.

CONCLUSION: There is an urgent need to take synergistic action to delay, as much as possible, the occurrence of CRB epidemics in West Africa.

Keywords: resistance to carbapenems, carbapenemase, alternative antibiotics to carbapenems, West Africa, carbapenem-resistant bacteria

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INTRODUCTION

Carbapenems are the last-resort antibiotics used to treat severe infections caused by multidrug-resistant bacteria [1, 2]. Unfortunately, the world has been witnessing the spread of carbapenem-resistant bacteria (CRB) for the last two decades [3-5]. According to the World Health Organization (WHO), carbapenem-resistant *Enterobacteriaceae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* should be considered critical priority pathogens, posing the greatest threat to human health [6].

Three major mechanisms can lead to carbapenem resistance: (i) production of carbapenemases (enzymes hydrolyzing carbapenems); (ii) overexpression of efflux pumps; and (iii) quantitative loss of and/or mutations in outer membrane porins combined with the production of extended-spectrum β-lactamases (ESBL) or cephalosporinases [1, 7, 8].

As new antibiotics are rarely discovered [9], it is imperative to conduct epidemiological, preventive, and curative actions in every part of the globe to contain or postpone the occurrence of carbapenem-resistant bacterial epidemics as much as possible. Currently, there is no information on the overall status of carbapenem resistance in West Africa. With an area of 6,064,060 km^2, West Africa consists of 16 countries with a population of 442,006,171, representing approximately 5.47% of the world population [10].

This study aimed to conduct a systematic and comprehensive review of clinical carbapenem resistance in West Africa. The specific objectives were to: (i) report the prevalence of CRB in West Africa; (ii) describe the genetic determinants involved in carbapenem resistance in West Africa, such as resistance genes and mobile genetic elements; (iii) discuss methods used to study carbapenem resistance in West Africa; and (iv) list the alternative antibiotics with good activity against CRB isolated in the West African region.

MATERIALS AND METHODS

Literature review

Keywords (carbapenem resistance, carbapenemase, West Africa, and country name) were used to perform a comprehensive literature search covering PubMed, Embase, Google Scholar, African Journals Online, and Scopus. All articles published in French or English from January 1, 2000, to August 25, 2023, were included to ensure comprehensive and relevant data.

Study selection criteria

This study included peer-reviewed research articles published in French or English, reporting clinical carbapenem-resistant bacterial samples collected from one of the 16 West African countries. These countries are Benin, Burkina Faso, Cape Verde, Côte d'Ivoire or Ivory Coast, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, and Togo. The articles that reported at least one isolated bacterium resistant to carbapenem, the prevalence of carbapenem resistance, or a bacterium and its carbapenemase gene(s) were included in the study. Data on bacteria from human populations (from hospitals and communities) of all ages were included in this study. As this review focused on carbapenem-resistant bacteria of human origin, data on bacteria isolated from animal and environmental samples were excluded. Articles reporting clinical CRB collected from outside the sixteen West African countries were also excluded.

Data extraction and synthesis

The following data were extracted from the publications: country in which the samples were collected, year of sampling, type of study, number of isolates tested for carbapenem resistance, carbapenem resistance prevalence, the species (or genera) of the CRB, sample type, carbapenemase genes and their prevalences, mobile genetic elements, method used to detect CRB, community-acquired or hospital-acquired strains, age group, antibiotics active against CRB, and references (Table 1). To calculate the total prevalence of CRB, we only considered data displaying both the number of CRB and the total number of samples.

Method for obtaining the number of samples types

In studies reporting carbapenem-resistant bacteria (CRB) isolated from urine, pus, and blood the number of sample types equals 3. Similarly, in studies reporting CRB isolated only from urine, the number of sample types is equal to 1.

Method for calculating CRB prevalence

The prevalence of carbapenem-resistant bacteria was determined by studies that specified both the number of CRB and the total number of strains tested. Therefore, at the West African or country level, the prevalence of CRB was calculated as the ratio of the total number of CRB reported in the corresponding studies to the total number of strains tested in these studies.

Method for carbapenemase gene type description

For example, in a study reporting bla_{NDM-1}, bla_{NDM-2}, bla_{NDM-3}, bla_{OXA-48}, and $bla_{OXA-181}$, the number of carbapenemase gene types will be equal to bla_{NDM}=1 and bla_{OXA}=1. Additionally, a single study can report several bacterial strains (or bacterial pathotypes), each of which contains more than one carbapenemase gene (or gene type). This can lead to the sum of percentages of carbapenemase genes (or gene types) exceeding 100%.

Method for calculating values of other parameters

The number of cases with a defined parameter was divided by the total number of cases in which this type of parameter was studied.

Statistical analysis

Statistical analyses were performed by the χ^2 test at 5% level of significance using Microsoft Excel 2016.

RESULTS

Literature search and eligible studies

A literature search of databases such as PubMed, Embase, Google Scholar, African Journals Online, and Scopus generated 547 research articles. Subsequently, 329, 72, and 44 research articles were excluded due to duplication, data from countries outside West Africa, and data from animal and environmental sources, respectively. The data from the remaining 102 research articles were included in this systematic review (Fig. 1).

Sample collection and article publication periods

Out of the 102 studies included in this review, 89 (87.3%) reported the year of the sample collection. The sample collection period was from 2001 to 2022. The number of articles published per year ranged from 0 (2008, 2009, 2010) to 19 (January to August 2023) (Fig. 2).

Number of studies in each country

The number of articles published on carbapenem resistance per country was 30 (29.4%) in Nigeria, 15 (14.7%) in Ghana, 12 (11.8%) in Senegal, 10 (9.8%) in Burkina-Faso, 8 (7.8%) in Benin, 6 (5.9%) in Togo, 6 (5.9%) in Sierra Leone, 4 (3.9%) in Côte d'Ivoire, 4 (3.9%) in Mali, 3 (2.9%) in Gambia, 2 (2%) in Mauritania, 1 (1%) in Cape Verde, and 1 (1%) in Niger. We did not find any published studies on carbapenem resistance in Guinea, Guinea-Bissau, or Liberia (Fig. 3).

Type of studies

The type of study was specified in 57 publications (55.9%), including prospective, retrospective, descriptive, cross-sectional, case report, antimicrobial resistance surveillance, and screening program studies.

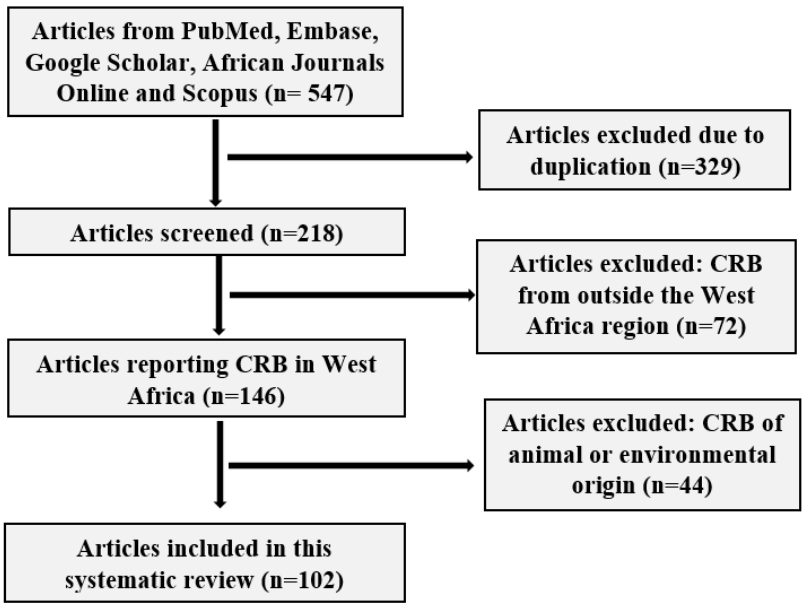

Fig. 1. Selection process of research articles included in this systematic review.

Table 1. Review of studies on carbapenem resistance in West Africa

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
	2019-2020	Descriptive cross-sectional	12/180 (6.7)	*E. coli*, *P. aeruginosa*, *P. mendocina*, *E. cloacae*, *A. baumannii*	Pus	bla_{OXA-48} (33.3), bla_{NDM} (33.3), bla_{VIM} (33.3)	NA	Kirby-Bauer DDM, PCR	Hospital (adult)	Amikacin	[11]
	2021-2022	NA	28/103 (27.18)	*Enterobacteriaceae*	Urine	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[12]
	2021-2022	Prospective descriptive	(100) (30) 0	*P. putida*, *S. paucimobilis*, *K. pneumonia*, *E. coli*	Urine	- bla_{NDM} (11.1), bla_{NDM} (10)	NA	Kirby-Bauer DDM, Vitek 2 (AST-N233 card), standard PCR	Hospital, community (children, adults, seniors)	NA	[13]
	NA	NA	(9) (25)	*E. coli*, *P. aeruginosa*	Wound	NA	NA	Kirby-Bauer DDM	Hospital	NA	[14]
Benin	2012-2013	NA	3/84 (3.6)	*E. coli*	Urine, pus, VS, sperm, blood, CSF	NA	NA	Kirby-Bauer DDM	Hospital	NA	[15]
	2017-2020	Prospective antimicrobial resistance surveillance	2/49 (4.1) 2/44 (4.5)	*E. coli* *E. cloacae*	Blood	NA	NA	Kirby-Bauer DDM, E-Test	Hospital (children, adults)	NA	[16]
	2019-2020	Cross-sectional	3/21 (14.3) 1/20 (5) 3/38 (8) 5/62 (8)	*E. cloacae*, *A. baumannii*, *P. aeruginosa*, *E. coli*	Pus, wound	NA	NA	Kirby-Bauer DDM, microdilution	Hospital	NA	[17]
	2005	Prospective	2/39 (5) 3/150 (2)	*E. coli*, Non ESBL *E. coli*	Urine, wound, blood, VS, rectal swab	NA	NA	Kirby-Bauer DDM	Hospital	NA	[18]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Burkina-Faso	2009-2010	Prospective sectional	2/5 (40)	*E. coli* (5 pathotypes)	Stool	bla_{KPC} (40), bla_{VIM} (40), bla_{IMP} (40)	NA	Kirby-Bauer DDM, PCR	NA (children)	Ciprofloxacin, netilmicin	[19]
	2020	Retrospective	15/53 (28.3)	*E. coli* (15 strains)	Urine, pus	bla_{NDM} (86.7), bla_{VIM} (33.3)	NA	PCR, Kirby-Bauer DDM	Hospital, community (adults, children, seniors)	NA	[20]
	NA	Case report	4*	*E. coli*	Urine, pus	$bla_{OXA-181}$	Tn*2013* transposons located on IncX3-type plasmids	E-test, PCR, DNA sequencing, PRaseT, PCR-based replicon typing	NA (adults, children, seniors)	NA	[21]
	2013-2015	NA	5/31 (16.1)	*E. coli*	Stool	NA	NA	PCR, Kirby-Bauer DDM	Hospital, community (children)	Ciprofloxacin	[22]
	2022	Retrospective descriptive	3/123 (2.4)	*E. coli, K. pneumoniae*	NA	NA	NA	Kirby-Bauer DDM	NA	NA	[23]
	2016	NA	17/601 (2.8)	*Enterobacteriaceae, Acinetobacter* spp.	Urine, wound, pus, stool, blood	bla_{NDM-1}, bla_{OXA-58}, $bla_{OXA-181}$, bla_{VIM-2}	IncX3-, IncX1-, IncF-type plasmids	Kirby-Bauer DDM, PCR, PRaseT	Hospital, community (children, adults, seniors)	Amikacin	[24]
	2009-2013	NA	2/17 (11.8)	*Klebsiella* spp.	Urine, pus, CSF	bla_{IMP} (17.6)	NA	Kirby-Bauer DDM, PCR	NA (children)	NA	[25]
	NA	NA	5/52 (9.6)	*P. aeruginosa, S. maltophilia*	blood, urine, pus, VS, stool	NA	NA	Kirby-Bauer DDM, Vitek 2	NA	NA	[26]
	2014-2015	Cross-sectional	1/486 (0.2)	*Enterobacteriaceae*	Urine, pus, blood, stool, VS, PF	NA	NA	Kirby-Bauer DDM	NA (children, adults, seniors)	NA	[27]
	2013-2015	NA	2/53 (3.8)	*Salmonella* spp.	Stool	NA	NA	Kirby-Bauer DDM	Hospital, community (children)	NA	[28]
Cape Verde	2021	NA	6/98 (6.1)	*Enterobacteriaceae*	Rectal swab	$bla_{OXA-181}$ (66.7), bla_{OXA-48} (16.7), $bla_{OXA-244}$ (16.7)	IncFI-, IncX3-types plasmids	Kirby-Bauer DDM, PCR-based replicon typing	Hospital (adult)	Ceftazidime/avibactam	[29]

Table 1. (*continued*)

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Côte d'Ivoire	2010-2016	Transverse	14/174 (8)	*P. aeruginosa*	Urine, pus, blood, CSF, catheter, BF, PF	NA	NA	Kirby-Bauer DDM	Hospital, community	NA	[30]
	2002-2012	NA	8/48 (16.7)	*P. aeruginosa*	NA	$bla_{\text{VIM-2}}$	NA	Kirby-Bauer DDM, PCR, Sequencing	Hospital	NA	[31]
	2009-2011	NA	12*	*P. aeruginosa*	Urine, blood	$bla_{\text{VIM-2}}$	Class 1 integron	PCR, DNA sequencing	Hospital	Aztreonam, colistin	[32]
	NA	NA	4/20 (20)	*A. baumannii, A. nosocomialis*	Urine	$bla_{\text{NDM-1}}$, $bla_{\text{OXA-58}}$, $bla_{\text{OXA-66}}$	Tn*125*	Kirby-Bauer DDM, PCR, WGS	Hospital (children, adults)	NA	[33]
Gambia	2015	Cross-sectional	16/89 (18)	*Enterobacteriaceae, Pseudomonas* spp.	Stool	NA	NA	Kirby-Bauer DDM	Community (adults)	NA	[34]
	2015	Cross-sectional	1/28 (3.6)	*Enterobacteriaceae*	Stool	NA	NA	Kirby-Bauer DDM	Community (adults)	NA	[35]
	2017	Cross-sectional cohort	112*	*E. coli, K. pneumoniae, Acinetobacter* spp.	Perianal, skin, rectovaginal	$bla_{\text{SHV-75}}$, $bla_{\text{SHV-65}}$, $bla_{\text{SHV-61}}$, $bla_{\text{SHV-27}}$, $bla_{\text{SHV-187}}$, $bla_{\text{SHV-157}}$, $bla_{\text{SHV-13}}$, $bla_{\text{SHV-106}}$, bla_{MBL}, $bla_{\text{CTX-M-27}}$	NA	WGS	Hospital, community (children, adults)	NA	[36]
Ghana	2016-2017	NA	2/36 (5.6)	*Acinetobacter* spp.	Urine, sputum, wound, HVS, blood, semen, CSF	$bla_{\text{OXA–23}}$, $bla_{\text{OXA–58}}$, $bla_{\text{OXA–420}}$, $bla_{\text{OXA-70}}$, $bla_{\text{OXA-699}}$, $bla_{\text{OXA-51}}$	Tn*2007*, IS*15DII*, plasmids	WGS, broth microdilution	NA	Amikacin, minocycline	[37]
	2014-2015	Retrospective	52/87 (59.8)	*Acinetobacter* spp.	Wound, urine, aspirate, ear, eye swab	bla_{NDM}	NA	Kirby–Bauer DDM, PCR	NA (children, adults)	Amikacin	[38]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Ghana	2020-2021	Cross-sectional	8/144 (5.6)	*E. coli*, *K. pneumoniae*	Wound, urine, sputum, blood, pus, PF, aspirate, ear, eye swab, HVS	$bla_{\text{OXA-48}}$ (80), bla_{NDM} (20)	NA	Kirby-Bauer DDM, MIC, PCR	NA (children, adults, seniors)	NA	[39]
	2012-2014	Prospective	111/3840 (2.9)	*A. baumannii*, *Enterobacteriaceae*, *P. aeruginosa*	Wound, urine	$bla_{\text{NDM-1}}$ (14.4), $bla_{\text{VIM-1}}$ (7.2), $bla_{\text{OXA-48}}$ (1.8)	NA	Kirby-Bauer DDM, E-test, PCR, sequencing	Hospital (children, adults, seniors)	NA	[40]
	NA	NA	43/600 (7.2)	*Enterobacteriaceae*, *A. baumannii*	NA	NA	NA	Kirby-Bauer DDM, E-test	NA	Amikacin, colistin, fosfomycin	[41]
	2017-2021	Cross-sectional	42/14554 (0.3)	*E. coli*,	Urine	NA	NA	Kirby-Bauer DDM	NA (adults, children, seniors)	NA	[42]
			1/48 (2.1)	*Acinetobacter* spp.,							
			19/100 (19)	*Pseudomonas* spp.,							
			56/3090 (1.8)	*Klebsiella* spp.,							
			3/1110 (0.3)	*Proteus* spp.							
	NA	Case report	2*	*E. coli*	Stool	$bla_{\text{OXA-181}}$	IS*26* forming composite transposon on IncX3-, IncFIC(FII)-type plasmids	Broth microdilution, WGS	NA (children)	NA	[43]

Table 1. (*continued*)

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Ghana	2017-2018	Prospective	22/45 (48.9)	*A. baumannii* (22 strains)	Wound	$bla_{\text{NDM-1}}$ (90.9), $bla_{\text{OXA-23}}$ (90.9), $bla_{\text{OXA-420}}$ (9.1), $bla_{\text{OXA-378}}$ (13.6), $bla_{\text{OXA-69}}$ (77.3)	NA	Broth microdilution, Vitek 2 (AST-N248 card), PCR, Sequencing	NA	NA	[44]
	2017-2018	NA	27/91 (29.7) 18/48 (37.5)	*K. pneumonia,* *K. oxytoca*	Blood, HVS, sputum, urine, wound	$bla_{\text{OXA-48}}$ (2.2), bla_{NDM} (0.7)	NA	Kirby-Bauer DDM, PCR	Hospital (adults)	Amikacin	[45]
	2018-2019	Cross sectional	2/135 (1.5)	*E. coli*	Urine	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[46]
	2017-2018	Laboratory surveillance of antimicrobial resistance	35/168 (21)	*Enterobacteriaceae*	Urine, wound, blood, throat swab, stool, ear swab	$bla_{\text{OXA-48}}$, bla_{NDM}, bla_{KPC}	NA	Kirby-Bauer DDM, microscan auto-SCAN system, PCR	Hospital, community	NA	[47]
	2017-2019	NA	29*	*K. pneumoniae*	Swabs of neonates, blood	$bla_{\text{OXA-181}}$	IncX3-, IncF1B (Mar)-, IncQ1-, IncColKP3-type plasmids	WGS	Hospital (children)	NA	[48]
	2019	Cross-sectional	2/19 (10.5)	*K. pneumoniae*	Stool	NA	NA	Vitek 2	Community (children)	NA	[49]
	NA	Cross-sectional	2/736 (0.3)	*Enterobacteriaceae*	NA	$bla_{\text{NDM-1}}$, $bla_{\text{CMY-2}}$	NA	NA	Community	NA	[50]
	2015	Cross-sectional analytical	22/220 (10)	*Enterobacteriaceae*	Urine	NA	NA	E-test	Community (children, adults)	NA	[51]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Mali	2001-2008	Screening program	41*	*Salmonella* spp.	Stool	$bla_{\text{SHV-12}}$ (51.2)	NA	Kirby-Bauer DDM, PCR, Sanger DNA sequencing	Community (children)	NA	[52]
	2010-2019	Retrospective	5/317 (1.6)	*P. aeruginosa*	Urine, pus, VS, sputum, blood, PF, CSF, ProF, PeriF, BAF, AF, GF	NA	NA	Kirby-Bauer DDM	Hospital, community	Colistin, ceftazidime, amikacin, piperacillin	[53]
	2019-2022	NA	2/48 (4.2)	*K. pneumoniae*	Urine, pus, sputum, blood, PL	NA	NA	Kirby-Bauer DDM	NA	NA	[54]
	2014	Prospective	1/31 (3.2)	*E. coli*	Blood	$bla_{\text{OXA-181}}$	NA	Kirby-Bauer DDM, E-test, PCR, sequencing	Hospital (adults, children, seniors)	NA	[55]
Mauritania	2014	Prospective	4/366 (1.1)	*E. coli*	Urine	NA	NA	Kirby-Bauer DDM	Hospital, community	NA	[56]
	2019-2020	Retrospective	4/120 (3.3)	*Enterobacteriaceae*	Urine	NA	NA	Vitek 2, Kirby-Bauer DDM	Hospital, community (adults, children)	NA	[57]
Niger	2021	Descriptive cross-sectional	4/50 (8) 7/9 (77.8)	*Enterobacteriaceae* *P. aeruginosa*	Urine, pus, stool	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[58]

Table 1. (*continued*)

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Nigeria	2019	Prospective descriptive, epidemiological	19/292 (6.5)	*Enterobacteriaceae*	Urine, sputum, stool	$bla_{\text{NDM-5}}$ (71.4), $bla_{\text{OXA-181}}$ (28.6)	NA	RT-PCR, modified Kirby-Bauer DDM	NA	NA	[59]
	2016-2020	Antimicrobial resistance surveillance	54/86 (62.8) 2* 16*	*A. baumannii*, *A. haemolyticus*, *A. nosocomialis*	Rectal swab, blood, CSF	$bla_{\text{OXA-23}}$ (34.9), $bla_{\text{NDM-1}}$ (27.9), $bla_{\text{OXA-214}}$, $bla_{\text{OXA-420}}$, $bla_{\text{OXA-58}}$ (11.6)	Tn*2006*, Tn*2006*-like, Tn*125*	Vitek 2 (AST N281 card), WGS	Hospital	Minocyclin, tigecycline	[60]
	2015	Cross-sectional	13/64 (20.4) 21/108 (19.4)	*E. coli,* *K. pneumoniae*	Urine	NA	NA	Modified Kirby-Bauer DDM	NA (children, adults, seniors)	NA	[61]
	2019	NA	16/200 (8)	*Enterobacteriaceae*	NA	$bla_{\text{NDM-7}}$ (12.5), $bla_{\text{SHV-37}}$, $bla_{\text{ACT-29}}$	NA	E-test, BDM, standard PCR, WGS	NA	Amikacin, colistin, tigecyclin	[62]
	NA	NA	13/25 (52) 11/35 (31.4) 9/30 (30)	*K. pneumoniae,* *E. coli,* *P. aeruginosa*	Urine	NA	NA	Kirby-Bauer DDM	NA	NA	[63]
	2019	NA	47/158 (29.7)	*Enterobacteriaceae,* *P. aeruginosa*	Urine, wound, eye swab, sputum, tracheal aspirate	NA	NA	EDTA double-disc synergy test, mCIM	Hospital, community	NA	[64]
	2015-2016	NA	17/46 (37)	*Klebsiella* spp.	Urine, sputum, ear swab, wound, VS	NA	NA	Kirby-Bauer DDM	NA	NA	[65]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
	2017-2018	NA	105/1741 (6)	*A. baumannii*, *Enterobacteriaceae*, *P. aeruginosa*	Urine, wound, stool, sputum, VS, ear swab, PF	bla_{NDM} (24.8), bla_{VIM} (3.8)	NA	MicroScan Walk-Away 40, RT-PCR	NA	NA	[66]
	2018	NA	7/21 (33.3)	*A. baumannii*	Urine, CSF, wound, blood, sputum, tissue	bla_{NDM-1}, bla_{OXA-51}, bla_{OXA-58}, bla_{OXA-67}, bla_{OXA-68}, bla_{OXA-69}, bla_{OXA-23}, $bla_{OXA-180}$, bla_{OXA-91}, $bla_{OXA-130}$, bla_{OXA-64}, bla_{OXA-91}, $bla_{OXA-203}$, $bla_{OXA-235}$	NA	WGS, Kirby-Bauer DDM	NA (children, adults, seniors)	NA	[67]
Nigeria	2014	Descriptive cross-sectional	28/225 (12.4)	*Enterobacteriaceae*	Blood, urine, CSF, stool	bla_{KPC} (47.8%), bla_{NDM-1} (21.4), bla_{VIM} (30.4%)	NA	Kirby-Bauer DDM, PCR	Hospital (children, adults, seniors)	NA	[68]
	2014-2015	Laboratory-based	35/171 (20.5)	*P. aeruginosa*	Urine, wound, blood, bone	NA	NA	Kirby-Bauer DDM	NA	NA	[69]
	2018	Retrospective, epidemiological and surveillance	39/177 (22)	*Enterobacteriaceae*, *A. baumannii*, *P. aeruginosa*	Urine, pus, wound, tracheal aspirate, tissue biopsy, sputum	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	Colistin, nitrofurantoin	[70]
	2016-2017	Cross-sectional	19/59 (32.2)	*Enterobacteriaceae*	Blood, urine	NA	NA	Kirby-Bauer DDM	Hospital (children, adults, seniors)	NA	[71]

Table 1. (*continued*)

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Nigeria	2016-2021	NA	32/49 (65.3)	*Enterobacteriaceae* (49 species)	Blood, urine, wound	*bla*$_{NDM-1}$ (35), *bla*$_{NDM-5}$ (25), *bla*$_{OXA-181}$ (3), *bla*$_{OXA-48}$ (9.1), *bla*$_{SHV-67}$ (6.1), *bla*$_{SHV-187}$ (44.9), *bla*$_{SHV-11}$ (4.1), *bla*$_{OXA-320}$ (2), *bla*$_{OXA-534}$ (2), *bla*$_{OXA-9}$ (2)	IS*Ec33*, IS*5*, IS*Kpn19*, IS*Kra4* family, IncFII-type plasmids	BD Phoenix Automated Microbiology System, WGS	Community	Tigecycline, fosfomycin, amikacin, colistin	[72]
	2018	Descriptive cross-sectional	8/76 (10.5)	*Enterobacteriaceae*	Blood, urine, sputum, tracheal aspirate	*bla*$_{VIM}$ (62.5), *bla*$_{NDM}$ (25), *bla*$_{KPC}$ (12.5)	NA	Kirby-Bauer DDM, PCR	Hospital (children, adults)	NA	[73]
	2018-2019	NA	55/128 (43.0)	*K. pneumoniae* (128 phenotypes)	Urine, blood, sputum, wound, HVS, pus, stool, tracheal aspirate, semen	*bla*$_{VIM}$ (43), *bla*$_{OXA-48}$ (28.9), *bla*$_{IMP}$ (22.7), *bla*$_{NDM}$ (17.2), *bla*$_{KPC}$ (13.3)	NA	Kirby-Bauer DDM, broth microdilution methods, PCR	Hospital, community (children, adults, seniors)	Polymyxin B	[74]
	2018-2019	NA	54/123 (44)	*P. aeruginosa*	Wound, urine, sputum/tracheotomy aspirates, ear swabs, VS	*bla*$_{VIM-2}$, *bla*$_{VIM-5}$-like, *bla*$_{NDM-1}$, *bla*$_{GES-5}$, *bla*$_{GES-1}$, *bla*$_{GES-9}$	Plasmids	Vitek 2 (AST-N-232 card), WGS	Hospital, community (adults)	NA	[75]
	2016-2019	NA	33/95 (34.7)	*Enterobacteriaceae*	Stool, urine	*bla*$_{SHV-11}$, *bla*$_{SHV-28}$	IncFIB-, IncFIB(K)-, IncFII-, IncFIA-, IncFII(K)-, IncR-type plasmids	broth dilution method, Kirby-Bauer DDM, WGS	NA	NA	[76]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Nigeria	2011	NA	67/182 (36.8)	*Enterobacteriaceae*, *Pseudomonas* spp.	Urine, wound, stool, blood, sputum, ear swab	bla_{NDM}, bla_{VIM}, bla_{GES}	Plasmids	Kirby-Bauer DDM, PCR, sequencing	Hospital, community	NA	[77]
	2015	NA	9/218 (4.1)	*Enterobacteriaceae*	Urine, peritoneal fluid, endocervical swab	bla_{NDM-1}, bla_{OXA-48}, $bla_{OXA-181}$, bla_{SHV-11}, bla_{SHV-28}, bla_{ACT-5}	IncL/M-type plasmids	Kirby-Bauer DDM, E-test method, WGS	NA	NA	[78]
	2012	NA	3/5 (60)	*A. baumannii*	NA	bla_{OXA-23}	NA	RT-PCR, standard PCR	NA	Colistin	[79]
	2016-2018	Antimicrobial resistance sentinel surveillance	134*	*K. pneumoniae*	Blood, cerebrospinal fluid, urine	bla_{NDM-1} (6), bla_{NDM-5} (1.5), bla_{OXA-48} (0.7), bla_{SHV-89}, bla_{SHV-80}, bla_{SHV-32}, $bla_{SHV-215}$, bla_{SHV-36}, $bla_{SHV-212}$, $bla_{SHV-223}$, bla_{SHV-75}, $bla_{SHV-172}$, bla_{SHV-84}	IncL/M-, IncFIB-(AP001918), IncN-, IncR-types plasmids	Vitek 2, WGS	NA	NA	[80]
	NA	NA	66/140 (47.1) 48/108 (44.4)	*E. coli*, *K. pneumoniae*	Urine, wound, abscess	NA	NA	Modified Kirby-Bauer DDM,	NA	NA	[81]
	2016-2018	NA	48/175 (27.4)	*Enterobacteriaceae* (48 species)	Urine, wound, blood	bla_{NDM} (85.4), $bla_{OXA-181}$ (25), bla_{OXA-48} (2.1), bla_{CMY-2} (22.9)	NA	Vitek 2, standard PCR, isothermal amplification, WGS	NA (children, adults, seniors)	Fosfomycin, ceftazidim/avibactam/aztreonam	[82]
	NA	NA	(12.5)	*Enterobacteriaceae*	NA	NA	NA	Kirby-Bauer DDM	Hospital	Colistin, tigecycline	[83]
	2013	NA	27/177 (15.2)	*Enterobacteriaceae*	Urine, blood, sputum, wound, pus	NA	NA	Modified Kirby-Bauer DDM	Hospital	NA	[84]

Table 1. (*continued*)

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Nigeria	2020	Prospective descriptive	3/8 (37.5)	*K. pneumoniae*	Urine, sputum, wound	NA	NA	Kirby-Bauer DDM, PCR	NA	NA	[85]
	2013-2014	Prospective cross-sectional	1/220 (0.5)	*E. coli*	Urine, blood, diverse aspirates	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[86]
	2014	NA	52/157 (33.1)	*Enterobacteriaceae, P. aeruginosa*	Urine, blood, wound, sputum, semen, HVS, endo cervical swab	NA	NA	Kirby-Bauer DDM	NA	NA	[87]
	NA	NA	9/97 (9.3)	*E. coli, K. pneumoniae*	Urine, blood, CSF, genitals	NA	NA	Kirby-Bauer DDM	(children, adults)	NA	[88]
Senegal	2018-2020	Retrospective	10/66 (15.2)	*K. pneumoniae*	Urine, pus, sputum, BF, VS	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[89]
	2018-2020	Retrospective	3/78 (3.8)	*E. coli*	Urine, pus, sputum, BF, VS	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	Fosfomycin	[90]
	2014-2018	Prospective	30/807 (3.7) 23/295 (7.8) 20/95 (21.1)	*E. coli,* *Klebsiella* spp., *Enterobacter* spp.	Urine	NA	NA	Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[91]
	2019-2022	Prospective	13/240 (5.4)	*Enterobacteriaceae*	Urine, pus, blood, VS, puncture fluid, sputum	bla_{NDM} (5.4), bla_{OXA-48} (5.8)	NA	Kirby-Bauer DDM, RT-PCR, standard PCR	Hospital, community (children, adults)	Colistin	[92]
	2015-2016	Retrospective	12/1185 (1)	*Enterobacteriaceae*	Urine	NA	NA	Kirby-Bauer DDM	Hospital, community	NA	[93]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Senegal	NA	NA	NA/49	*K. pneumoniae* (5 isolates)	Urine	$bla_{\text{OXA-48}}$ (100), $bla_{\text{SHV-28}}$ (40), $bla_{\text{SHV-11}}$ (20), $bla_{\text{SHV-61}}$ (20), $bla_{\text{SHV-110}}$ (20)	Tn*1999.2*-type transposon located on IncL/M-type plasmids	PCR, WGS	NA	NA	[94]
	2018-2021	Retrospective	10/28 (35.7)	*K. pneumoniae*	Urine, blood, wound	$bla_{\text{OXA-48}}$ (21.4)	NA	Kirby-Bauer DDM, PCR	Hospital	NA	[95]
	2016	Cross-sectional	62/1205 (5.1)	*Enterobacteriaceae*	Wound, urine, LF, genitals, blood, stool	NA	NA	Kirby-Bauer DDM	Hospital, community (adults, seniors)	Amikacin, fosfomycin	[96]
	NA	NA	29/29 (100)	*A. baumannii* (29 strains)	Urine, BS, pus, PL, blood	$bla_{\text{OXA-51}}$ (100), $bla_{\text{OXA-23}}$ (89.7), $bla_{\text{NDM-1}}$ (3.4)	NA	Kirby-Bauer DDM, standard PCR	Hospital	Amikacin, colistin	[97]
	2011	Case report	3*	*A. baumannii*	BAL, blood	$bla_{\text{OXA-23}}$, $bla_{\text{OXA-51}}$	IS*Aba1*	Genome sequencing	Hospital (children, adults)	Netilmicin, colistin	[98]
	2008-2009	NA	2/11 (18.2)	*Enterobacteriaceae*	Urine, post-surgical specimen	$bla_{\text{OXA-48}}$	Tn*1999* transposon located on a plasmid	Kirby-Bauer DDM, E-test method, PCR	Hospital, community	NA	[99]
	2008-2011	Prospective	2*	*A. baumannii*	Stool	$bla_{\text{OXA-23}}$	NA	PCR, E-test	Community (children, adults)	Colistin, rifampicin	[100]

Table 1. (*continued*)

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
	2010-2011	Molecular epidemiology surveillance program	20*	*Enterobacteriaceae, Pseudomonas* spp.	NA	$bla_{\text{OXA-51}}$-like, $bla_{\text{OXA-58}}$, $bla_{\text{DIM-1}}$, $bla_{\text{VIM-2}}$, $bla_{\text{VIM-10}}$, $bla_{\text{VIM-16}}$, $bla_{\text{VIM-17}}$, $bla_{\text{VIM-30}}$	Class 1 integron, IS*Aba3*- related transposons	PCR, DNA sequencing, WGS	NA	NA	[101]
	2018	Cross-sectional	1/1 (8.7) (13)	*B. cepacia, A. baumannii E. cloacae*	Urine, sputum	NA	NA	Vitek 2	Hospital (adults, seniors)	NA	[102]
Sierra-Leone	2018	NA	56*	NA	Stool	bla_{NDM} (10.7), $bla_{\text{OXA-48}}$-like (1.8), bla_{PER} (1.8)	Class 1 integron, IS*CR1*	RT-PCR	Hospital	NA	[103]
	2019-2020	NA	4*	*M. morganii, Proteus* spp.	Wound	NA	NA	Vitek 2 (AST-N214 card), Kirby-Bauer DDM	Hospital, community (children, adults, seniors)	NA	[104]
	2013-2014	NA	2/70 (2.9)	*Enterobacteriaceae*	Urine	NA	NA	Kirby-Bauer DDM, E-test	Community (children, adults)	Tigecycline	[105]
	2021	Prospective	1/2 (50) 2/6 (33)	*P. mirabilis P. aeruginosa*	Surgical wound, urinary catheter	NA	NA	Vitek 2	Hospital (adults, seniors)	Amikacin	[106]

Country	Year of sampling	Type of study	CR isolates / total tested (%)	Species (number of strains studied)	Isolate source	Carbapenemase genes (prevalence among the studied strains, %)	Mobile genetic element	Method used	Setting (age group)	Effective antibiotic against CRB	Ref.
Togo	2016	Cross-sectional	28/903 (3.1)	*A. baumannii, E. cloacae, P. aeruginosa, K. pneumoniae, E. coli*	Urine, pus, CSF	NA	NA	Kirby-Bauer DDM	Hospital, community	Tobramycin, amikacin, colistin	[107]
	2016	NA	8/152 (5.2)	*E. xiangfangensis, E. cloacae* subsp. *cloacae, E. hormaechei* subsp. *oharae*, *E. coli, K. pneumoniae*	Urine, pus	bla_{NDM-5}, bla_{ACT-16}, bla_{ACT-7}, $bla_{OXA-181}$, bla_{OXA-9}	IncX3-, ColKP3-type plasmids	WGS	Hospital, community (children, adults)	Fosfomycin	[108]
	2013-2015	Retrospective	7/1979 (0.35) 5/197 (2.5)	*E. coli,* *A. baumannii, P. aeruginosa,*	Pus, spit, urine, sperm, stool, articular fluids, ascitic fluids, BS	NA	NA	Kirby-Bauer DDM	Hospital, community	NA Amikacin	[109]
	2017-2018	NA	4/35 (11.4)	*E. coli*	NA	NA	NA	Kirby-Bauer DDM	Hospital, community	Gentamicin	[110]
	2009-2011	NA	(0.68) (3.7)	*E. coli,* *Klebsiella* spp.	VS, urine, pus, blood	NA	NA	Kirby-Bauer DDM	NA	NA	[111]
Togo	2013-2015	Prospective	2/91 (2.2) 1/64 (1.6)	*E. coli,* *K. pneumoniae*	Urine, VS, pus, sperm, wound, sputum	NA	NA	Kirby-Bauer DDM	NA	NA	[112]

NA - not available; CRB - carbapenem-resistant bacteria; CSF - cerebrospinal fluid; WGS - whole genome sequencing; * - tested isolates; BF - bronchial fluid; VS - vaginal secretion; LF - liquid of effusion; BS - bronchial secretion; PL - puncture liquid; BAL - bronchoalveolar lavage; CR - carbapenem-resistant; BDM - broth dilution method; PF - pleural fluid; ProF - prostatic fluid; PeriF - peritoneal fluid; BAF - bronchoalveolar fluid; AF -articular fluid; GF - gastric fluid; MLST - multilocus sequence typing; PBRT - PCR-based replicon typing method; HVS - high vaginal swabs; mCIM - modified carbapenem inactivation method; CIM - carbapenem inactivation method; MIC - minimum inhibitory concentration; Kirby-Bauer DDM - Kirby-Bauer disk diffusion method; RS - respiratory secretion; PRaseT - plasmid relaxase gene typing.

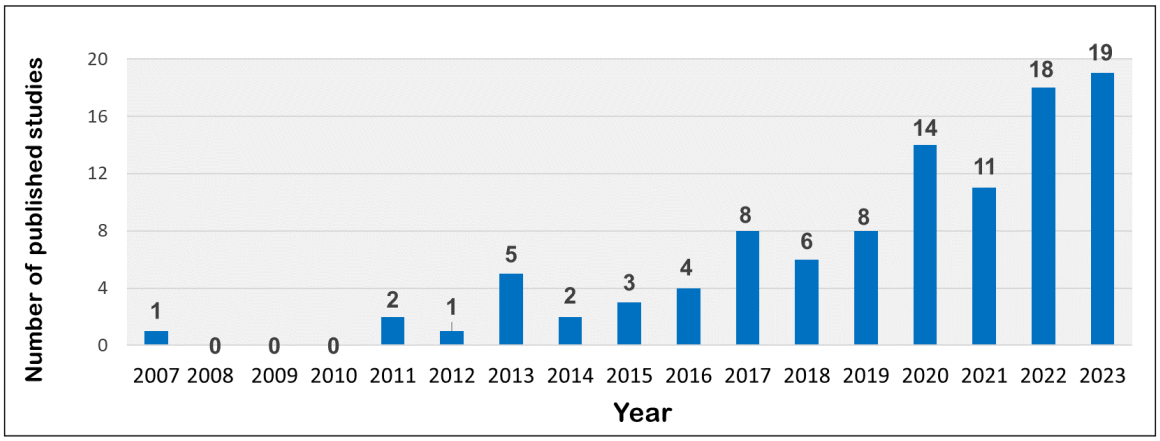

Fig. 2. Number of studies reporting CRB and/or carbapenemase genetic determinants in West African countries (2007 – August 2023).

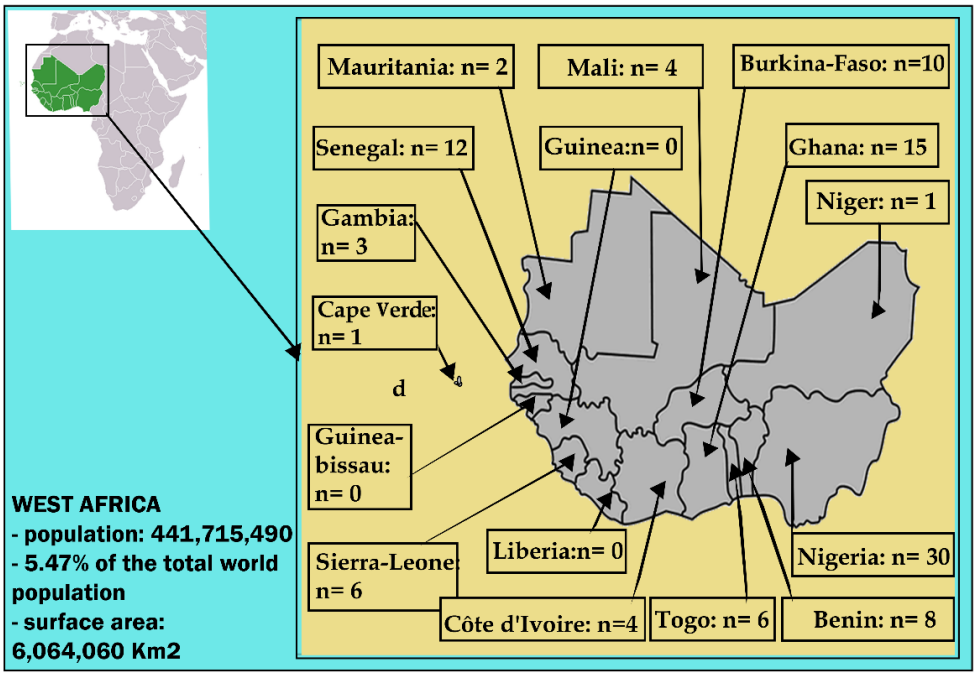

Fig. 3. Map of the West African region with the number of studies per country (adapted from https://www.mewc.org/index.php/countries/west-africa).

Samples

The origin of the samples of CRB strains was specified in 93 studies (total 300 cases). The number of sample types per study varied from 1 to 12. CRB were mainly isolated from urine and wound/pus samples ($p<0.0001$). The sample types included isolates from urine 73/300 (24.3%), pus/wounds 69/300 (23%), blood 39/300 (13%), sputum's/tracheal aspirates 29/300 (9.7%), stool/rectal samples 26/300 (8.7%), vaginal and endocervical samples 24/300 (8%), samples from pleural fluids 13/300 (4.3%), cerebrospinal fluids 11/300 (3.7%), semen samples 7/300 (2.3%), articular fluids 2/300 (0.7%), peritoneal fluids 2/300 (0.7%), tissues 2/300 (0.7%), bone samples 1/300 (0.3%), skin swabs 1/300 (0.3%), and samples from gastric fluids 1/300 (0.3%) (Table 1, Fig. 4). Eye and ear swabs were considered pus samples.

Prevalence of carbapenem-resistant bacteria in West Africa

The average prevalence of CRB in West Africa was (1902/41635; 4.6%), and the prevalence of CRB per country ranged from 1.6% to 18.6%. More specifically, Niger (11/59; 18.6%) and Nigeria (968/5396; 17.9%) exhibited the highest prevalence of CRB, followed by Gambia (17/117; 14.5%), Côte d'Ivoire (26/262; 9.9%), Benin (64/790; 8.1%), Sierra Leone (6/79; 7.6%), Cape Verde (6/98; 6.1%), Senegal (214/4039; 5.3%), Burkina Faso (52/1421; 3.7%), Mali (8/396; 2%), Ghana (467/25071; 1.9%), Mauritania

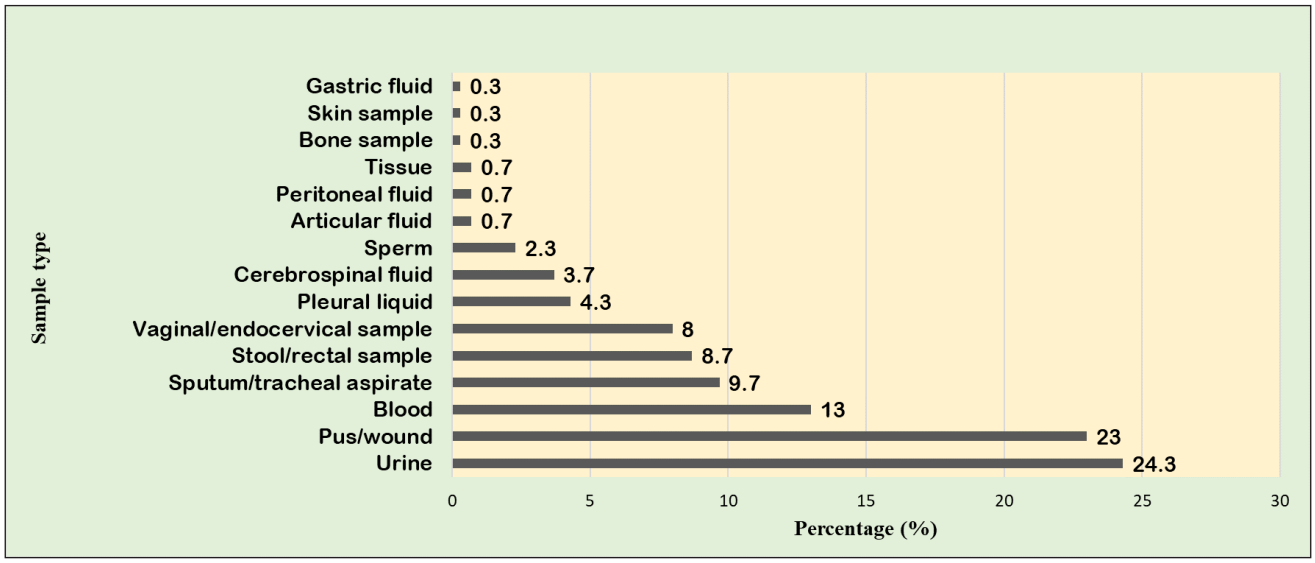

Fig. 4. Distribution of sample types from which CRB were isolated in West African countries.

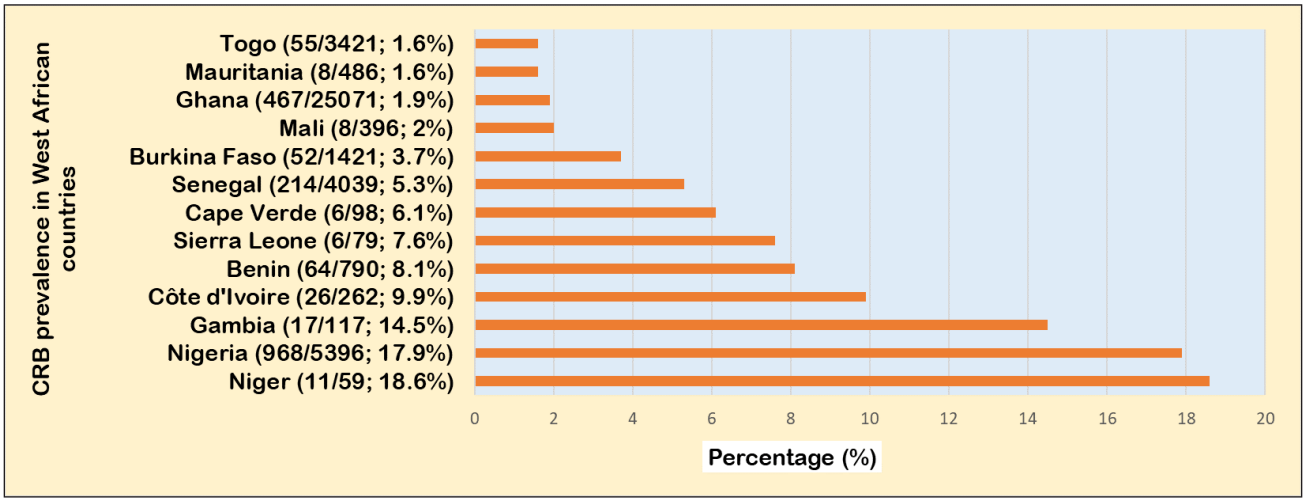

Fig. 5. Prevalence of CRB in West African countries.

(8/486; 1.6 %), and Togo (55/3421; 1.6%), according to the antibiotic susceptibility assays reported in the articles incorporated into this systematic review (Fig. 5).

Distribution of carbapenem-resistant genera in West Africa

All studies included in this review reported CRB belonging to the order Enterobacterales. In total, 101 studies mentioned carbapenem-resistant bacterial species, genera, or families. Among 101 studies, 36 cases of the *Enterobacteriaceae* family were reported without a specified genus. Studies that specified genera or species (total 130 cases) reported a total of 11 genera, including *Escherichia* spp. 34/130 (26.1%), *Klebsiella* spp. 27/130 (20.8%), *Pseudomonas* spp. 26/130 (20%), *Acinetobacter* spp. 25/130 (19.2%), *Enterobacter* spp. 9/130 (6.9%), *Proteus* spp. 3/130 (2.3%), *Salmonella* spp. 2/130 (1.5%), *Sphingomonas* spp. 1/130 (0.8%), *Stenotrophomonas* spp. 1/130 (0.8%), *Burkholderia* spp. 1/130 (0.8%), and *Morganella* spp. 1/130 (0.8%) (Fig. 6, Table 1). CRB were mainly *Escherichia spp.*, *Klebsiella* spp., *Pseudomonas* spp., and *Acinetobacter* spp. ($p<0.0001$).

Carbapenemase genes reported in West Africa

Fifty studies (49%) from 11 countries described the carbapenemase genes involved in bacterial carbapenem resistance (total 104 cases). Carbapenemases encoded by these genes belonged to the four Ambler classes and included 13 types: bla_{OXA}-type carbapenemases (34/104; 32.7%), bla_{NDM} (31/104; 29.8%), bla_{VIM} (13/104; 12.5%), bla_{SHV}-type carbapenemases (8/104; 7.7%), bla_{KPC} (4/104; 3.8%), bla_{ACT} (3/104; 2.9%), bla_{IMP} (3/104; 2.9), bla_{CMY}-type carbapenemases (2/104; 1.9%), bla_{GES} (2 /104; 1.9%), bla_{CTX-M}-type carbapenemases (1/104; 1%), bla_{PER} (1/104;

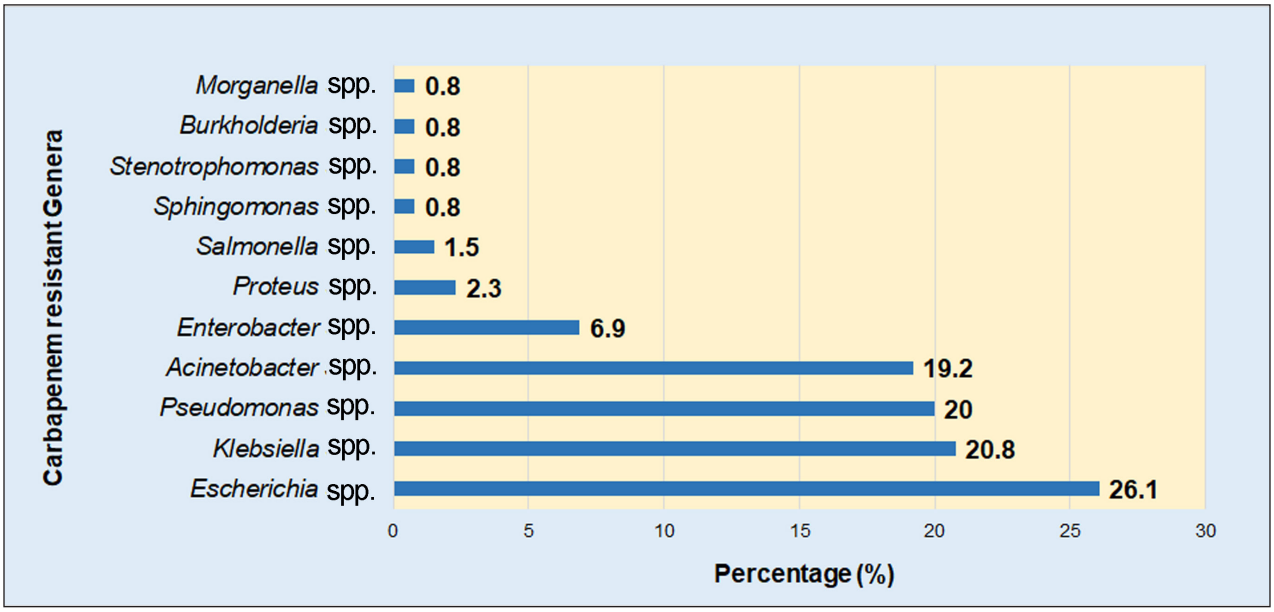

Fig. 6. Prevalence of carbapenem-resistant bacterial genera in West African countries.

Table 2. Carbapenemase genes reported in studies from West African countries

Country	Carbapenemase genes												
	Class A					Class B					Class C		Class D
	bla$_{KPC}$	*bla*$_{CTX-M}$*	*bla*$_{SHV}$*	*bla*$_{GES}$	*bla*$_{PER}$	bla$_{NDM}$	*bla*$_{VIM}$	*bla*$_{IMP}$	*bla*$_{DIM}$	*ble*$_{MBL}$	*bla*$_{ACT}$	*bla*$_{CMY}$*	*bla*$_{OXA}$*
Nigeria	■		■	■		■	■	■			■	■	■
Ghana	■					■	■					■	■
Senegal			■			■							■
Burkina-Faso	■					■	■	■					■
Benin						■	■						■
Togo						■					■		■
Sierra-Leone					■	■	■		■				■
Côte d'Ivoire						■	■						■
Mali			■										■
Gambia		■	■							■			
Cape Verde													■

Gray color means that a carbapenemase gene was reported in study from this country; *gene encoding carbapenem hydrolyzing enzyme variants

1%), *bla*$_{DIM}$ (1/104; 1%), and *ble*$_{MBL}$-type carbapenemases (1/104; 1%) (Table 1, 2). OXA-type and NDM-type carbapenemases were the most prevalent in West Africa ($p<0.0001$). The distribution of carbapenemase genes by country is shown in Table 2.

Mobile genetic elements carrying carbapenemase genes

Twenty-one out of 102 studies (20.6%) reported and specified mobile genetic elements carrying the genetic determinants of carbapenemases (Table 1). The mobile genetic elements included plasmids, integrons, and composite transposons delimited by insertion sequences (IS). The gene *bla*$_{NDM-1}$ in *Acinetobacter* spp. described in studies from Nigeria and Côte d'Ivoire was generally carried by IncF-type plasmids or Tn*125* composite transposons delimited by IS*Aba125* (Table 1). The gene *bla*$_{NDM-5}$ was usually carried by IncX3-type plasmids. The gene *bla*$_{NDM-5}$ carried by *E. xiangfangensis* isolated in Togo was part of composite transposons delimited by IS*5* (Table 1). The gene *bla*$_{OXA-181}$ carried by *Enterobacter* spp., *Klebsiella* spp., and *E. coli* (studies from Togo, Ghana, and Burkina-Faso) was generally carried by IncX3-, ColKP3-, IncFIC(FII)-, and IncFI-type plasmids. When *bla*$_{OXA-181}$ was carried by IncX3-like plasmids, it was part of Tn*2013* (Table 1). The gene *bla*$_{OXA-48}$ reported in papers from Burkina-Faso, Senegal, and Cape Verde

was located on Tn*1999* or Tn*1999.2* carried by IncL/M-type plasmids. Moreover, several IncFI- and IncX3-type plasmids were reported to be bla_{OXA-48} carriers (Table 1). In *Acinetobacter* spp. reported in studies from Nigeria and Senegal, bla_{OXA-23} was mainly associated with Tn*2006* and Tn*2007*, delimited respectively by IS*Aba1* and IS*Aba4* (Table 1). In studies from Ghana and Nigeria, the bla_{OXA-58} gene carried by *Acinetobacter* spp. was found within composite transposons delimited by IS*Aba3* (Table 1). The gene $bla_{OXA-420}$ was part of a composite transposon delimited by IS*Aba3*-like insertion sequence, while bla_{VIM-2}, carried by *P. aeruginosa*, was part of class 1 integrons (Table 1).

Methods used to study carbapenem resistance in West Africa

One hundred and one studies have reported total 172 cases where phenotypic and genotypic methods were used to assess carbapenem resistance in West Africa. The Kirby-Bauer disc diffusion method (74/172; 43.0%) was the most used phenotypic method (p<0.0001), followed by the Vitek 2 automated system (12/172; 7.0%), E-test (12/172; 7.0%), broth dilution and microdilution methods (7/172; 4.1%), MicroScan WalkAway Plus System (2/172; 1.2%), and the BD Phoenix™ automated system (1/172; 0.6%) (Table 3). Among genotypic methods, PCR (standard PCR and RT-PCR) was the most used (38/172; 22.1%) (p=0.03), followed by whole-genome sequencing (17/172; 9.9%), and partial genome sequencing (9/172; 5.2%) (Table 3).

Origins and age groups of CRB carriers

The origin of CRB was reported in 104 cases published in 67 out of 102 studies. CRB were mainly hospital-acquired (59/104; 56.7%), whereas community-acquired CRB accounted for 43.3% (45/104; p=0.003). In addition, 54 studies specified the age groups of people carrying CRB (total 118 cases) including adults (46/118; 39.0%), children/neonates (45/118; 38.1%), and elderly people (27/118; 22.9%). Overall CRB were most frequently isolated from adults and children/neonates (p=0.0002).

Alternative antibiotics retaining good activity against CRB

According to the antimicrobial susceptibility testing results in thirty-one studies (30.4%), 51 successful cases of antibiotics with good activity against CRB were reported. The list of antibiotics active against CRB includes amikacin 14/51 (27.5%), colistin 12/51 (23.5%), fosfomycin 6/51 (11.8%), tigecycline 4/51 (7.8%), netilmicin 2/51 (3.9%), gentamicin 2/51 (3.9%), ciprofloxacin 2/51 (3.9%), minocycline 2/51 (3.9%), nitrofurantoin 1/51 (2%), polymyxin B 1/51 (2%), ceftazidime/avibactam/aztreonam 1/51 (2%), rifampicin 1/51 (2%), tobramycin 1/51 (2%), ceftazidime/avibactam 1/51 (2%), and aztreonam 1/51 (2%) (Fig. 7). Amikacin and colistin were the two most frequently reported alternative antibiotics (p=0.002).

DISCUSSION

This systematic review revealed that, in the countries of West Africa, CRB were mostly isolated from patients' urinary tracts (24.3%), pus/wounds (23%), blood (13%), sputum/tracheal aspirates (9.7%), stool/rectal samples (8.7%), and vaginal/endocervical samples (8%). Overall, this aligns with studies conducted in other regions of the world. Thus, a significant number of CRB were isolated from the urinary tract (19%) and wound/pus (18%) samples of patients in East Africa, although the distribution was shifted towards the respiratory tract (23%) and blood (22%) samples [113]. In the USA [114], CRB were isolated mainly from patients' urine (87.1%) and blood (10.8%). In Japan [115], the urinary tract was also the main source of CRB (33%), followed by the

Table 3. Summary of methods used to study carbapenem resistance in West Africa

	Method	n/N (%)	p value
Phenotypic	Kirby-Bauer Disc diffusion method	74/172 (43.0)	<0.0001
	Vitek 2 automated system	12/172 (7.0)	
	E-test	12/172 (7.0)	
	Broth dilution and microdilution method	7/172 (4.1)	
	MicroScan WalkAway plus System	2/172 (1.2)	
	BD Phoenix™ automated system	1/172 (0.6)	
Genotypic	Standard PCR and RT-PCR	38/172 (22.1)	0.03
	Whole genome sequencing	17/172 (10.0)	
	Partial genome sequencing	9/172 (5.2)	

n- the number of particular tests; N- the total number of tests. Data were compared by χ^2 test.

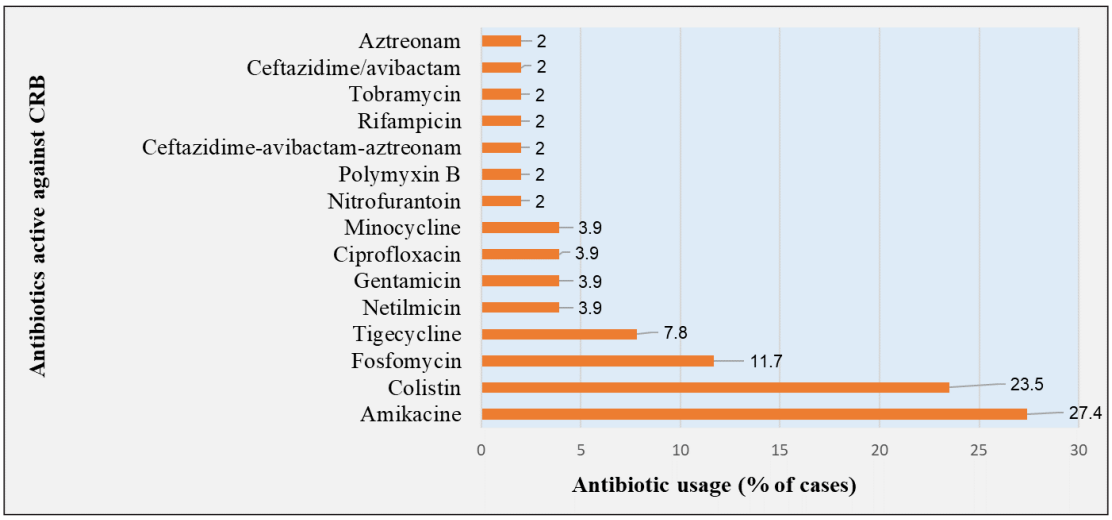

Fig. 7. Antibiotics active against CRB in countries of West Africa.

respiratory tract (21%) and blood (11%). The urinary tract, pus/wound, blood, and respiratory tract appear to be the main sources of CRB worldwide.

The average prevalence of CRB in West Africa was 4.6% (1902/41635), ranging from 1.6% to 18.6%. This average of 4.6% is low compared to the prevalence of CRB reported on the Indian subcontinent (18-31%) [116, 117], Africa and the Middle East (5.7-26.9%) [118], and Saudi Arabia 38-46% [119]. However, the prevalence of CRB reported in the USA was 4.5% [120]. In addition, prevalence rates of up to 7% for CR-*E. coli*, 33.4% for CR-*K. pneumoniae*, 38.2% for CR-*P. aeruginosa* spp., and 82.1% for CR-*Acinetobacter* spp. were reported in endemic areas of Europe (Albania, Greece, Romania, and Croatia) [121]. The reason for the significant variation in CRB prevalence among West African countries (1.6% to 18.6%) remains to be determined. Larger-scale studies, especially in countries where no studies on CRB have been conducted yet, could help estimate the average prevalence of CRB in West Africa more accurately.

This systematic review identified that the most reported CRB genera in West Africa were *Escherichia* spp. (26.1%), followed by *Klebsiella* spp. (20.8%), *Pseudomonas* spp. (20%), and *Acinetobacter* spp. (19.2%). These results are similar to values reported in studies from East Africa and the Asia-Pacific region (*P. aeruginosa*, 17-18.9%; *A. baumannii*, 23%) [113, 117]. However, Lee et al. [122] reported a much higher prevalence of carbapenem-resistant *A. baumannii* (71.7%) in the Asia-Pacific region. Furthermore, it seems that carbapenem-resistant *Klebsiella* spp. is much more common in Asia and the USA than in West Africa. Indeed, at least two papers [114, 123] reported a 53-73.9% prevalence of CR-*K. pneumoniae* in Asia and the USA.

In West Africa, 13 types of carbapenemases have been reported, with a predominance of the bla_{OXA}-type (32.7%) and bla_{NDM} (29.8%), followed by bla_{VIM} (12.5%), bla_{SHV} (7.7%), bla_{KPC} (3.8%), bla_{ACT} (2.9%), bla_{IMP} (2.9%), bla_{CMY} (1.9%), bla_{GES} (1.9%), bla_{CTX-M} (1%), bla_{PER} (1%), bla_{DIM} (1%), and ble_{MBL} (1/104; 1%). These numbers are somewhat similar to results obtained in South Africa and Central Africa, which showed a predominance of bla_{NDM}-type and bla_{OXA}-type carbapenemases [124-126]. However, the patterns of carbapenemase genes reported in this review diverge significantly from those observed in the East African region, Asia-Pacific region, Canada, Brazil, and the USA. Six types of carbapenemases have been reported in studies from East Africa, with a predominance of bla_{VIM} (28.6%), followed by bla_{NDM} (25%), bla_{OXA}-type (17.9%), bla_{IMP} (14.3%), bla_{KPC} (7.1%), and bla_{SPM} (7.1%) [113]. Seven types of carbapenemases have been listed in papers from the Asia-Pacific region, with a predominance of bla_{VIM} (29.0%), followed by bla_{NDM} (24.9%), bla_{VEB} (20.8%), bla_{IMP} (18.0%), bla_{GES} (5.7%), bla_{TEM}-type (3.3%), and bla_{KPC} (1.6%) [117]. Five types of carbapenemases have been described by scientists from the USA: bla_{KPC} (62.4%), bla_{NDM} (2%), bla_{OXA}-type (1.6%), bla_{VIM} (0.4%), and bla_{IMP} (0.2%) [127]. In Canada, bla_{NDM} (37%) and bla_{KPC} (31%) predominated, while in Brazil and Russia, the prevalence of bla_{KPC} (94.7%) and bla_{OXA-48} (65.6%) correspondingly was reported [126].

The mobile genetic elements (MGE) carrying carbapenemase genes described in this systematic review are very similar to those reported elsewhere. Thus, similar to the results from this review, Pagano et al. [128] noted that the bla_{NDM-1} gene is carried by Tn*125* composite transposon delimited by IS*Aba125*. Li et al. and Yang et al. [129, 130] reported the bla_{NDM-5} gene within composite transposons (delimited by IS*5*) carried by IncX3-type

plasmids in China, which is in accordance with the results obtained in West African countries. The *bla*$_{OXA-181}$ gene was also reported within Tn*2013* transposon carried by IncX3- and ColKP3-type plasmids in China, India, and Germany [131-133]. Furthermore, IncL/M-type plasmids carrying the *bla*$_{OXA-48}$ gene were reported in China and Europe [134-137]. Our analysis of literature data showed that, in most cases, the *bla*$_{OXA-48}$ gene was carried by Tn*1999.2* and Tn*1999* transposons. The *bla*$_{OXA-23}$ gene in *A. baumannii* was also reported in association with Tn*2006* and Tn*2007* transposons in studies from Algeria, Spain, Tahiti, France, Turkey, Vietnam, Romania, Libya, Australia, and France [128], which corresponds to our results. In papers from China, Italy, Taiwan, and Lebanon, as in our review, the *bla*$_{OXA-58}$ gene was observed within composite transposons delimited by IS*Aba3* [128]. Furthermore, the *bla*$_{OXA-420}$ gene was also reported within composite transposons delimited by IS*Aba3* in a study from India [138], while in papers from Korea, East Africa, and Italy [139-141], the *bla*$_{VIM-2}$ gene was reported as a cassette in class 1 integrons carried by plasmids. An in-depth analysis and comparison of carbapenemase gene-associated MGEs reported from West Africa with the corresponding data from other parts of the world could provide a better understanding of the evolution and dissemination of carbapenemase gene-associated MGEs worldwide.

This systematic review revealed that the Kirby-Bauer disc diffusion (43.0%), PCR (22.1%), whole-genome sequencing (9.9%), Vitek 2-system (7.0%), E-test (7.0%), and partial genome sequencing (5.2%) were the most used methods for the detection of carbapenem resistance. It should be noted that more than one method was used to detect CRB in several studies. With a few exceptions, the methods, and technologies for detecting carbapenem resistance reported in studies from West Africa are the same as those used in Europe and East Africa. To illustrate, according to [121] the disc diffusion method and MIC determination methods were used in 90% of European labs while PCR and WGS – in 50% and 11% of labs correspondingly whereas the disc diffusion method (64.7%), PCR (47.1%), sequencing (23.5%), WGS (5.9%), BD Phoenix™ automated system (5.9%), and E-test (5.9%) were the most commonly used techniques in the labs of East African countries [113].

This systematic review revealed that amikacin, colistin, fosfomycin, and tigecycline are alternative antibiotics with the highest activity against CRB. In Africa, the Middle East, the Asia-Pacific region, and the USA, the most frequently reported alternative antibiotics active against CRB were amikacin and colistin, followed by ceftazidime/avibactam, tigecycline, ceftolozane/tazobactam, minocycline, and gentamycin [114, 117, 118, 122, 127]. Colistin and amikacin seem to be the two most reported alternative antibiotics worldwide. Therefore, in West Africa, the administration of amikacin and colistin should be strictly monitored to delay, as much as possible, the appearance and generalization of mutant bacterial clones resistant to these antibiotics.

CONCLUSION

Our systematic review shows the past and present of carbapenem resistance in West Africa in detail. According to our results, the West African region has a low prevalence of CRB compared to other African, European, and Asian regions. Additional publications on carbapenem resistance in West Africa may provide more accurate data. It seems that there are similar patterns of carbapenemase gene distribution among bacteria from the West, Central, and Southern Africa while mobile genetic elements carrying carbapenemase genes appeared to be like those reported worldwide. The transfer of bacteria by international travelers may have played an important role in bacterial distribution in Africa and worldwide. Additional WGS, multilocus sequence typing (MLST), and phylogenetic analyses could deepen our understanding of CRB strains circulating in West Africa. Additional funds should be allocated to African researchers to better prevent and counter CRB epidemics. Moreover, the use of the few antibiotics still effective against CRB circulating in West Africa should be restricted to emergency cases to help preserve their activity as much as possible. Preliminary phytotherapy studies have shown that several plants contain natural compounds that may be effective against CRB. Therefore, phytotherapy should be further investigated as a new approach to fighting CRB in West Africa. This could lead to discovering phytomedicines that are highly effective against CRB.

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