frontiers | Frontiers in Public Health

TYPE Review
PUBLISHED 02 April 2024
DOI 10.3389/fpubh.2024.1357345



OPEN ACCESS

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RECEIVED 17 December 2023
ACCEPTED 12 March 2024
PUBLISHED 02 April 2024

CITATION
Hoarau AOG, Mavingui P and Miltgen G (2024) Comprehensive analysis of antimicrobial resistance in the Southwest Indian Ocean: focus on WHO critical and high priority pathogens.
*Front. Public Health* 12:1357345.
doi: 10.3389/fpubh.2024.1357345



# Comprehensive analysis of antimicrobial resistance in the Southwest Indian Ocean: focus on WHO critical and high priority pathogens

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The spread of antimicrobial resistance (AMR) is a major global concern, and the islands of the Southwest Indian Ocean (SWIO) are not exempt from this phenomenon. As strategic crossroads between Southern Africa and the Indian subcontinent, these islands are constantly threatened by the importation of multidrug-resistant bacteria from these regions. In this systematic review, our aim was to assess the epidemiological situation of AMR in humans in the SWIO islands, focusing on bacterial species listed as priority by the World Health Organization. Specifically, we examined Enterobacterales, *Acinetobacter* spp., *Pseudomonas* spp. resistant to carbapenems, and *Enterococcus* spp. resistant to vancomycin. Our main objectives were to map the distribution of these resistant bacteria in the SWIO islands and identify the genes involved in their resistance mechanisms. We conducted literature review focusing on Comoros, Madagascar, Maldives, Mauritius, Mayotte, Reunion Island, Seychelles, Sri Lanka, and Zanzibar. Our findings revealed a growing interest in the investigation of these pathogens and provided evidence of their active circulation in many of the territories investigated. However, we also identified disparities in terms of data availability between the targeted bacteria and among the different territories, emphasizing the need to strengthen collaborative efforts to establish an efficient regional surveillance network.

KEYWORDS

**antimicrobial resistance, Enterobacterales, *Pseudomonas* spp., *Acinetobacter* spp., *Enterococcus* spp., carbapenem resistance, vancomycin resistance, Indian Ocean**

## 1 Introduction

The spread of antimicrobial resistance (AMR) is recognized as an increasing global threat. It was estimated that in 2019, there were 4.95 million deaths worldwide associated with AMR, among which 1.27 million were directly attributable to AMR (1). This alarming situation originates from the emergence of multidrug-resistant strains and the lack of new effective therapeutic approaches. In 2017, the World Health Organization (WHO) established its first-ever priority list of antibiotic resistant pathogens (2). For instance, Gram-negative bacteria including Enterobacterales, *Acinetobacter* spp., and *Pseudomonas* spp. resistant to carbapenems,

were classified as critical priority pathogens (2). Similarly, Gram-positive bacteria, such as *Enterococcus* spp. (specifically *Enterococcus faecium*), resistant to vancomycin (known as vancomycin resistant Enterococci or VRE), were classified as high priority pathogen (2).

The Southwest Indian Ocean (SWIO) is made up of multitude islands. Despite their relative isolation, these territories face significant pressure from the importation of antibiotic-resistant pathogens from Southern Africa and the Indian subcontinent, and they are highly concerned about AMR. In 2015, the Indian Ocean Commission (IOC), which includes Comoros, Madagascar, Mauritius, Reunion Island, and Seychelles, declared AMR a priority health issue (3). Gay et al. (4) conducted a systematic review of the literature in 2016 to assess the prevalence of AMR for bacterial species prone to develop multidrug resistance, and fecal-oral foodborne bacteria in humans and animals within the IOC and Mayotte. They pointed out that many resistant strains were circulating in both humans and animals (4). The main concerns were extended-spectrum β-lactamase-producing Enterobacterales and carbapenemase-producing Enterobacterales (CPE) (4).

In the present review, our aim is to portray the current AMR epidemiological situation in the SWIO, six years after the initial review. We will focus specifically on bacterial species that are registered on the WHO priority list, including Enterobacterales, *Acinetobacter* spp., and *Pseudomonas* spp. resistant to carbapenems, as well as *Enterococcus* spp. resistant to vancomycin. The objectives of our study were to *(i)* map the distribution of these resistant bacteria in the SWIO, and *(ii)* identify the specific resistance genes that may be involved.

## 2 Method

Our study was conducted between August and November 2023. We chose to include the following territories in the screening: Comoros, Madagascar, Maldives, Mauritius, Mayotte, Reunion Island, Seychelles, Sri Lanka, and Zanzibar. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (5), we used published data by searching in the Google Scholar (RRID:SCR_008878), PubMed (RRID:SCR_004846), and Web of Science (RRID:SCR_022706) databases for articles, posters, and conference abstracts, in French or English from 1990 until November 2023. We collected relevant information on carbapenem-resistant Enterobacterales (previously named Enterobacteriaceae), *Pseudomonas* spp. and *Acinetobacter* spp. in each territory by combining bacteria names and locations with the keywords "carbapenem resistance" or "carbapenemase resistance." Similarly, we collected information on vancomycin-resistant *Enterococcus* spp. by using the keywords "vancomycin resistance *Enterococcus*" or "vancomycin resistance Enterococci." Only studies reporting the detection of at least one resistant isolate were included. References and data were discarded when original sources were not identified.

Abbreviations: AMR, antimicrobial resistance; CPE, carbapenemase-producing Enterobacterales; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRE, carbapenem-resistant Enterobacterales; IOC, Indian Ocean commission; ST, sequence type; SWIO, Southwest Indian Ocean; VRE, vancomycin resistant enterococci; WHO, world health organization.

## 3 Results

A total of 102 studies were identified. Out of these, 58 were excluded for not meeting the inclusion criteria. The final analysis included 44 studies (Supplementary Table S1). None of these studies were published before 2010, and the number of studies has been increasing over time (Figure 1). The number of published studies varied according to territories (Figure 2), with Sri Lanka and Reunion Island accounting for 31 out of 44 studies (70.5%). Among the selected studies, 29 (65.9%) investigated the presence of antimicrobial resistance genes in addition to antimicrobial susceptibility studies (Supplementary Table S2). However, studies investigating the localization of these genes were scarce, representing only 27.2% (12/44) of the total studies (Supplementary Table S2). Carbapenem-resistant Gram-negative bacteria were reported in 42 out of 44 studies (95.5%), while VRE were reported in 13.6% (6/44) of the studies (Supplementary Table S2).

### 3.1 Enterobacterales resistant to carbapenems

Carbapenem-resistant Enterobacterales (CRE) were reported in six territories (Figure 3; Supplementary Tables S2, S3). In Madagascar, there were four studies available. A study conducted from 2011 to 2013, spanning three years, identified three *Enterobacter cloacae* isolates (resistance rate: 15.0%, 3/20), two *Escherichia coli* isolates (resistance rate: 2.3%, 2/89), six *Klebsiella pneumoniae* isolates (resistance rate: 17.1%, 6/35), three *Klebsiella oxytoca* isolates (resistance rate: 13.6%, 3/22), and one *Proteus mirabilis* isolate (resistance rate: 4.2%, 1/24) with carbapenem resistance in the community population (6). Another study reported one carbapenem-resistant *Pantoea agglomerans* isolate in a hospitalized patient (resistance rate: 11.1%,1/9) (7). Between 2015 and 2017, four patients (CRE carrier rate: 1.2%) presented with CRE (8). Between 2018 and 2019, a pregnant woman was found to have one carbapenem-resistant *E. coli* isolate (resistance rate: 0.6%, 1/168) carrying the $bla_{\text{NDM-5}}$ gene (9).

For Mauritius, five studies were retained (Figure 3; Supplementary Table S2). In 2009, a carbapenemase-producing *K. pneumoniae* sequence type (ST) 231 isolate carrying the $bla_{\text{NDM-1}}$ gene on a plasmid of IncA/C type was identified (10). In 2010, another carbapenem-resistant *Klebsiella* spp. isolate was discovered (11). In July 2014, a study reported resistant rates of 3.0% for *E. coli* and 9.0% for *Klebsiella* spp. (12). From 2015 to 2016, 23 CRE strains (resistance rate: 30.3%, 23/76) were isolated in an intensive care unit (13). Lastly, between 2015 and 2017, a total of nine patients tested positive for CRE (CRE carriers rate: 8.1%) (8).

On Mayotte Island, only two studies have reported CRE (Figure 3; Supplementary Table S2). A three-year study conducted between 2015 and 2017 identified 14 patients carrying CRE (CRE carriers rate: 0.9%) (8). Another study conducted over 16 months between 2015 and 2017 reported the presence of 18 isolates of *E. cloacae* ST820 that harbored the $bla_{\text{IMI-1}}$ gene, which was carried on the integrative mobile element *Eclo*IMEX-8 (14).

In Figure 3 and Supplementary Table S2, we included seven studies related to Reunion Island. In November 2011 and March 2012, two patients who were repatriated from Mauritius and India were found to have *K. pneumoniae* and *Salmonella enterica* subsp. *enterica* serotype Westhampton carrying the $bla_{\text{NDM-1}}$ gene, respectively (15). A

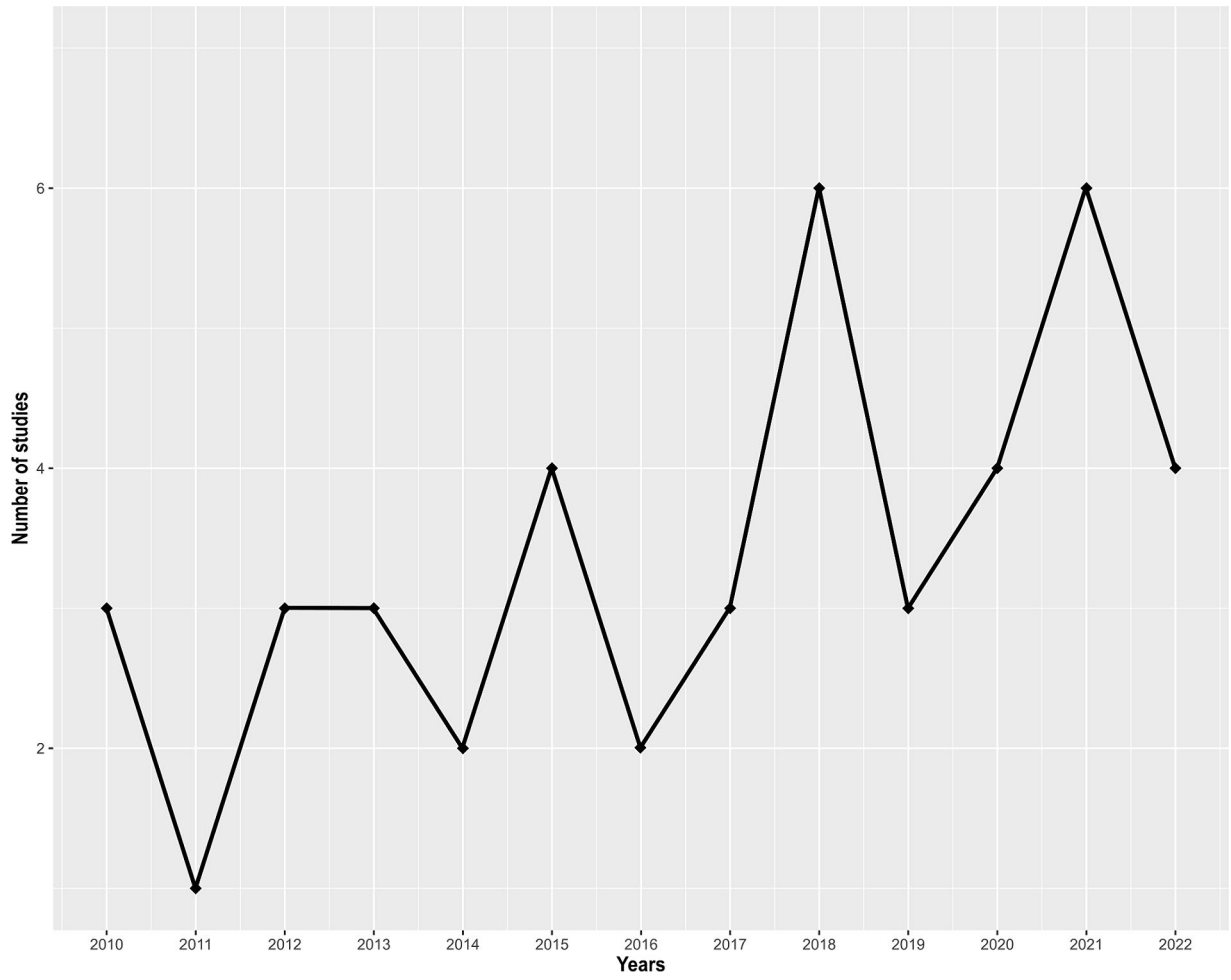


FIGURE 1
Number of studies identifying critical and high priority antibiotic-resistant bacteria in the Southwest Indian Ocean, per year, from 2010 to November 2023.

retrospective observational multicenter study conducted between January 2010 and December 2015 reported several species of CRE in 36 patients (16). These species included *K. pneumoniae* ($bla_{NDM-1}$), *E. coli* ($bla_{NDM-1}$, $bla_{NDM-4}$, $bla_{NDM-5}$, $bla_{NDM-6}$, $bla_{OXA-48}$), *E. cloacae* ($bla_{NDM-1}$ and $bla_{IMI-1}$), *Citrobacter freundii* ($bla_{NDM-1}$), *Morganella morganii* ($bla_{NDM-1}$), *Enterobacter aerogenes* ($bla_{OXA-48}$), *P. mirabilis* ($bla_{NDM-1}$), and *Salmonella enteritidis* ($bla_{NDM-1}$) (16). In early 2017, a patient was reported to be infected with carbapenemase-producing *K. pneumoniae*. This isolate harbored the $bla_{NDM-1-like}$ gene. Additionally, an extensively-drug resistant *E. coli* carrying $bla_{NDM-1-like}$ and *mcr-1* genes was also isolated from this patient (17). In the same year, a patient returning from Mauritius was found to be carrying a carbapenemase-producing *K. pneumoniae* isolate with the $bla_{NDM-1}$ and $bla_{OXA-181}$ genes (18). From 2011 to 2016, 61 Enterobacterales from 53 patients on Reunion Island were identified to have carbapenem resistance (19). Among them, 13 *E. coli* belonging to eight STs (ST10, ST12, ST167, ST349, ST354, ST405, ST410, ST1284) were recovered. These isolates carried five resistance genes: $bla_{NDM-1}$, $bla_{NDM-4}$, $bla_{NDM-5}$, $bla_{NDM-6}$, $bla_{OXA-181}$, and one isolate even carried both $bla_{NDM-1}$ and $bla_{VIM-2}$ genes (19). Twenty-six carbapenemase-producing *K. pneumoniae* isolates belonging to 13 STs: ST14, ST15, ST17, ST37, ST101, ST147, ST307, ST359, ST524, ST1562, ST1864, ST2193, and ST4507 were also retrieved. They were found to carry $bla_{NDM-1}$, $bla_{NDM-5}$, $bla_{NDM-7}$, and one isolate even carried both $bla_{NDM-1}$ and $bla_{OXA-181}$ (19). Nine *E. cloacae* isolates belonging to ST106, ST820, ST1304 and carrying $bla_{NDM-1}$ and $bla_{IMI-1}$ genes, six *C. freundii* isolates belonging to ST22, ST116, ST124, ST248, ST502 carrying $bla_{NDM-1}$, three *Serratia marcescens* isolates carrying $bla_{IMP-10}$, one *Enterobacter asburiae* isolate carrying $bla_{IMI-13}$, one *Enterobacter kobei* isolate carrying $bla_{NDM-1}$, one isolate of *P. mirabilis* and one isolate of *S. enterica* subsp. *enterica* harboring $bla_{NDM-1}$ were detected (19). Between 2015 and 2017, a total of 10 patients tested positive for CRE (CRE carrier ratio: 0,5%, 10/2,184) (8). Finally, in June 2020, *E. cloacae* ST190 carrying $bla_{NDM-1}$ gene located in a truncated insertion sequence IS*Aba125* on a IncC plasmid was reported in four patients (20). Additionally, one *E. coli* isolate and one *K. pneumoniae* isolate both carrying $bla_{NDM-1}$ were also identified (20).

For Sri Lanka, a total of 15 studies addressed the presence of CRE in the country (Figure 3; Supplementary Table S2). In 2012, a four-month study detected 22 *K. pneumoniae* isolates belonging to ST14, ST147, ST380, carrying $bla_{OXA-181}$ and $bla_{NDM-1}$ genes in a hospital (21). In early 2013, one isolate of *K. pneumoniae* ST394 with $bla_{NDM-1}$ on a IncHI plasmid, which included the insertion sequence IS*Aba125* upstream, was detected (22). Throughout the 2013 year, four *E. coli* isolates (resistance rate: 7.5%) and ten *K. pneumoniae* isolates (resistance rate: 40.0%) were identified in a tertiary hospital

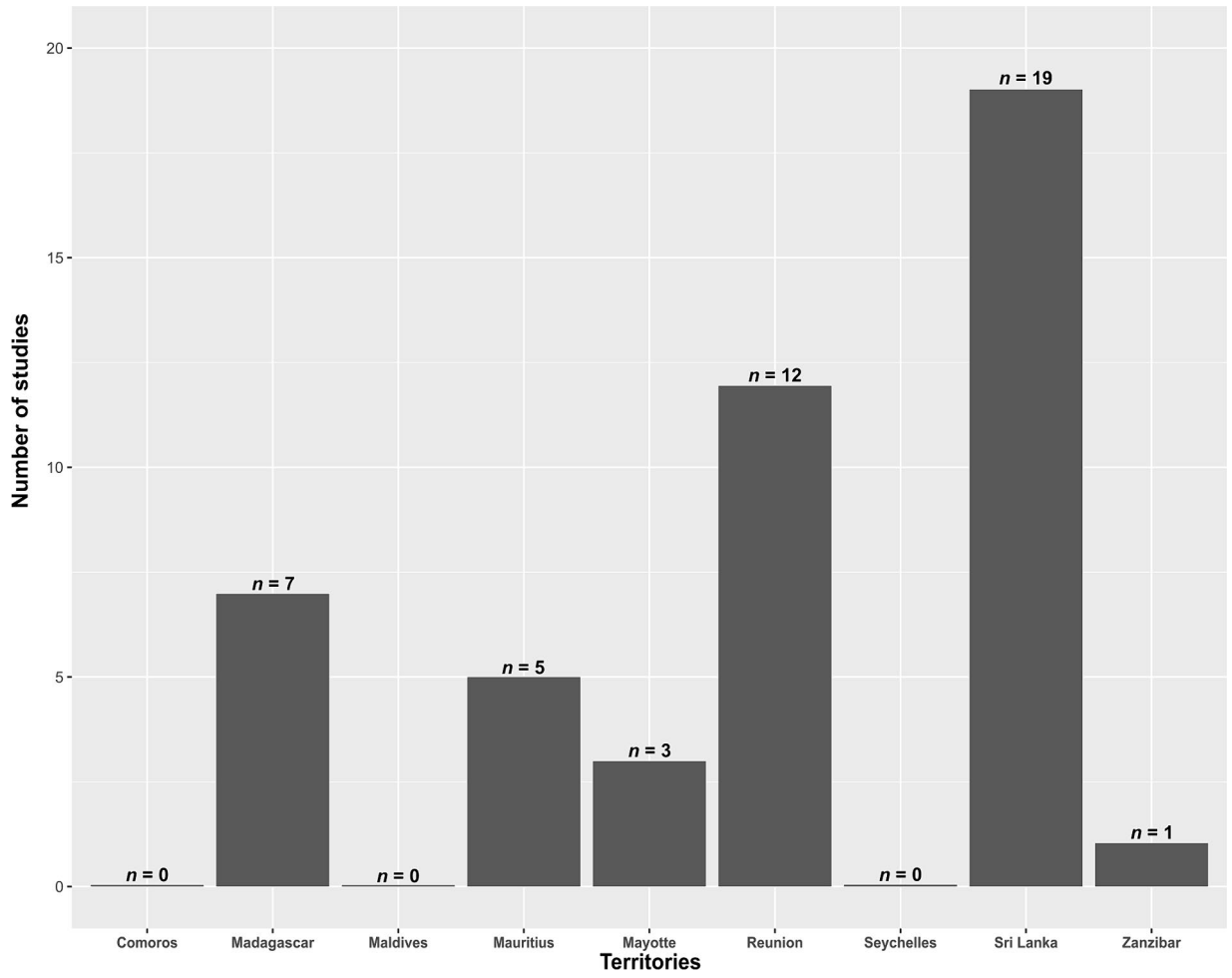


FIGURE 2
Number of studies identifying critical and high priority antibiotic-resistant bacteria in the Southwest Indian Ocean, for each investigated territory, from 2010 to November 2023.

(23). In 2014, a national laboratory-based surveillance recorded a total of 149 CRE isolates (resistance rate: 9.0%) (24). During the first semester of 2015, a descriptive cross-sectional study reported the presence of *E. coli* (resistance rate: 4.9%) and *Klebsiella* spp. resistant to carbapenems (25). In addition, an eight-month study conducted in 2015 described carbapenemase-producing *K. pneumoniae* ST147 and ST437 with $bla_{\text{OXA-181}}$ gene in ten patients. Three plasmids, CUHK_SL-A, CUHK_SL-B, and CUHK_SL-C, were identified to carry the gene, with the CUHK_SL-A plasmid harboring the insertion sequence IS*Ecp*, while the CUHK_SL-B plasmid did not have this insertion sequence (26). The CUHK_SL-C plasmid presented both IS*Ecp1* and a mobile gene (*mobC*) deletion (26). Between March and September 2015, *E. coli* and *K. pneumoniae* were also reported during a retrospective study in a hospital (27). In 2015–2016, three isolates of *K. pneumoniae* ST147 carrying the $bla_{\text{OXA-181}}$ gene, two isolates of *K. pneumoniae* ST16 harboring $bla_{\text{OXA-181}}$ and $bla_{\text{OXA-232}}$ genes, one isolate of *Enterobacter hormaechei* subsp. *steigerwaltii* (*E. cloacae* complex) ST93 carrying $bla_{\text{OXA-181}}$ were reported in patients presenting hospital-acquired urinary tract infections. All resistance genes were localized on the ColKP3 plasmid and flanked by the insertion sequence IS*Ecp1* (28). In a neonatal unit between October 2015 and January 2016, one carbapenem-resistant *Klebsiella* spp. isolate was detected (29). Additionally, between 2015 and 2016, the hospital reported 15 isolates of *E. coli* (resistance rate: 5.1%) carrying the $bla_{\text{NDM-1}}$ gene, 24 isolates of *K. pneumoniae* (resistance rate: 36.9%) presenting $bla_{\text{NDM-1}}$, $bla_{\text{OXA-181}}$ and $bla_{\text{OXA-232}}$ genes, three isolates of *Enterobacter* spp. (resistance rate: 11.5%) harboring $bla_{\text{NDM-1}}$, $bla_{\text{NDM-4}}$ and $bla_{\text{OXA-181}}$, as well as four other Enterobacterales isolates (resistance rate: 10.5%) (30). In December 2016 and March 2017, one isolate of *E. coli* and one isolate of *K. pneumoniae* (resistance rate: 2.7%) resistant to carbapenem were retrieved (31). Between December 2017 and February 2018, a prospective cross-sectional study identified 57 CRE isolates in 57 patients (32). These isolates included *K. pneumoniae* carrying $bla_{\text{KPC}}$, $bla_{\text{OXA-48-like}}$, and both $bla_{\text{NDM}}$ and $bla_{\text{OXA-48-like}}$; *E. coli* carrying the $bla_{\text{OXA-48-like}}$ gene, *C. freundii* carrying $bla_{\text{OXA-48-like}}$ and $bla_{\text{NDM}}$, *Providencia rettgeri* and *E. cloacae* both carrying $bla_{\text{NDM}}$; and *Klebsiella aerogenes* harboring both $bla_{\text{NDM}}$ and $bla_{\text{OXA-48-like}}$ (32). In a separate study between August 2016 and January 2017, four carbapenem-resistant *K. pneumoniae* isolates were detected in four infants in a post-partum ward (33). Additionally, between 2018 and 2019, a nine-month descriptive cross-sectional study reported the presence of 37 CRE isolates (resistance rate: 41.1%) among patients with cancer in a hospital (34). Finally, in another study, 119 CRE

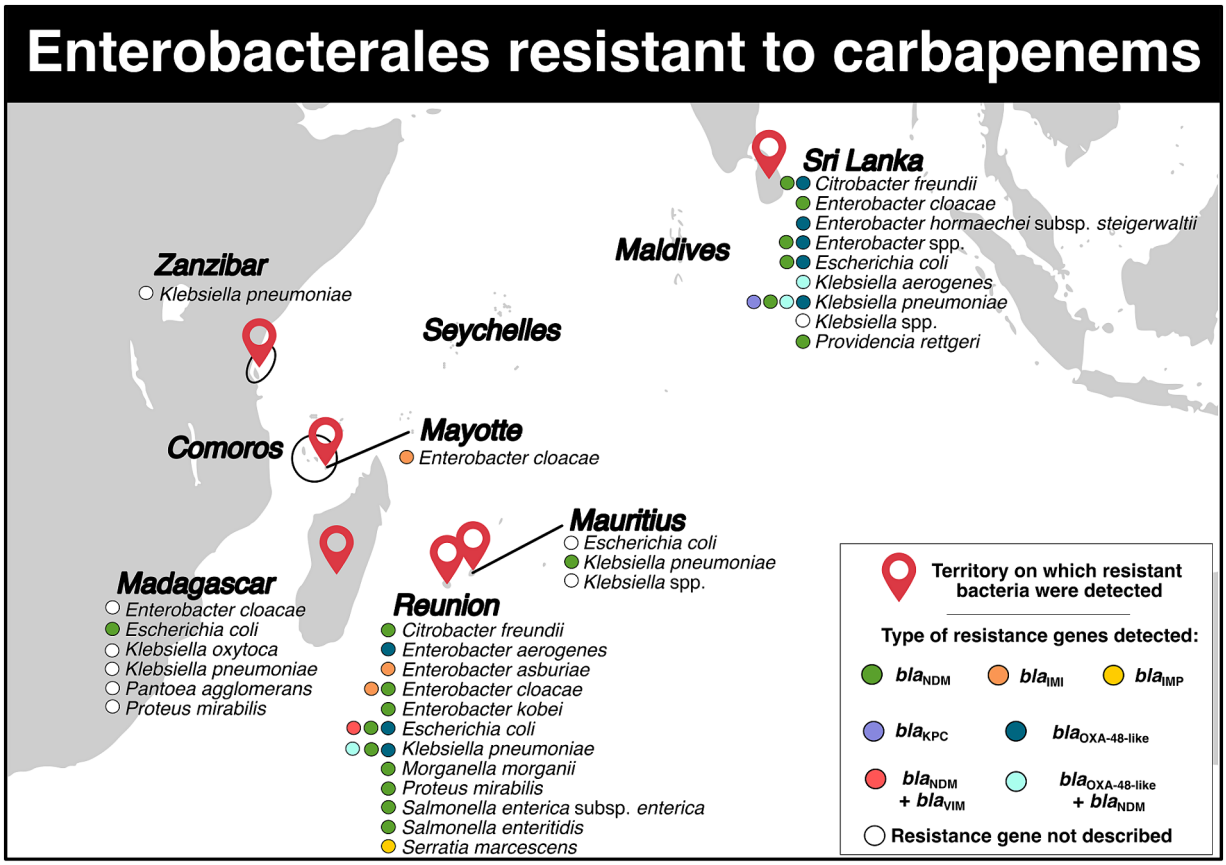


FIGURE 3
Distribution of carbapenem-resistant Enterobacterales and genes associated with resistance mechanisms in the Southwest Indian Ocean Islands.

isolates originating from 93 patients with cancer (rate of CRE carriers: 35.2%) were detected and found to carry $bla_{NDM}$, $bla_{OXA-48}$ and $bla_{KPC}$ genes (35).

For Zanzibar, only one study reported the detection of a carbapenem-resistant *K. pneumoniae* isolate in a neonatal unit (resistant rate: 9.1%, 1/11; carrier rate: 0.2%, 1/469) (Figure 3; Supplementary Table S2) (36).

## 3.2 *Acinetobacter* spp. resistant to carbapenems

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) was detected on five territories (Figure 4; Supplementary Tables S2, S3). Three studies were available for Madagascar. From September 2006 to March 2008, 50 isolates of CRAB (resistance rate: 44.7%) were identified in patients in intensive care and surgery wards (37). From September 2006 to March 2009, 53 CRAB isolates were identified in various Malagasy hospitals (resistance rate: 44.0%) (38). All isolates contained the $bla_{OXA-23}$ gene carried by the insertion sequence IS*Aba1* (38). Finally, between 2008 and 2016, 15 CRAB isolates belonging to four STs (ST1, ST2, ST1195, ST1196) were detected, and the $bla_{OXA-23}$, $bla_{OXA-24}$ and $bla_{OXA-58}$ genes were identified. The $bla_{OXA-23}$ gene was located in Tn*2006* and Tn*2008* transposons on the bacterial chromosome, with the insertion sequence IS*Ab1* upstream (39). The $bla_{OXA-24}$ was flanked by XerC/XerD recombination sites on the small designated pOXA-24_AB334 plasmid (39).

For Mauritius, three studies were included (Figure 4; Supplementary Table S2). In 2010 and 2014, the resistance rates for *Acinetobacter* spp. isolates were 68.0 and 74.0% respectively, indicating that a majority of the isolates were carbapenem-resistant in hospitalized patients (11, 12). Another retrospective study conducted between July 2015 and December 2016 identified 32 CRAB isolates, with a resistance rate of 86.5% (13).

On Mayotte Island, one study mentioned the detection of two CRAB isolates in May and August 2011 (Figure 4; Supplementary Table S2). These isolates belonged to ST23 and carried the $bla_{OXA-58}$ gene on the bacterial chromosome, with the insertion sequence IS*Aba3* downstream (40). It was suggested that these isolates likely originated from the Comoros archipelago, specifically from Grande Comore and Mohéli islands (40).

On Reunion Island, a comparative study conducted between 1997 and 2005 revealed a decrease in carbapenem resistance for *A. baumannii* from 12.9 to 8.3% (41). Another study reported the presence of a CRAB isolate belonging to ST2 and carrying the $bla_{OXA-23-like}$ gene in hospital (Figure 4; Supplementary Table S2) (42). In 2017, a woman who had previously traveled to Saudi Arabia was found to have a OXA-23 carbapenemase-producing *A. baumannii* (17). More recently, during an outbreak from April 2019 and June 2020, CRAB isolates were obtained from 13 patients. The isolates belonged to $ST^{Pas}1/ST^{Ox}231$ clonal complex and carried the $bla_{NDM-1}$ and $bla_{OXA-23}$

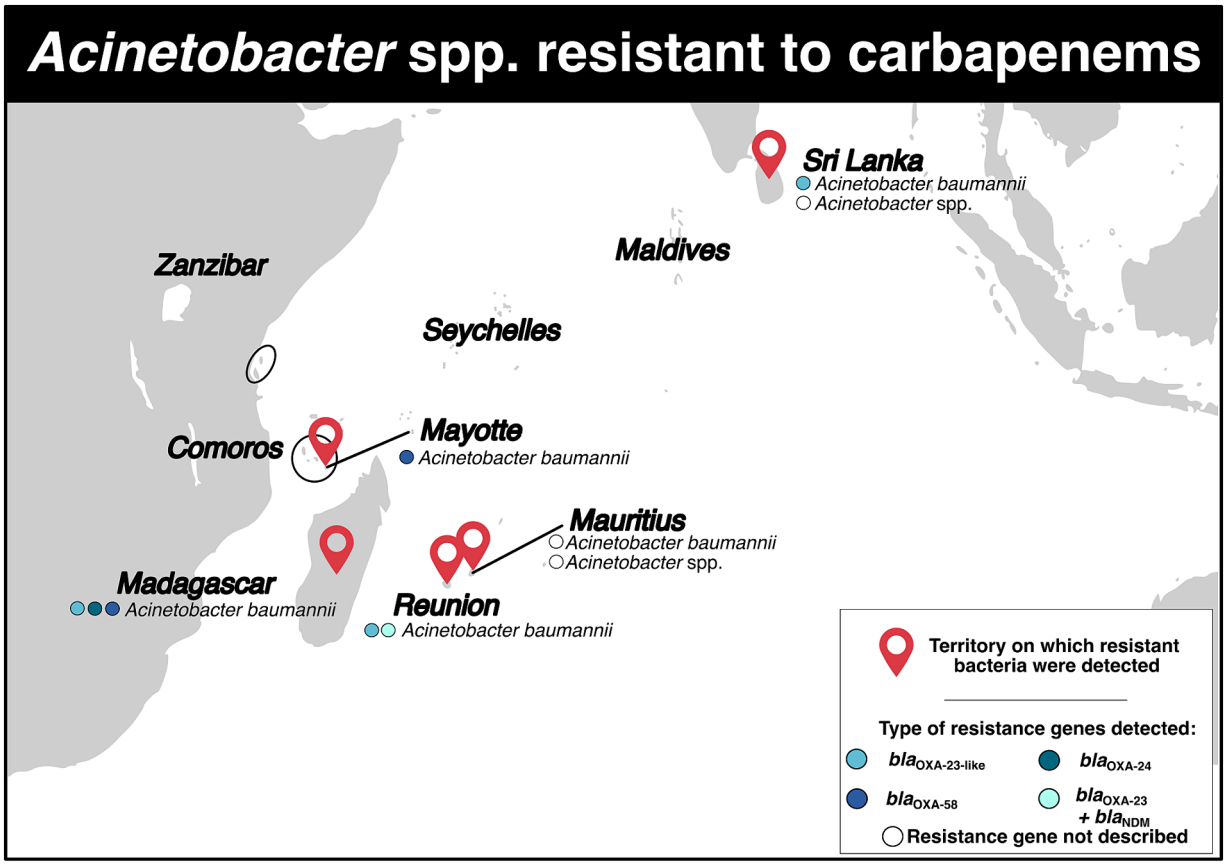


FIGURE 4
Distribution of carbapenem-resistant *Acinetobacter* spp. and genes associated with resistance mechanisms in the Southwest Indian Ocean Islands.

genes. The $bla_{\text{NDM-1}}$ gene was located on the Tn*125* transposon, while the $bla_{\text{OXA-23}}$ gene was located on the Tn*2006* transposon (Figure 4; Supplementary Table S2) (43). All the 13 isolates displayed resistance to colistin (43).

In Sri Lanka, three studies were included in the analysis (Figure 4; Supplementary Table S2). In a one-year study conducted in 2013, it was reported that 18 carbapenem-resistant *Acinetobacter* spp. were detected in in a tertiary care hospital with resistance rate of 87.5% (23). Another study from March to September 2015 found 30 carbapenem-resistant *Acinetobacter* spp. in an intensive care unit (27). These isolates were also found to be multidrug-resistant (27). More recently, 46 CRAB isolates carrying $bla_{\text{OXA-23-like}}$ were isolated (44).

## 3.3 *Pseudomonas* spp. resistant to carbapenems

Carbapenem-resistant *Pseudomonas* spp. isolates were reported in four territories (Figure 5; Supplementary Tables S2, S3). In Madagascar, only two studies have described the detection of these bacteria. The first study, conducted between September 2006 and March 2008, reported a resistance rate of 1.9% for *Pseudomonas* spp. in an intensive care unit (37). The second study, published in 2015 and conducted in a hospital and community setting, reported the detection of three *Pseudomonas putida* isolates that were intermediate susceptible to carbapenems (resistance rate: 60%), but still susceptible to other antibiotics (7).

In Mauritius, a study in 2010 reported a 40.0% resistance rate to carbapenems in *Pseudomonas aeruginosa* (86 isolates) in a hospital setting (11). Similarly, another study in July 2014 reported a 27.0% resistance rate, also in a hospital (12). A retrospective study conducted between July 2015 and December 2016 reported a total of 16 *Pseudomonas* spp. isolates resistant to carbapenems (resistance rate: 80.0%) (Figure 5; Supplementary Table S2) (13).

Between 1997 and 2005, there was a stable resistance rate to carbapenems in Reunion Island. The rate of *P. aeruginosa* resistant to carbapenems ranged from 5.9 to 6.1% (41). From January 2010 to June 2012, three isolates of *P. aeruginosa* producing VIM-2 and one producing VIM-6 were identified (Figure 5; Supplementary Table S2) (45).

In Sri Lanka, in 2000, three carbapenem-resistant *P. aeruginosa* isolates belonging to ST235 and carrying the $bla_{\text{VIM-2}}$ gene on their chromosome were detected (46). Between January and December 2013, a tertiary care hospital reported two isolates of *Pseudomonas* spp. displaying resistance to carbapenems, with a resistance rate of 10.0% (Figure 5; Supplementary Table S2) (23). During a retrospective study conducted in a Sri Lankan intensive care unit between March and September 2015, two *P. aeruginosa* isolates resistant to carbapenem were detected, with a resistance rate of 13.3% (Figure 5; Supplementary Table S2) (27).

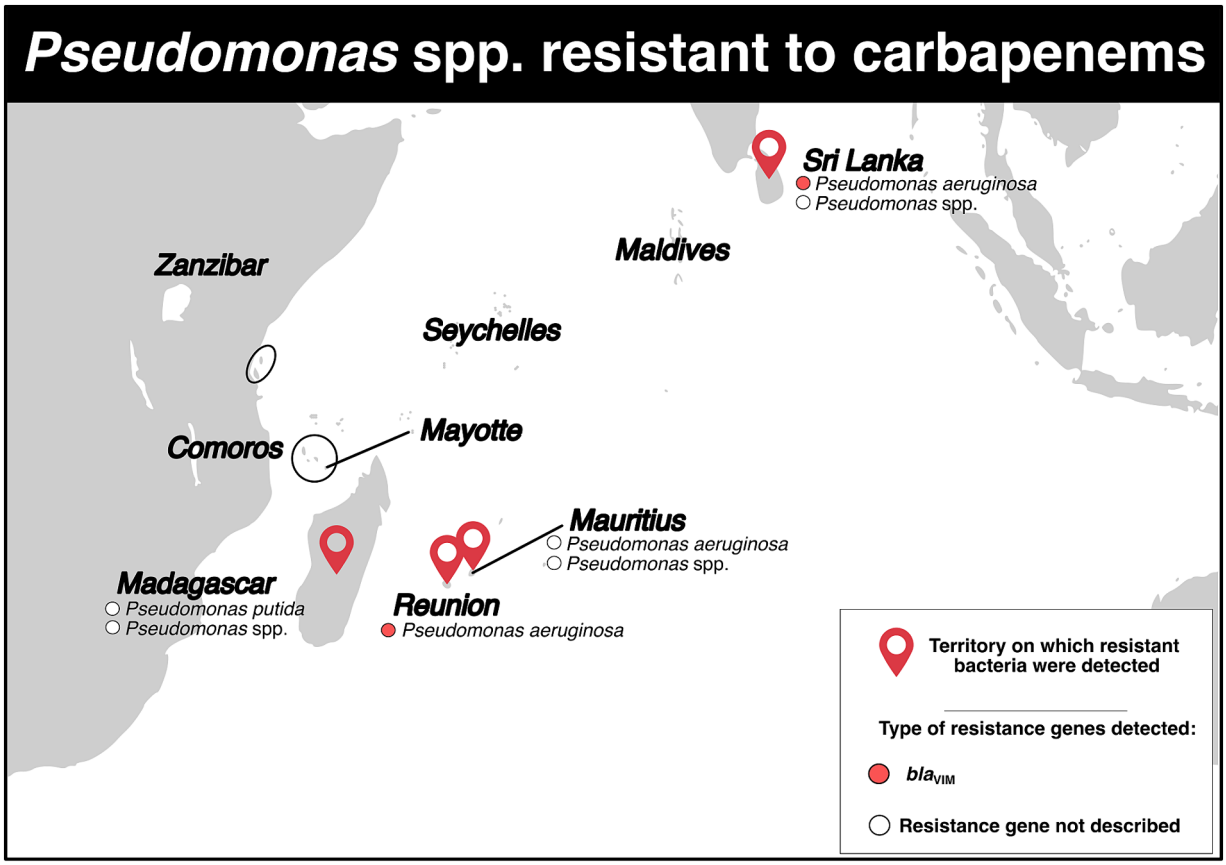


FIGURE 5
Distribution of carbapenem-resistant *Pseudomonas* spp. and genes associated with resistance mechanisms in the Southwest Indian Ocean Islands.

## 3.4 Enterococci resistant to vancomycin

VRE were reported in six studies across three territories (Figure 6; Supplementary Tables S2, S3). Two of the studies were performed in Madagascar. The first one, a cross-sectional survey conducted between 2006 and 2008 in surgery and intensive care wards, detected one resistant *Enterococcus* spp. isolate (resistance rate: 3.3%) (37). The second study, conducted between January 2011 and December 2013, detected one resistant *Enterococcus faecalis* isolate in the community population (resistance rate: 5.6%) (6).

On Reunion Island, three studies were identified (Figure 6; Supplementary Table S2). Between January 2015 and December 2017, one patient tested positive for resistant *Enterococcus faecium* (rate of VRE carriers: 0.05%) (8). In 2017, a patient repatriated from Mauritius tested positive for a resistant *E. faecium* that carried the *vanA* gene (18). Moreover, between January 2015 and December 2019, 16 resistant isolates of *E. faecium* harboring the *vanA* gene were detected. Half of these isolates were also resistant to linezolid. One isolate even exhibited simultaneous resistance to vancomycin, teicoplanin, linezolid and daptomycin. Among the 16 isolates, six (37.5%) showed a connection to a foreign country: two with India, two with Mauritius, one with Madagascar, and one with India/Saudi Arabia (47). Genotyping analyses identified five STs, with ST761 ($n = 8$), ST80 ($n = 4$) and ST5 ($n = 2$) being the most common.

Finally, in Sri Lanka, between January and March 2012, 11 *E. faecium* isolates were obtained from 11 patients (VRE carrier rate: 5.1%), and the *vanA* gene was detected in all isolates (Figure 6; Supplementary Table S2) (48).

# 4 Discussion

In this systematic review, we screened the literature to assess the current knowledge of critical- and high-priority resistant bacteria in several territories including Comoros, Madagascar, Maldives, Mauritius, Mayotte, Reunion Island, Seychelles, Sri Lanka, and Zanzibar. Similarly to Gay et al. in 2017, we encountered challenges due to the diverse study designs, resulting in uneven information across the available studies (4). However, our findings indicate that the targeted bacteria are actively circulating in the SWIO area. Gram-negative bacilli appeared to be most prevalent in the eastern islands of the region, particularly Mauritius and Sri Lanka, where resistance rates for some bacterial species can be alarmingly high (e.g., up to 87% of resistant *A. baumannii* in Mauritius and up to 100% in Sri Lanka). However, it is important to note that these findings may be affected by a bias, as studies were lacking for some territories. As far VRE, the limited number of studies and their distribution across different territories make it difficult to draw firm conclusions. Finally, cases of co-resistance have been recorded in the

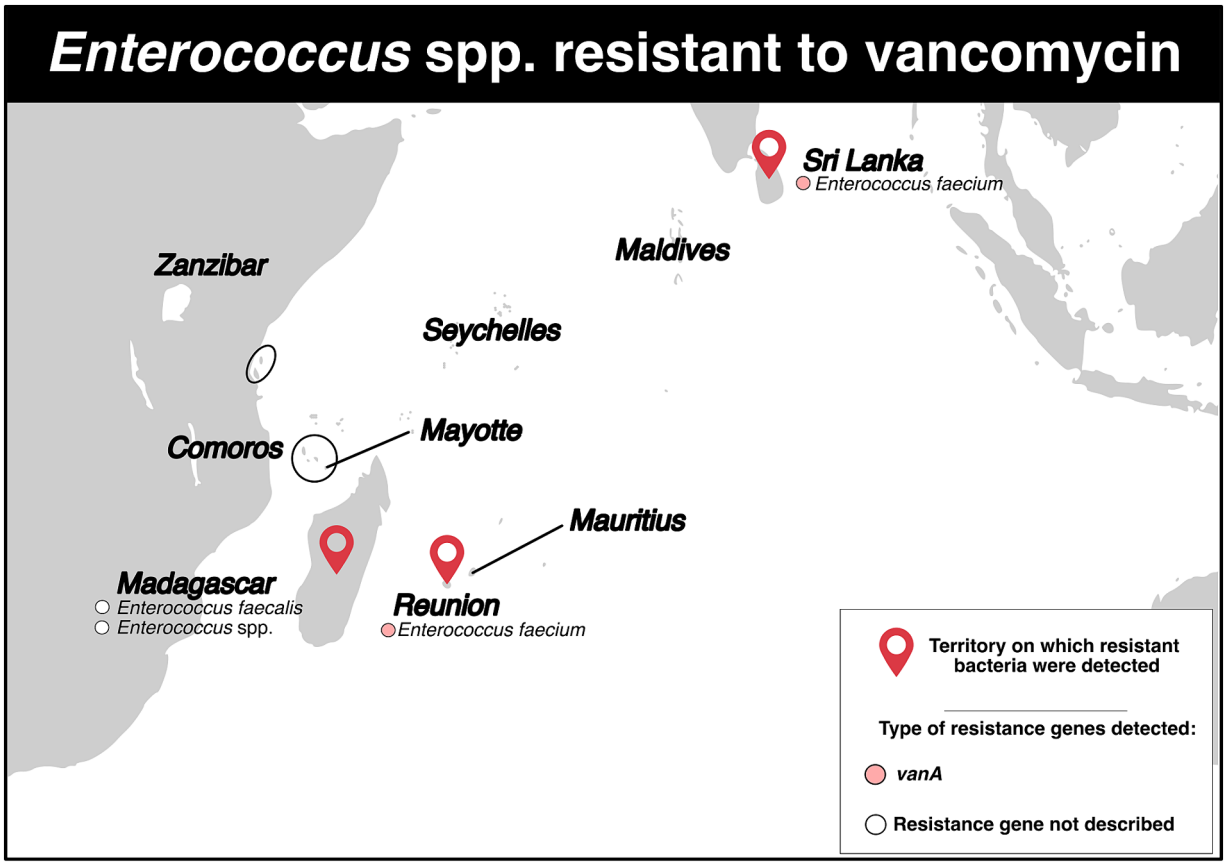


FIGURE 6
Distribution of vancomycin-resistant *Enterococcus* spp. and genes associated with resistance mechanisms in the Southwest Indian Ocean Islands.

region, such as carbapenem-colistin in *A. baumannii* or vancomycin-teicoplanin-linezolid-daptomycin resistance in *E. faecium*, raising serious concerns about the availability of effective therapeutic alternatives for infections caused by this type of extensively-drug resistant bacteria.

With further details, CPE were the bacteria for which more data were available. They were relatively widespread and were detected in two-thirds of the investigated territories. Six resistance genes families were associated with resistance mechanisms; however, the $bla_{NDM}$ and $bla_{OXA\text{-}48\text{-}like}$ families were the most represented, supporting the trend observed worldwide (49–51). Interestingly, during our literature screening, emerging high-risk clones were detected. Specifically, *K. pneumoniae* ST307/ST147 or *E. coli* ST167/ST405/ST410 were reported on Reunion Island and/or Sri Lanka (19, 21, 26, 28). These clones are considered a significant threat to public health due to their propensity to harbor multiple-resistance genes, promoting their spread (particularly in regions where antibiotic use is poorly controlled); and because they can be involved in serious infections, as limited therapeutic options exist to treat infected patients (52, 53). Their presence on these islands might likely originate from importation from territories on which they already circulate. For instance, *K. pneumonia* ST147 might have been imported from India, where it has been previously reported (52), and for which extensive human traveling exchanges exist between the Indian subcontinent and the SWIO region. Carbapenem-resistant *Acinetobacter* spp. and *Pseudomonas* spp. were detected in half of the investigated territories. However, compared to CPE, the number of studies and available information were less extensive. *A. baumannii* was the dominant species, and resistance mechanisms were only associated with $bla_{NDM}$ and $bla_{OXA}$ genes. For *Pseudomonas* spp., the main represented species was *P. aeruginosa* and $bla_{VIM}$ was the main gene involved in the resistance mechanisms. Finally, the bacteria that had the least number of available studies was *Enterococcus* spp. resistant to vancomycin. These bacteria were reported only in one third of the targeted territories. Both *E. faecalis* and *E. faecium* were identified and only the *vanA* gene was found to be associated with resistance to glycopeptides (47, 48). The contrasting level of information found between the four bacterial groups may be due to a bias in investigation and should be interpreted with caution when assessing the epidemiology of these critical and high-priority pathogens. It is possible that CPE has been the main focus for both scientific and medical communities in recent years, which may explain why there are more studies investigating their circulation compared to the other groups. However, these discrepancies might also originate from the socio-economic context of the region. The selected islands belong to eight countries with highly disparate gross domestic product *per capita* and healthcare systems. Health policies and resources allocated to investigate AMR, particularly through antimicrobial susceptibility testing, are not equal across these territories (Supplementary Table S2).

For instance, bacterial identification involving colorimetric/biochemical methodologies might be less precise than new approaches such as Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (54). Similarly, the use of traditional molecular biology test (PCRs) and limited access to sequencing analysis capabilities hinder performing Next Generation Sequencing for resistome/bacterial genotyping (55) may explain the scarcity of data regarding the localization of resistance genes. Variations in the number of available studies across the nine investigated territories could also be attributed to the socio-economic context. Additionally, in regions with limited resources, the use of broad-spectrum antibiotic molecules like third generation cephalosporins or carbapenems as probabilistic treatments may contribute to the selection and proliferation of these resistant isolates. More globally, these socio-economic disparities and contact with highly endemic regions could also drive the spread of AMR through population movements, such as tourism or medical evacuation, as observed in many published examples (18, 19, 40). However, collaborative efforts with the IOC provide opportunities for multicenter studies to overcome recruitment biases. It is worth noting that veterinary surveillance targeting these critical and high priority pathogens is scarce, and that no "One Health" study has looked at the cross-compartmental spread of these pathogens in this geographical area, indicating a need for improvement that should be highlighted.

In conclusion, our review highlights a growing interest in studying AMR in the SWIO region. The identification of critical and high priority pathogens emphasizes the alarming progression of this global silent pandemic, even in insular ecosystems, and provides an overview of the regional epidemiology. Nevertheless, the available information is still lacking consistency among these territories. Furthermore, there is shortage of research on resistance mechanisms and genotyping analyses. It is, therefore, necessary to enhance the diagnostic capabilities of laboratories to collect more comprehensive data in the future. Now more than ever, it is crucial to set up a regional surveillance network to prevent the spread of these pathogens. This should be done alongside implementing strict and uniform infection control measures, as well as effective antibiotics stewardship.

## Author contributions

AH: Data curation, Formal analysis, Writing – original draft, Writing – review & editing. PM: Writing – review & editing. GM: Writing – review & editing.

## Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This article was funded by the European Regional Development Fund "RESISTORUN" project (POE 2014–2020, grant number 20201126-0022906) and the Reunion Island Regional Council.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note



## Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1357345/full#supplementary-material

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