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## *Review article*

# Resistance Profile and Epidemiology of Carbapenem Resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* in Nigeria: A Review Update

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## Abstract

*Acinetobacter baumannii* and *Klebsiella pneumoniae* are clinically significant bacteria that cause hospital acquired infections worldwide, and resistance to carbapenems by these pathogens has been classified in the critical category by WHO. There is paucity of information on both pathogens in Nigeria, especially *Acinetobacter baumannii,* making it difficult to determine the resistance prevalence and public health impact of the bacteria. This study aimed at determining the resistance profile and epidemiology of carbapenem-resistant *Acinetobacter baumannii* (CRAB) and *Klebsiella pneumoniae* (CRKP) in Nigeria. Databases were searched using: PubMed, Scopus, Google Scholar and Google search engine for publications on CRAB and CRKP in Nigeria from 2014-2024. It was revealed that 55.6% of studies on these pathogens were from the South-West part of the country as compared to other geopolitical zones. The occurrence of *A. baumannii* in clinical samples was relatively low compared to *K. pneumoniae.* The overall prevalence of CRAB and CRKP was found to be high. The class of antibiotics to which *A. baumannii* and *K. pneumoniae* were resistant are those in the beta-lactam class while both pathogens showed a high sensitivity rate to the fluroquinolones. The two frequently identified resistance genes in *A. baumannii* isolates are *blaOXA-51* and *blaOXA-23* with most data reporting class B carbapenemase in *K. pneumoniae.* Conclusively, the incidence of CRAB and CRKP in Nigeria has increased over years and this is of great concern as these pathogens show multi-drug resistance. Thus, this study provides the current trends in resistance profile, which can serve as a starting point for further monitoring studies.

**Keywords:** *Acinetobacter baumannii*; *Klebsiella pneumoniae*; resistance profile; carbapenem-resistance; antimicrobial-resistance; Nigeria

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## 1. Introduction

In the early years of the 20th century, a medical scientists named Paul Ehrlich took the initiative to develop a chemical substance that would be fatal to microorganisms but would prevent the chemical agents from harming their host, which he termed a “magic bullet” (Onyedibe et al., 2018). After the discovery of these magic bullet (antibiotics), the public and clinicians believed that infections caused by microorganisms could be effectively controlled or prevented. However, shortly after this discovery, it was observed that microorganisms were capable of stopping or bypassing the effect of this magic bullet, which was later referred to as antimicrobial resistance. At the moment, resistance to antibiotics is a global phenomenon with the scourge much more pronounced in developing countries than in developed countries (Pandra et al., 2010). This global phenomenon is enhanced by bacterial, human and environmental factors and according to Bengtsson-Palme et al. (2018), antibiotic resistance is likely to result in 10 million fatalities by 2050 with a high proportion of mortality happening in Sub-Sahara, Africa (O’ Neill, 2016; Arowolo et al., 2023). The outbreak of antimicrobial resistance especially in Africa including many developing countries like Nigeria, has been enhanced by various factors such as poverty, unhygienic living conditions, overpopulation with a large percentage of uncontrolled use of antibiotics in hospitals, veterinary clinic and agricultural practices (Onanuga et al., 2019).

According to data on antimicrobial usage and resistance released by Nigeria Centre for Disease Control (NCDC) in 2017, Nigeria has the third highest percentage rate (48%) of antimicrobial prescriptions in Africa and the highest mean number of medications supplied to sick persons per visit (3.8/visit), coupled with other factors, led to an increase in emergence of antimicrobial resistance, with the most common antibiotics prescribed been in the penicillin group ranging between 25%-71.1% (Adisa et al., 2015; Joseph et al., 2015; NCDC, 2017).

The unfolding of resistance to *Klebsiella pneumoniae* strains has enhanced a crucial problem to public health at large due to its ability to spread quickly in the hospital surroundings (Rossolini, 2015). The swift spread of carbapenem-resistant *K. pneumoniae* and *A. baumannii* was one of the reasons why World Health Organization (WHO) enlisted these pathogens as ‘critical priority’ and is currently a worldwide threat to humans particularly, as it has been associated to cause an increase in morbidity and mortality over the years (WHO, 2017). The irrational use of antibiotics in the community and hospitals, inadequate infection prevention and control procedures, extended hospital stays, the use of indwelling devices (such as urinary catheters, central venous lines, and endotracheal tubes), stays in nursing homes, and the presence of immunosuppressive conditions are some factors that have contributed to the successful outbreak of carbapenem resistance (Freire et al., 2015). In Nigeria, the presence of resistance in these pathogens has been confirmed; however, there is scarcity of information on the epidemiology and resistance profiles of *Acinetobacter baumannii* and *Klebsiella pneumonia*e. Hence, in this review, insight to clinicians, researchers and general public on the risks posed by these priority pathogens in Nigeria are provided.

Carbapenems (meropenem, ertapenem, imipenem, doripenem, etc.) are broad spectrum βeta-lactam antibiotics with a penicillin-like mode of action, and are considered last-resort antibiotics for treating infections caused by multi-drug resistant Gram-negative bacteria (Codjoe & Donkor, 2017). They are highly potent antibiotics compared to other major beta-lactam antibiotics such as penicillin and cephalosporin because of the fortification of the beta-lactam ring of carbapenem, as shown in Figure 1. Carbapenem is

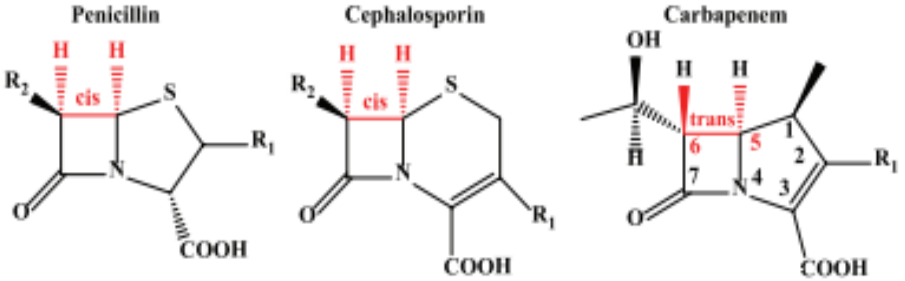



**Figure 1.** Chemical structure of carbapenem showing its "trans" fortified potency compared to penicillin and cephalosporin

ranked third among the commonly administered antibiotics worldwide which are used in treating both hospital and community-acquired infections that are caused by *Pseudomonas aeruginosa*, and species of *Klebsiella, Acinetobacter*, due to their good safety profiles and tolerance rates (Nguyen & Joshi, 2021). The global consumption of carbapenem increased by 45% between 2000 to 2010 (Patrier & Timsit, 2020). According to Meletis (2016), carbapenems are less harmful, and are more prescribed than other known last resort antibiotics such as polymyxins (Nguyen & Joshi, 2021).

Carbapenem-resistant organisms (CRO) have been shown to affect severely ill individuals leading to high mortality rates, prolonged hospitalization and they are accountable for an obvious proportion of hospital acquired infections, posing a great threat due to limited treatment options (Perez et al., 2010; Ayobami et al., 2022). Presently, the global epidemiology of carbapenem resistance, especially involving *Escherichia coli* and *Klebsiella pneumoniae* in the community and health-care facilities, and amongst livestock, remains a tremendous liability and may damage quality health-care delivery (Cai et al., 2016). Carbapenem-resistant Gram-negative bacteria are immensely life-threatening organisms exhibiting resistance to carbapenems and almost all other classes of antibiotics available now. Evidence suggests that those infected with pathogens that are resistant to carbapenem may have an increased likelihood of morbidity and mortality as compared with those infected by susceptible causative agents (van Duin et al., 2013; Ssekatawa et al., 2018; Nordmann & Poirel, 2019). The common mechanisms of resistance to carbapenem are the release of beta-lactamases, efflux pumps, and mutations that interfere with the expression and/or function of porins and penicillin binding proteins, with possible occurrence of combination of these mechanisms (Bashar & Ajibola, 2020; Robin et al., 2010). As stated by Fasuyi et al. (2020), the mechanisms of resistance to carbapenem by *Klebsiella pneumoniae* include the production of carbapenemase, modification of outer membrane permeability and upregulation of efflux systems. Oxacillinase production is the most common enzymatic mode of carbapenem resistance by *Acinetobacter baumannii* (Bergogne- Bérézin & Towner, 1996).

*Carbapenem resistant Klebsiella pneumoniae (CRKP)*: The bacterium *K. pneumoniae* has been linked to hospital acquired infections including burn infections, sepsis, gastrointestinal tract infections, soft tissue and wound infections, pyogenic liver abscesses, and urinary and respiratory tract infections (Ranjbar et al., 2019; Akinyemi et al., 2021). *Klebsiella pneumoniae* was identified as one of the frequent causative agents of lower respiratory tract infections, and bacteremia in children and newborn septicemia (Ogbolu et al., 2020; Akinyemi et al., 2021). It was estimated that respiratory tract infections

caused by different pathogenic microorganisms such as *Streptococcus pneumoniae*, *Haemphilus influenzae* and *Klebsiella pneumoniae,* potentially result in an annual death rate of one million children under the age of 5 and roughly 16% of preschool-age deaths in developing and low-income countries (UNICEF, 2019; Oyegoke et al., 2021). *Klebsiella pneumoniae* was also among the frequently isolated Gram negative bacteria in Sokoto, Northwest Nigeria, as reported by Olowo-Okere et al. (2020), with 14% of isolates showing multidrug resistance and carbapenemase activities. The prevalence of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) has been reported in the whole world particularly in developed countries with limited data on the prevalence in Africa.

*Carbapenem resistant Acinetobacter baumannii (CRAB): Acinetobacter baumannii* is a significant opportunistic bacterium that can result in nosocomial infections. There are about 60 species of *Acinetobacter* and of these diverse species, only *Acinetobacter baumannii* complex (*Acinetobacter baumannii, A. pittii, A. nosocomalis*) are the most clinically relevant species (Odewale et al., 2016; Kariuki et al., 2022). In Nigeria, the commonly isolated species of *Acinetobacter* that have been recovered in clinical samples are; *Acinetobacter baumannii, A. hemolyticus, A. nosocomalis*. These bacteria are recurrent colonizers of the respiratory tract, digestive tract, and throat; affecting people with compromised host defenses, frequently causing pneumonia with a high death rate. Other infections that this pathogen can cause are osteomyelitis, bacteremia, peritonitis, wound infections, keratitis, secondary meningitis, urinary tract infections and native-valve endocarditis (Ike et al., 2020).

Resistance to carbapenem by *Acinetobacter baumannii* has been reported worldwide with little information on the prevalence rate in Nigeria and Africa. Kariuki et al. (2022) previously reported that Nigeria was ranked 4$^{th}$ among seven African countries that were reviewed for prevalence of antimicrobial resistance rates of *A. baumannii* with 91.2% and 82.4% resistance to meropenem and imipenem respectively. Odih et al. (2022) explained that there was little information available on the molecular, epidemiology and resistance profiles of *A. baumannii* in Nigeria, which was mainly attributed to insufficient capacity to isolate, identify and determine the antibiogram of this pathogen in laboratories as well as inaccessible standard molecular methods of characterization. However, few reports describing carbapenem-resistant *Acinetobacter baumannii* causing clinical infections in Nigeria have been documented over time.

*Mechanism of carbapenem resistance:* Carbapenem resistant *K. pneumoniae* and *A. baumannii* pose a significant threat to public health. Bonomo et al. (2018) reported that carbapenem resistance in bacteria may result from one or more mechanisms including but not limited to;

a. release of carbapenemase enzymes (carbapenem-hydrolyzing enzymes) including class A carbapenemase (the *Klebsiella pneumoniae* carbapenemase types), class B or Metallo-beta-lactamases (MBLs), and class D oxacillinases (e.g., OXA-48-like enzymes).
b. extended spectrum beta-lactamase (ESBL) production
c. production of AmpC enzymes (mostly plasmid-mediated)
d. drug decreased permeability caused by porin loss
e. overexpression of efflux pumps

According to the Ambler classification system (Ambler, 1980), carbapenemases are classified into 4 groups (A, B, C and D) based on the central catalytic domain and substrate level, as seen in Figure 2. The class A group which is predominated by *Klebsiella pneumoniae* are the most common types of beta-lactamase enzymes encountered globally (Yusuf et al., 2015).

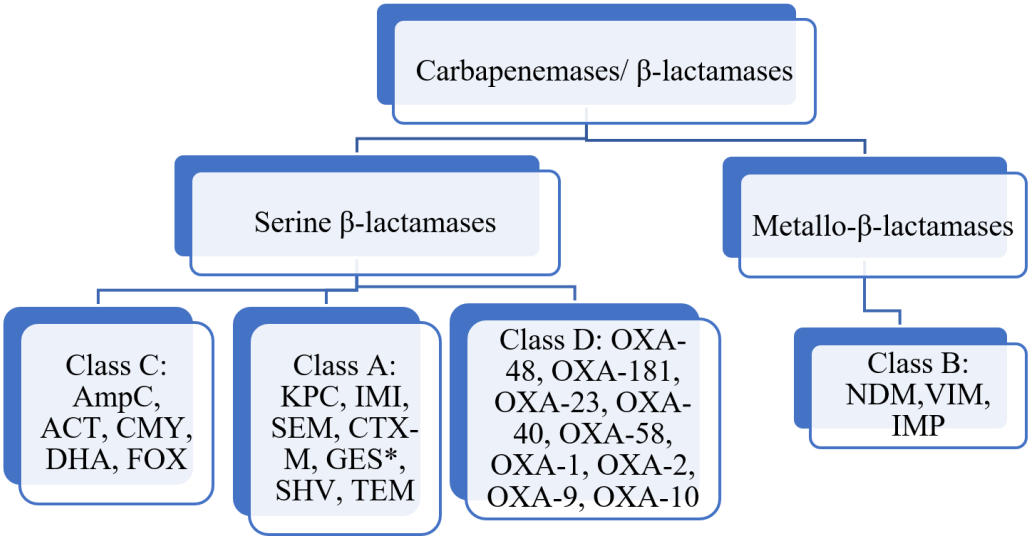



**Figure 2.** Classification of carbapenemases

## 2. Materials and Methods

### 2.1 Search strategy

Electronic databases (Google Scholar, Dove Press, Scopus, PubMed) were searched for published articles on carbapenem-resistant *A. baumannii* and *K. pneumoniae* in Nigeria from 2014-2024.

#### 2.1.1 Inclusion criteria

This study included articles published in Nigeria within the last 10 years (2014-2024). Articles or review that reported the incidence of *A. baumannii* and *K. pneumoniae* in humans taking into consideration studies that were retrospective, cross-sectional and longitudinal were included in the study. The keywords for the search include: carbapenem resistant *K. pneumoniae*, *A. baumannii*, carbapenem resistant, Nigeria and the year frame 2014 -2024. Reports on the prevalence of *A. baumannii* and *K. pneumoniae* in non-human samples and those that did not fall within the inclusion criteria were excluded from the search.

#### 2.1.2 Data extraction

Data were extracted from the selected articles which met the inclusion criteria and a table was designed (Table 1) from the eligible articles that met the inclusion criteria using the following headings; study design, study state, study objectives, sample size, organism prevalence, carbapenem-resistance prevalence, antimicrobial susceptibility testing method and carbapenem used with appropriate references. The data were analyzed using descriptive analysis (bar chart).

**Table 1.** Summary of studies on carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* in Nigeria

| Study Objectives | State | No. of Sample/ Isolates | Bacteria Prevalence (%) | % of Resistance | AST Method | Carbapenem Used | Resistance Genes Detected | Ref. |
|---|---|---|---|---|---|---|---|---|
| Estimating the occurrence of Gram-negative bacteria and resistance patterns | Lagos | 402 | *A. baumannii* (6.7) *K. pneumoniae* (7.7) | 17.7 | Disk diffusion | IMI ETP MRP | NA | Ettu et al. (2018) |
| Characterizing the molecular basis of CRAB isolated in clinical samples | South-West | 72 | *A. baumannii* (95.8) | 78.7 | Disk diffusion | MRP IMI | $bla_{OXA-23}$, $bla_{OXA-51}$ | Odih et al. (2022) |
| Investigating suspected outbreak of CRAB colonizing ICU patients | Osun Oyo | 108 | *A. baumannii* (31.5) | 18.5 | Vitex 2 | IMI DRP MRP | $bla_{OXA-23}$, $bla_{OXA-51}$, $bla_{NDM-1}$ | Odih et al. (2022) |
| Evaluating the antibiotic susceptibility pattern of *Acinetobacter* species isolated from clinical samples | Oyo | 87 | *A. baumannii* (70.3) | 38.5 | Disk diffusion | MRP IMI | NA | Dada-Adegbola et al. (2020) |
| Determining the prevalence of multi-drug resistant A. baumannii and its resistance genes | Osun | 150 | *A. baumannii* (8.5) | 63.6 | Disk diffusion | MRP IMI | $bla_{TEM}$, $bla_{CTX-M}$, $bla_{OXA}$ | Odewale et al. (2016) |

**Table 1.** Summary of studies on carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* in Nigeria (continued)

| Study Objectives | State | No. of Sample/ Isolates | Bacteria Prevalence (%) | % of Resistance | AST Method | Carbapenem Used | Resistance Genes Detected | Ref. |
|---|---|---|---|---|---|---|---|---|
| Characterizing CRAB isolated from clinical samples | Niger | 105 | *A. baumannii* (5.65) | 71.5 | Disk diffusion | MRP, IMI | $bla_{OXA-23}$, $bla_{OXA-51}$ | Ayams (2019) |
| Determining the mechanism of CRAB isolated from clinical samples | South-West | NA | *A. baumannii* (86) | 66.7-100 | Vitek 2 | MRP IMI | $bla_{OXA-23}$, $bla_{NDM-1}$ | Odih et al. (2023) |
| Evaluating the antibiotic susceptibility of CRKP and its mechanism of resistance | Lagos | 153 | *K. pneumoniae* (100) | 5.2 | Disk diffusion | MRP ETP | NR | Oshun & Ogunsola (2018) |
| Determining the prevalence of *A. baumannii* in two tertiary hospitals | Ebonyi | 300 | *A. baumannii* (7.0) | 14.3 | Disk diffusion | MRP IMI | NA | Ogbonna et al. (2023) |
| Determining the prevalence of antimicrobial and carbapenem resistant Enterobacteriaceae isolates | Abuja, Kuwait | 400 | *K. pneumoniae* (29) | 29.0 | NA | MRP | $bla_{NDM-7}$ | Jamal (2022) |

**Table 1.** Summary of studies on carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* in Nigeria (continued)

| Study Objectives | State | No. of Sample/ Isolates | Bacteria Prevalence (%) | % of Resistance | AST Method | Carbapenem Used | Resistance Genes Detected | Ref. |
|---|---|---|---|---|---|---|---|---|
| Monitoring the prevalence and antibiogram profile of CRKP among patients with UTIs | Ebonyi | 500 | *Klebsiella pneumoniae* (7.2) | 2.0 | Disk diffusion | MRP IMI | NR | Nomeh et al. (2022) |
| Determining the prevalence of CPO causing infections among ICU patients | Benin | 64 | *Klebsiella pneumoniae* (10.9) | 100 | Disk diffusion | MRP IMI | NR | Ibadin et al. (2023) |
| Characterizing the antibiotic susceptibility profile and resistance genes of *A. baumannii* | Sokoto | 23 | *A. baumannii* (75.0) | NS | Disk diffusion | MRP | $bla_{SHV}$, $bla_{TEM}$ | Mohammed et al. (2024) |
| | Lagos | 175 | *K. pneumoniae* (35.4) | 68.8 | Vitek 2 | MRP | $bla_{NDM}$, $bla_{OXA-}$ | Olalekan et al. (2019) |
| Determining the proportion of CR isolates among ESBL producing Enterobacterales | Lagos | 127 | *K. pneumoniae* (34) | 7.0 | Disk diffusion, micro-dilution | IMI | $bla_{SHV}$, $bla_{CTX-M-1}$, | Akinyemi et al. (2021) |
| | Ogun | 140 | *A.baumannii* (18) | 88.9 | Disk diffusion | MRP | $bla_{OXA-51}$ | Fasuyi et al. (2020) |

**Table 1.** Summary of studies on carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* in Nigeria (continued)

| Study Objectives | State | No. of Sample/ Isolates | Bacteria Prevalence (%) | % of Resistance | AST Method | Carbapenem Used | Resistance Genes Detected | Ref. |
|---|---|---|---|---|---|---|---|---|
| Determining the prevalence of *K. pneumoniae* and burden of CRKP in clinical isolates | Rivers | 172 | *K. pneumoniae* (62.8) | 35-48 | Disk diffusion | ETP | NA | Onanuga et al. (2019) |
| Investigating the prevalence, AMR, and profile plasmid of *A. baumannii* isolated | Kaduna | 90 | *K. pneumoniae* (17) | 7.7 | Disk diffusion | IMI | $bla_{TEM}$, $bla_{OXA}$, | Oyegoke et al. (2021) |

MRP- Meropenem, IMI- Imipenem, ETP- Etarpenem, DRP- Doripenem, NA- Not applicable, NR- Not reported, ICU- Intensive care unit, UTI- Urinary tract infections, CPO- Carbapenem producing organisms, CR- Carbapenem resistant, AST- Antibiotic susceptibility testing, CRAB- Carbapenem resistant *A. baumannii*, AMR- Antimicrobial resistance, CRKP- Carbapenem resistant *K. penumoniae*

# 3. Results and Discussion

## 3.1 Isolation and identification of *Acinetobacter baumannii* and *Klebsiella* species from clinical samples

*Acinetobacter baumannii* and *Klebsiell*a species could be isolated from an array of clinical samples but common clinical samples used were urine, sputum, blood and wound swabs. Ogbonna et al. (2023) isolated *A. baumannii* from wound samples while Dada-Adegbola et al. (2020) isolated 87 *A.baumannii* from different clinical samples such as blood, tracheal, pleural aspirates, wound biopsy, and confirmed 43 using Microbact with 37 further identified using Vitek 2. Suwaiba et al. (2020) isolated 46 (13.1%) *K. pneumoniae* from 300 urine samples. Generally, *Klebsiella* species and *A. baumannii* were isolated using similar technique and culture media although they had varying morphology and biochemical characteristics. Table 2 depicts the methods used in isolation and identification of the bacteria, the culture media frequently used in isolating these pathogens, and the prevalence of both pathogens that had been isolated successfully over time as well as the species isolated. Although some researchers used presumptive isolates and identified them using various methods.

## 3.2 Resistance profiles of *Klebsiella pneumoniae* and *Acinetobacter baumannii*

Across the six geo-political zones in Nigeria, there have been reports of carbapenem resistance in *K. pneumoniae* and *A. baumannii* of varying prevalence with more report coming from the South-Western part of Nigeria, as shown in Figure 3. The South-West (55.6%) had the highest number of published articles on carbapenem resistance detected in tertiary hospitals in Nigeria, with the least number seen in the North-East (5.6%), as shown in Figure 4. In the South-Western region, there were reported findings on the prevalence on carbapenem resistance particularly in Lagos, Ogun and Oyo. Nomeh et al. (2022) reported the prevalence rate of 7.4% for carbapenem resistant *K. pneumoniae* in Abakaliki, 37.5% and 5.2% CRKP in Ibadan and Lagos were reported by Olalekan et al. (2019) and Fasuyi et al. (2020) respectively. However, the prevalence of carbapenem resistant *A. baumannii* was significantly high even when the pathogen isolation frequency was low. Ike et al. (2020) and Ettu et al. (2018) published resistance rates of 78.7% and 59.3%, respectively to meropenem. The Kirby-Bauer's disk diffusion method of antimicrobial susceptibility test was the most common method used to determine the antimicrobial profile with only a few using other methods such as agar well method and Vitek 2, as seen in Table 1. The prevalence of CRKP and CRAB reported in published articles from 2014-2024 is depicted in Figure 5. The highest prevalence of CRKP and CRAB was reported in the year 2020.

**Table 2.** Data extraction for carbapenem resistant *A. baumannii* and *Klebsiella pneumoniae* studies

| Type of Clinical Samples | Total Number | Culture Media Used | Method of Identification | Bacteria Isolated (%) | Species Isolated | Ref. |
|---|---|---|---|---|---|---|
| Urine, Blood, Sputum, CSF, Wound swab, Tracheal aspirate | 150 | MacConkey (aerobically) | Gram reaction<br>Biochemical tests<br>API 20E | 8.5 | *A. baumannii* | Odewale et al. (2016) |
| Rectal swabs | 180 | CHROM™ agar - Acinetobacter media | VITEK 2 | NS | *A. baumannii*<br>*A. nosocomalis*<br>*A. pittii* | Odih et al. (2022) |
| Urine (26)<br>Blood (22)<br>Wound swabs (24) | 72 | Constituted multidrug resistant Leeds Acinetobacter medium (MDR-LAM) | 12E Microbact ™ Gram negative identification system<br>16SrRNA | NS | *A. baumannii* | Ike et al. (2020) |
| Wound swabs | 150 | Leeds Acinetobacter media | 12E Microbact ™ Gram- negative identification system | 12.8 | *A. baumannii* | Ayams, (2019) |
| Urine | 23 | Cysteine Lactose Electrolyte Deficient (CLED) agar | Gram staining<br>Oxoid Microbact™ Gram-negative identification system | 75.0 | *A. baumannii* | Odih et al. (2023) |
| Sputum | 300 | Blood agar<br>MacConkey agar<br>Mannitol salt agar | Microgen ID kits | 32 | *Acinetobacter* spp. | Oyegoke et al. (2021) |
| Urine<br>Sputum<br>Wound | 105 | MacConkey agar<br>Leeds Acinetobacter media | Gram staining<br>Biochemical tests<br>PCR | 0.81<br>1.61<br>3.23 | *A. baumannii* | Ettu et al. (2018) |

NS: Not stated, CSF- Cerebrospinal fluid, API- Analytical profile ındex, PCR- Polymerase chain reaction

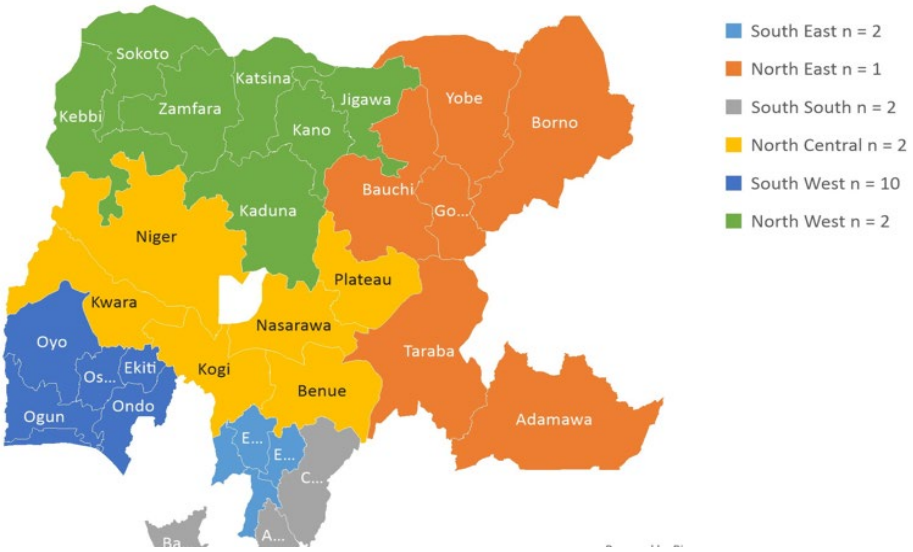



**Figure 3.** Map showing the frequency of study of carbapenemase resistant *Acinetobacter* and *Klebsiella* spp. across the geopolitical zones in Nigeria

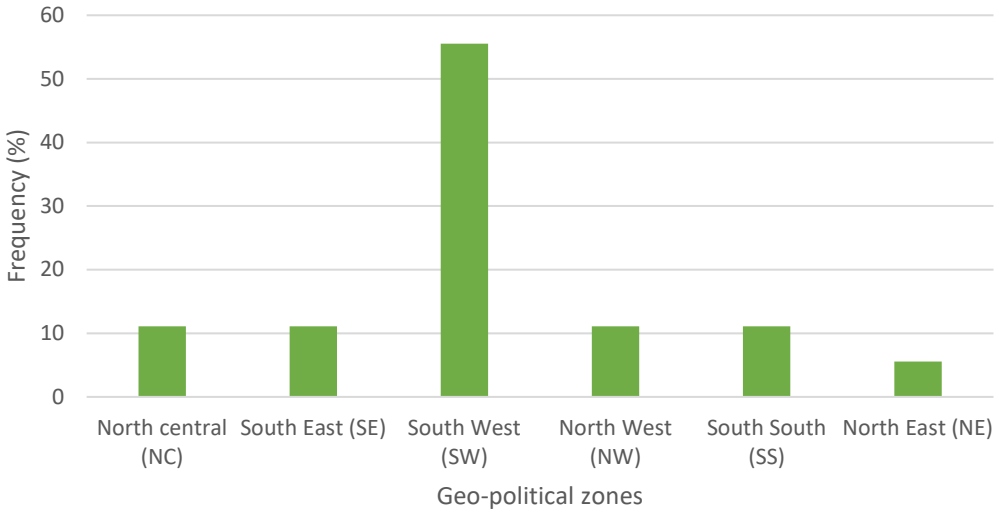



**Figure 4.** Percentage of study of capabenemase resistant *Acinetobacter* and *Klebsiella* spp. across the geopolitical zones in Nigeria

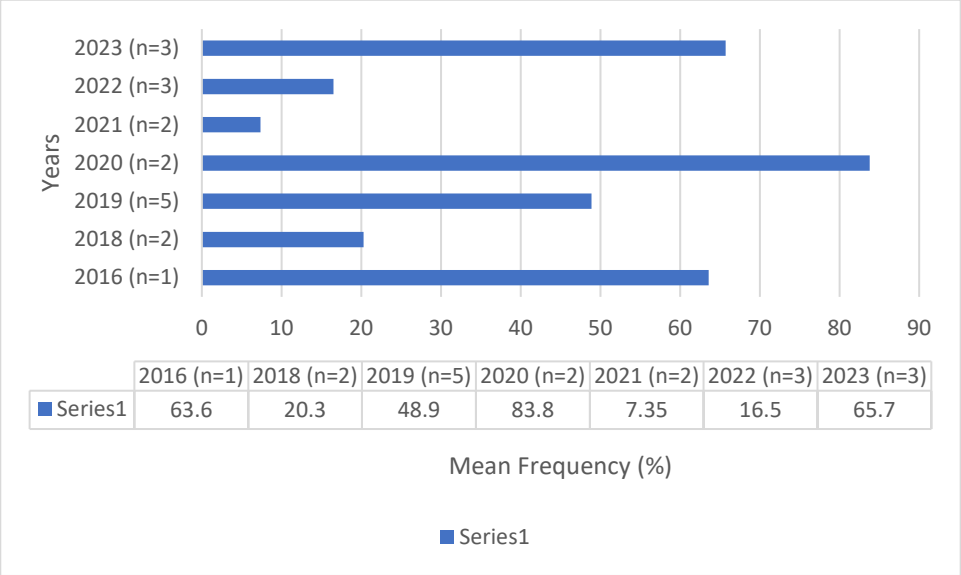



**Figure 5.** Prevalence of CRKP and CRAB reported in published articles from 2014-2024

Ogbonna et al. (2023) suggested from his findings that meropenem and imipenem still remain the most potent antibiotics against *A. baumannii*. This suggestion corroborates the findings of Mohammed et al. (2024) who reported 100% sensitivity to meropenem. However, Odih et al. (2022) reported a 100% resistance to doripenem, meropenem and imipenem from all seven *Acinetobacter* isolates from one selected hospital in South West, Nigeria. The discrepancy in both results could be the methods used in determining antimicrobial resistance, while the first researcher used the disk diffusion method, the second researcher used the Vitek 2 system in profiling antimicrobial resistance. The findings of Ayams (2019) aligned with those of Odih et al. (2022) who reported full resistance to meropenem from two *Acinetobacter* isolates but intermediate resistance to imipenem, while other isolates showed complete resistance to imipenem but were intermediate to meropenem. The variation in the resistivity and sensitivity to carbapenem could be the result of the specific carbapenem adopted as some types are more active than others, particularly to certain microbes despite being generally very potent and a broad-spectrum antibiotic. Perez et al. (2016) reported that ertapenem had limited activity against species of *Pseudomonas* and *Acinetobacte*r while meropenem showed a slightly higher success rate than imipenem. Imipenem on the other hand, inhibited about 98% of clinically important pathogens when given at a concentration of 8mg/L (Perez et al., 2016). The upsurge in carbapenem resistance over the years could be a result of the increase in the use of this medication, its misuse/abuse, or a lack of awareness of the implications of resistance. Akinyemi et al. (2021) reported imipenem resistance of 7% in *Klebsiella pneumoniae* with presence of the carbapenemase genes *blaCTX-M-1*, *blaSHV* and *blaTEM* isolated from patients in Lagos hospitals. Correspondingly, the resistance profile of these pathogens to other groups and classes of antibiotics was captured in this review. Antibiotics among the major classes of antibiotics were used in most studies including penicillins, cephalosporins, aminoglycosides, fluroquinolones, and beta-lactamase inhibitors.

Most researchers reported high resistance rates to penicillins (amoxicillin, ampicillin, piperacillin and ticarcillin). Ike et al. (2020) reported 100% resistance to amoxicillin, amoxicillin/clavulanic acid ampicillin, ceftizoxime and ceftazidime by *A. baumannii* which all fell into the beta-lactam class of antibiotics. The findings of Ike et al. (2020) were in line with the findings of Nomeh et al. (2022), who reported 100% resistance to amoxicillin/clavulanic acid, aztreonam, ticarcillin/clavulanic acid, ceftazidime and cefotaxime by *K. pneumoniae*. However, Dada-Adegbola et al. (2020) used third generation cephalosporins when determining the resistance of carbapenem resistant *K. pneumoniae* and recorded a 63.7% resistance to ceftazidime, and 78.4% to ceftizoxime. The choice of third generation cephalosporins by these researchers was due to the fact that these groups of antibiotics were the most used antibiotics in The Lagos University Teaching Hospital (LUTH), accounting for 34% of antibiotic prescriptions based on point prevalence study. The aminoglycoside class of antibiotics functions by inhibiting the protein synthesis ability of microorganisms. Ayams (2019) recorded a percentage resistance of 88.9 % to tetracycline and gentamicin which then reduced drastically after curing. The percentage prevalence of resistance to aminoglycosides reported by Ayams (2019) was very similar to the result of Onanuga et al. (2019), who reported a percentage resistance of 88.6% to gentamicin. It was observed from all the articles used in the review that antibiotics in the fluroquinolone class showed a reduced resistance rate compared to other classes. Akinyemi et al. (2021) published a resistance rate of 55.8% to ofloxacin while Nomeh et al. (2022) reported 100% susceptibility to ofloxacin and ciprofloxacin. A larger percentage of the published articles reported a high prevalence of multi-drug resistance pathogens suggesting that they were resistant to many antibiotics other than carbapenems. As of 2020, it was suggested that cephalosporins may no longer be effective in treating infections caused by *A. baumannii* (Ike et al., 2020).

Of the 19 articles screened for the prevalence of CRAB and CRKP, only one article failed to state the prevalence percentage, with others reporting the prevalence (percentage) in the range of 20-100. The highest frequency was documented in the Southwestern part of the country with the lowest in the Southeastern region. The Southwestern part of the country showed the burden of carbapenem resistance with respect to the microorganisms of interest compared to other parts. However, this review did not consider CRAB and CRKP prevalence in animals, non-animate objects and in environment which could give a clearer view of the extent at which the region was burdened with carbapenem resistance. Moreover, the trends of CRAB and CRKP over the last decade could not be fully elucidated in this review as there were few or no data reported on the prevalence of carbapenem resistance over certain periods of time. In addition to the discovery of the prevalence of CRKP and CRAB, resistance was conferred mostly through the production of carbapenemase enzymes. Those that were not carbapenemase producers suggested that resistance was conferred through mechanisms such as biofilm formation, efflux pump action. It was established by Kuo et al. (2021) that non-carbapenemase producers were less of a threat to healthcare systems than carbapenemase producers owing to the fact that non-carbapenemase mechanisms of resistance were nontransferable, thereby, making treatment much easier. Many publications did not report much on the resistance genes as carbapenemase production was commonly detected using various phenotypic screening methods and this was a major limitation of many studies. A reason for the lack of molecular examination in most articles could be a result of financial constraints as only a few of the reviewed articles received funding for the study and the little that had funding had affiliation with international bodies. The most commonly identified resistance genes in the compared studies were the bla*OXA*-23-like and bla*OXA-51-like* genes for *Acinetobacter baumannii*, which were categorized in

class D of the Ambler classification system. The bla*OXA-51*-like gene is an intrinsic gene for *A. baumannii* while other genes such as bla*OXA*-23-like, bla*OXA*-24-like, bla*OXA*-58-like are acquired (Ike et al., 2020). Few researchers were able to identify these genes in their publications. Ike et al. (2020) identified the bla*OXA*-23-like gene only while Ayams (2019) identified both the bla*OXA*-23-like, bla*OXA-51*-like genes with the prevalences of 42.86% and 100%, respectively, for CRAB. Odih et al. (2023) identified all the resistance genes present in CRAB using whole genome sequencing. The molecular method of detection was mostly the polymerase chain reaction with only a few researchers using other methods such as whole genome sequencing and nanopore technology that allowed the identification of a wider array of resistance in the virulence genes as well as in the specific strains harboring these genes. For instance, Shettima et al. (2020) reported an unknown mechanism for 10 isolates of *A. baumannii* and 3 isolates of *K. pneumoniae* after PCR has been carried out to detect bla*NDM* and bla*VIM*. This was of great concern as this publication was the only representative article from the Northeastern region. A more holistic molecular approach beyond PCR is suggested to fully elucidate not only the prevalence of CRAB and CRKP but also the mechanisms of resistance and this can be achieved when researchers are encouraged to do more through funding by government and collaborative research. It is also suggested that researchers should focus and do more molecular studies rather than phenotypic methods because phenotypic methods are limited to specific genes while molecular/genotypic methods as stated earlier can identify broader arrays of resistance and virulence genes as well as the percentages of resistance in the pathogenic strains. The routine susceptibility tests performed by clinical laboratories in Nigeria have failed to detect the bacteria harboring these enzymes, which have led to inappropriate and unsuccessful therapy of patient and unnecessary use of drugs.

The pooled frequency data during 2014-2024 optimally explains the current status of CRKP and CRAB in Nigeria (Tables 1 and 2). However, there are few published reports on CRAB and some of those published were not comprehensive enough to fully elucidate the impact of CRAB in Nigeria. Moreover, most published reports are from the South West part of the country with few or no reports from other geopolitical zones that can provide the current trends and prevalence of CRAB in Nigeria. A lack of enough articles coming from other parts of the country asides the Southwestern part and particularly in the northern region is likely the insecurity in the region. In West Africa, Nigeria and Ghana are the leading countries in the region that have documented carbapenemase resistant Enterobacteriaceae (CRE) (Sekyere et al., 2016). The prevalence of CRAB and CRKP is high in Nigeria when compared to other countries. Komla & Kpalma (2024) reported the prevalence of carbapenem resistant bacteria (CRB) per country in West Africa and Niger (18.6%) and Nigeria (17.9%) exhibited the highest prevalence of CRB, followed by Gambia (14.5%), Côte d'Ivoire (9.9%), Benin (8.1%), Sierra Leone (7.6%), Cape Verde (6.1%), Senegal (5.3%), Burkina Faso (3.7%), Mali (2%), Ghana (1.9%), Mauritania (1.6 %), and the least prevalence in Togo (1.6%). The overall findings of this review revealed that the burden of carbapenem resistance was high in Nigeria and this has detrimental implication. First and foremost, due to high prevalence of carbapenem resistance, there is the likelihood of an increase in hospital stay which will then lead to increase in cost of treatment. Nigeria is a developing country with a large number of its citizens earning less than $100 per month, making it difficult to afford the increase in cost of hospitalization, thereby, resulting to the option of self-care in case of no intervention. Secondly, there could be loss in productivity time which might be a threat to the economic at large. However, Nigeria is not the only Sub-Saharan country facing this menace as there have been studies and reports from other developing nations and advanced countries in other parts of the world such as USA, China, and Europe.

This study has provided an update report on the carbapenemase-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae*. Most of the research examined were concentrated around hospitals making it hard to establish the origin of *Acinetobacter baumannii* and *Klebsiella pneumoniae* outside hospital. Additional or more review that is focus on carbapenem-resistant bacteria outside hospital settings in Nigeria is advised.

## 4. Conclusions

The frequency of the CRAB and CRKP carbapenem- resistant pathogen strains reported in Nigeria raised an alarm of resistivity to carbapenem and other classes of antibiotics as there has been an increase in the degree of resistance of the pathogens. Awareness regarding the consequences of antibiotic abuse and poor antibiotic stewardship should be reinforced. There is an urgent need for a broader monitoring of hospital environments and communities to determine the true prevalence rate of these multi-drug resistant pathogens in Nigeria. Moreover, policies on infection control should be made and enforced to promote individual and community hygiene. Antibiotics need to be more appropriately administered by clinicians and veterinarians if the prevalence of carbapenem- resistant pathogens such as CRAB and CRKP in the country is to be reduced.

## 5. Conflicts of Interest

The authors declare no conflicts of interest.

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