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Research article

Acinetobacter baumannii from the one health perspective in Nigeria: A systematic review of literature in the last decade (2011-2021)

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Abstract

Multidrug drug-resistant (MDR)-*Acinetobacter baumannii* (*A. baumannii*) is one of the most feared nosocomial bacterial agents worldwide, and the World Health Organization classified carbapenem-resistant strains as a priority "1" critical pathogen. In Nigeria, the paucity of information on this pathogen makes it difficult to estimate its potential impact on public health and veterinary medicine. This systemic review was done to prepare an impact assessment for One Health based on the occurrence of *A. baumannii* in different environments and the antimicrobial resistance. A detailed search of articles on *A. baumannii* in Nigeria was conducted using search strings in the following databases: PubMed, Scopus, Google search engine, and Google scholars. This study revealed that 14 out of the 36 states in Nigeria reported *A. baumannii*. Specifically, 19/24 articles described isolates from clinical settings, 4/24 from the environment, and 1/24 from animal sources. *A. baumannii* occurrence of 9.15% (503/5496) was recorded from 8.4% (418/4950), 16.06% (80/498), and 10.42% (5/48) of samples of clinical, environmental, and animal origin by culture, respectively. The most common antibiotics to which *A. baumannii* was resistant were chloramphenicol, ampicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, cefuroxime, ceftazidime, ceftriaxone, gentamycin, and tetracycline. Seventeen resistance determinants were described for *A. baumannii* isolates originating mostly from clinical sources with *bla*OXA-51 and *bla*OXA-23 gene makers frequently reported. This study demonstrates the lack of data on *A. baumannii* from animals. Clinical MDR- *A. baumannii* isolates, particularly in Intensive Care Units (ICUs), are a severe public health concern in Nigeria. Thus, findings from this review will form a baseline for future surveillance research.

Keywords: *Acinetobacter baumannii*, Multidrug-resistant, One-health, Resistant determinants

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Introduction

Acinetobacter baumannii (*A. baumannii*) is generally regarded as an opportunistic nosocomial pathogen capable of causing various infections. Most often, the respiratory tract is affected and especially by ventilator-associated pneumonia. But bacteremia, mediastinitis, infections of skin wounds or surgical sites, catheter-related sepsis, soft tissue infections, osteomyelitis, urinary tract infections, cholangitis, meningitis, and rare community-acquired disease have also been reported (Dijkshoorn et al., 2007; Lee et al., 2017). Common risk factors for the acquisition of multidrug-resistant (MDR), extensively drug-resistant (XDR), or Pan-drug resistant (PDR) *A. baumannii* include previous antibiotic abuse, mechanical ventilation, length of stay in intensive care unit/hospital, the severity of illness, use of medical devices and the status of the immune system.

The World Health Organization (WHO) considers *A. baumannii* as one of the most dangerous ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *A. baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) organisms as it effectively escapes the effects of antibacterial drugs. This bacterium can move on surfaces (Wareth et al., 2021b). It also up-regulates or acquires resistance determinants fastly and survives harsh environmental conditions (Peleg et al., 2008; Lee et al., 2017; Vázquez-López et al., 2020). Rapid emergence and global spread

of carbapenem-resistant *A. baumannii* (CRAB) within the past decade left them to become a threat to public health (Kim et al., 2012; Lee et al., 2014; Huang et al., 2019). In the USA, a national surveillance study in 2010 found an occurrence of 44.7% and 49.0% *A. baumannii* strains resistant to imipenem and meropenem, respectively (Huang et al., 2019). Mortality of CRAB infections has risen to 76.0% from 16.0% (Huang et al., 2019). Similarly, in Korea and China, CRAB causes 79.8% and 70.0% mortality in bloodstream infection (DBI), respectively (Kim et al., 2012; Lee et al., 2014)).

Antimicrobial resistance and virulence determinants in *A. baumannii*

Genetic analyses have reported several virulence factors in *A. baumannii* isolates from clinical samples. Genes coding for outer membrane porins (*Omp*), pathogenicity islands (*PAI*), P fimbriae (*pap*), phospholipases, S fimbriae adhesion and F1C (*sfa*), fimbriae adhesion and *dr* antigen (*afa/dra*), proteases, type 1 fimbriae (*fimH*), fibronectin receptor (*fbn*), lipopolysaccharides (LPS), serum resistance (*traT*), curli fibers (*csg*), aerobactin (*iutA*), yersiniabactin (*fyuA*), polysaccharide coatings of group II and III capsules (*kpsMT*), cytotoxic necrotizing factors (*cnf*), invasins factors (*IbeA*), colicin V production (*cvaC*), iron-chelating systems and protein secretory system, responsible for adhesion, colonization, and invasion of different target cells as well as genes of various resistance mechanisms to several antibiotic classes have been identified (Lee et al., 2017; Tavakol et al., 2018; Vázquez-López et al., 2020). Some of the resistance mechanisms of *A. baumannii* include target modification, altered binding proteins, enzymatic degradation of drugs, multidrug efflux pumps, ribosomal (16S rRNA) methylation, damage to permeability, and ribosomal protection (Vázquez-López et al., 2020).

The virulence factors of *A. baumannii* extend to cytotoxicity, chemotaxis, bacterial killing, and persistence (Nocera et al., 2021). *A. baumannii* strains of human, animal, environmental origin, and foodstuffs also harbor a plethora of resistance genes against different classes of antibiotics at an alarming rate. Most common genes found are intrinsic chromosomal (OXA)-51-like (carbapenem), *bla*OXA-23, 24 (OXA-40-like), -58-like, and -123-like (acquired carbapenem) genes, *aad*A1 (streptomycin), *aac*(3)-IV (gentamicin), *sul*1 (sulfonamides), *bla*SHV and *bla*CTX-M (cephalosporins), *cat*1 and *cml*A (chloramphenicol), *Lpx*A, *Lpx*C, and *Lpx*D (colistin), *tet*A and *tet*B (tetracycline), *dfr*A1, (trimethoprim), *qnr* (fluoroquinolones), *imp*, *sim* and *vim* (carbenicillin), and *bla*KPC, *bla*GES, *bla*NDM, *bla*SIM, *bla*VIM, *bla*IMP (beta-lactams) are mainly responsible for the occurrence of severe antibiotic resistance that are often encoded in the chromosome and extra-chromosomal structures such as plasmid, integrons, and transposon (Lee et al., 2012; Tavakol et al., 2018; Ike et al., 2020; Vázquez-López et al., 2020).

***A. baumannii* from a "One Health" perspective**

A. baumannii, as an agent of public health concern, has been reported in food animals/livestock (cattle, poultry, and swine) and pet animals (cats, dogs, horses, etc.) in some parts of the world (Wareth et al., 2019) but no data are available in Nigeria yet. This could be attributed to researchers' interest and the emerging nature of *Acinetobacter*-associated diseases in Nigeria. Thus, *A. baumannii* needs an interdisciplinary approach for which human, environmental, and animal health is considered, and antibiotic resistance is addressed with care (Scott et al., 2019). Based on this One-Health approach, environmental, animal, and human (clinical) isolates are investigated to determine the sources and routes of infections. The detection and lack of knowledge on the occurrence of *A. baumannii* in livestock call for further investigation.

In Lebanon, Al Bayssari et al. (2015) reported the detection of VIM-2-producing and OXA-23-producing carbapenem-resistant *A. baumannii* (CRAB) and *P. aeruginosa*, respectively. Also, Tavakol et al. (2018) reported that sixteen out of 22 *A. baumannii* isolates from raw meat had different genetic clusters. Only 12 (54.54%) had similar genetic clusters. These *A. baumannii* strains were resistant to tetracyclines (90.90%), trimethoprim (59.09%), cotrimoxazole (54.54%), and gentamicin (50.00%), with *tet*A (81.81%), *tet*B (72.72%), *dfr*A1 (63.63%), *aac*(3)-IV (63.63%), *sul*1 (63.63%) and *aad*A1 (45.45%) being the most commonly detected antibiotic resistance genes. *Fim*H (81.81%), *afa/dra*BC (63.63%), *csg*A (63.63%), *cnf*1 (59.09%), *cnf*2 (54.54%) and *iut*A (50.00%) were the most commonly detected virulence factors. Notably, *A. baumannii* strains isolated from chicken meat samples had the highest genetic similarities. Furthermore, Klotz et al. (2019) reported that cattle harbored *A. baumannii* predominantly in the nose. Some of these bovine *A. baumannii* strains shared the same genotype as human strains. *A. baumannii* in cattle has different occurrences in beef cattle (6.8%), dairy cows (21.1%), and calves (2.4%).

Hrenovic et al. (2019) reported an important public health risk. They isolated *A. baumannii* ST195 strains from pigs on a Croatian farm, representing the predominant clinical isolates from humans in Europe. Habitats can be shared by wildlife and poultry, and these wild bird species are considered potential reservoirs of *A. baumannii* (Nocera et al., 2021). Kanaan et al. (2020) showed that poultry products such as meat of turkeys and chickens might be of concern as they may vector for transmitting MDR, XDR, and PDR *A. baumannii*. Zhang et al. (2013) isolated MDR *A. baumannii* strains carrying NDMI Metallo-β-lactamase [high potential carbapenemase] from blood samples of animal origin suffering from pneumonia in China. Hamouda et al. (2011) reported the isolation of bovine *A. baumannii* strains that were generally susceptible to antibiotics but discovered three new *bla*OXA-51 types for the first time beta-lactamase genes (*bla*OXA-148, *bla*OXA-149, and *bla*OXA-150) so far not found in human isolates. Cho et al. (2018) characterized 42 *A. baumannii* isolates from dry milk samples. All strains were of the European clonal lineages II and III, were PCR positive for *bla*OXA-51, and were resistant to chloram-

phenicol and oxacillin. Genome sequencing of nine isolates revealed that four isolates harbored *bla*OXA-530 and another four harbored *bla*OXA91 and *bla*OXA-430 genes of the *bla*OXA-51-like family. Moreover, the strains contained a blaADC-25-like gene encoding for an intrinsic AmpC beta-lactamase Tavakol et al. (2018); Nocera et al. (2021).

Therefore, significant attention needs to be given to the meat of cattle, sheep, goats, and camels in both community and hospital settings, as the source of *A. baumannii* MDR genes (Askari et al., 2020). Global Clones 1 (GC1) and 2 (GC2) have already been spread to more than 30 countries since 2011 Holt et al. (2016). Even though the spread of this bacterium in the hospital setting is well known, information on its ecology within the environment and food animals is still scarce and neglected in Nigeria; thus, a literature study of the last decade occurrence and antibiotic resistance of *A. baumannii* in Nigeria is required.

Materials and methods

Search strategy, eligibility, and validity assessment

A meta-analysis of original research on *A. baumannii* from clinical, environmental, and animal sources across 36 states of Nigeria's six geopolitical zones, including the Federal Capital Territory (FCT) Abuja, was conducted using the systematic review protocol PRISMA-P 2015 checklist Moher et al. (2015). Full-length research publications, abstracts, and keywords in English (such as MESH terms in PubMed) were considered. The search results were restricted to full-length publications and abstracts between January 1, 2011, and December 31, 2021. The electronic databases PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Google search (https://www.google.com), Google scholar (https://scholar.google.com/), Medline, and Scopus were searched. Following search items were by 10th March 2022: (*Acinetobacter* [ti], *baumannii* [ti], "*Acinetobacter*" [Mesh] or "*A. baumannii*" [Mesh]) and (synerg* [ti], combin* [ti], "MDR Combinations" [Mesh] or "Antimicrobial resistance, combination" [Mesh] for PubMed, Medline and Google Scholar). The same search without the MESH terms was also conducted in Scopus. While '' *Acinetobacter*" or '' *baumannii*" or a combination of both words, or '' Occurrence" or Antimicrobial resistance" or ''Nigeria" or ''Food" or ''clinical" OR ''Environment" or a combination of all were used as search criteria in Google search engine. The title and abstract of each publication and the full text of selected articles were analyzed. Any study type (including *in-vitro*, animal models, and clinical studies) was eligible.

Duplicate reports were sorted and removed from the analysis. Sorting was done by grouping all reports according to state and then comparing variables, which included study time, name, location of the study site, and the number of isolates. The occurrence was calculated in this study as the percentage of positive samples for *A. baumannii* in the total samples recorded. The study's validity was determined by carefully evaluating all original research publications for the inclusion and exclusion criteria outlined above, ensuring that only credible data were included.

Results

Data analysis

A flow chart of the review is depicted in Figure 1. Twenty-four relevant publications (Table 1 & Table 2) were identified as eligible for describing 503 [418 clinical, 80 environmental, and 5 animals] *A. baumannii* isolates. All (100%) studies were published in the last 10 years, while most (83.33%) articles were published in the last 5 years. Most studies (n=16) were conducted in the South-West region (62.5 %), three (16.67%) in North-west, and two (8.33%) in the South-South region as depicted in Figure 2. The number of eligible isolates per study was small in 45.83% of studies with less than 10 isolates. In particular, 16.67 % (4/24) of published studies from 2014 to 2020 included *Acinetobacter* species other than *A. baumannii*. The analysis revealed that *A. iwoffii* (n=22), *A. haemolyticus* (n=20), and *A. calcoaceticus* (n=1) are among the other species studied. Finally, most studies were single-center studies (62.5%), and multicenter studies (33.33%) that were conducted in two to six centers.

Spatiotemporal distribution of *A. baumannii* in human and non–human reservoirs in Nigeria

A total of 24 published articles were recorded between 2013 and 2021, with the year of studies ranging from 2011 to 2021. Six published articles on *A. baumannii* were recorded between 2013 and 2016. Fourteen published articles were observed between 2017 and 2020, an indication of an increase in publication drive. However, in 2021, there were four published articles on *A. baumannii* recorded (Table 1 & Table 2). As a result, human-to-human, animal-to-animal, food-to-food, and environment-to-food transmission mechanisms are now being debated. To tackle this public health issue, a thorough understanding of the current state of resistance development and epidemiology of this organism in clinical and non-human sources is required.

The situation in humans

Several clinical samples, such as urine, wound smears, blood, and sputum, have been reported to harbor MDR *A. baumannii* in Nigeria during the usual clinical surveillance studies for *A. baumannii*. Notably, the first report of *A. baumannii* in the clinical setting was dated back to 2002 by Iregbu et al. (2002), who reported 50 *A. baumannii* isolates from Lagos University Teaching Hospital (LUTH). All reported isolates were beta-lactamases producers and MDR. Then a total of 19 articles reported MDR *A. baumannii* from different geopolitical zones in Nigeria except for North-central within the last decade. Interestingly, from 19 published articles reviewed in this study, seven (37%) discussed Hospital-Acquired (HA), and Community-Acquired (CA) infections, four (21%) dealt with CA infections only, seven (37%) discussed HA infections only, and one (5%) article was devoided of any information about the case of the study (Table 1). These publications documented 8.4% (418/4950) of clinical *A. baumannii* isolates in random samples. Nine

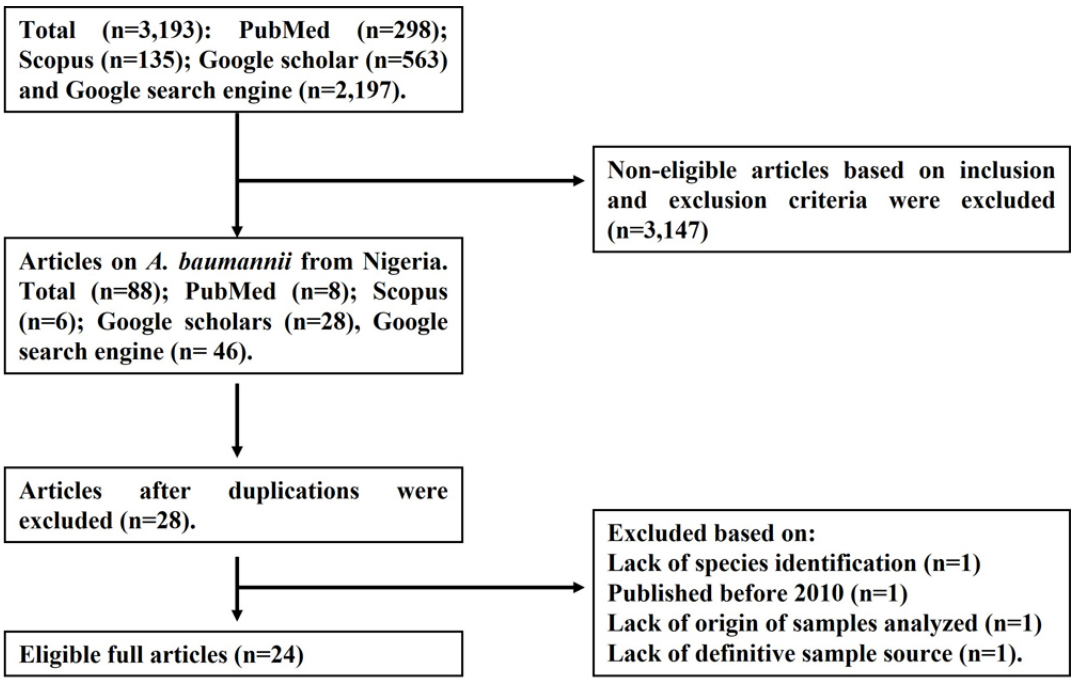

Figure 1: Flow chart of the systematic literature review of research on *A. baumannii* isolated in Nigeria.

papers (47.36%) reported phenotypic MDR *A. baumannii* without resistance genes characterization from three [South-West, North-West, and South-East) of the six geopolitical zones of Nigeria. Noteworthily, the 19 articles reported MDR of *A. baumannii* for most commonly used antibiotics such as TET: Tetracycline; SXT: Trimethoprim/Sulfamethoxazole; CHL: Chloramphenicol; Gen: Gentamycin; AMK: Amikacin; STR: Streptomycin; AMC: Amoxicillin/Clavulanic acid; SU: Sulfamethoxazole; PEN: Penicillin; APX: Ampiclox; CTX: Cefotaxime; CAZ: Ceftazidime; CRX: Cefuroxime; CRO: Ceftriaxone; AMP: Ampicillin; CFX: Ceftriaxone; and AMS: Ampicillin/Sulbactam; and growing emerging resistance to IMP: Imipenem; MER: Meropenem; CXC: Cloxacillin; AUG: Augmentin; AML: Amoxicillin; CPZ: Cephazolin; AZT: Aztreonam; CPT: Cephalothin; KAN: Kanamycin; and COL: Colistin. Nevertheless, ten (52.63%) articles reported *bla*OXA-51 intrinsic carbapenemases producing genes and *bla*OXA-23 acquired resistant genes. Most of the articles reported several other resistant makers also, including *bla*KPC, *bla*NDM, *bla*VIM, *bla*IMP, *bla*TEM, *bla*CTX-M, and *bla*SHV (Figure 3). Notably, most (60%) of these articles were from South-west Nigeria and published between 2018 and 2021. One article each (5%) described research/work from North-west, North-east, South-south, and an unspecified state/zone and was published in 2021, 2019, 2019, and 2020, respectively (Table 1 & Figure 2).

The situation in the environment and animal sources

A. baumannii can be found in soil, vegetables, wastewater, and on environmental surfaces. Four articles were published between 2015 and 2021 and reported 80 isolates from 498 samples giving an occurrence of 16.06%, while one article reported 10.42% (5780) *A. baumannii* from animal samples. The only published article on animal sources was conducted on fecal wild bird droppings collected in the vicinity of two irrigation farms (the Sharada Canal Wastewater Irrigation farm and Jakara Waste Canal Irrigation farm) in Kano North-West Dahiru and Enabulele (2015). These occurrences were recorded from randomly sampled studies on environmental and animal sources. Interestingly, the five MDR strains isolated out of 48 samples were resistant to first-generation cephalosporins and four to streptomycin. Notably, two (50%) of the four published articles on environmental sources reported the presence of resistant genes in *A. baumannii* strains from the soil, lake, and drinking water.

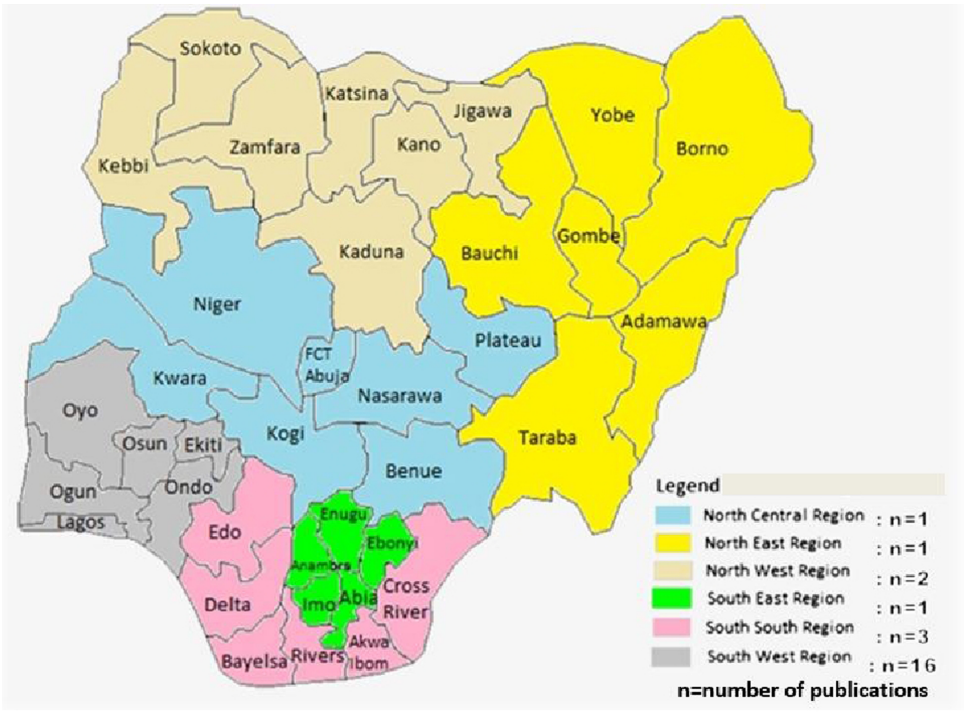

Figure 2: Map showing the distribution of published articles on *A. baumannii* from the geopolitical zones in Nigeria from 2010-2021.

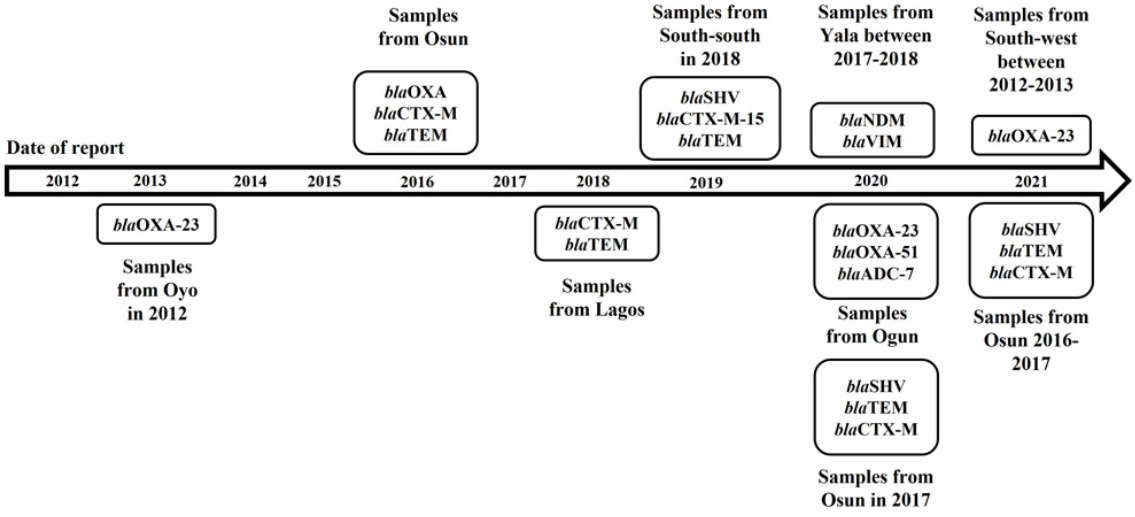

Figure 3: Chronological emergence of the number of genes coding for AMR in *A. baumannii* in Nigeria (2012–2021).

Table 1: Distribution of MDR clinical *A. baumannii* strains in Nigeria as reported in literature published within the last decade (2011-2021).

Study case	Patient age (years)	Origin of isolates	Sample size	No. of isolates	Time Month/Year	State/zones	Method of detection	AMR profile	Resistant genes	Reference
CA	ND	Wound swab	50	10	ND	Lagos [SW]	Microbact 12A and B system	ND	ND	Ilomuanya et al. (2022)
HA	≥6	Sputum	90	6	June–August 2018	Kaduna [NW]	Microgen	ID ERY, TET, SXT, AMC, STR, AML	OXA-51, TEM, and ermB	Oyegoke et al. (2021)
HA, CA	ND	Urine, wound, and blood	107	72	Jan.2012–May.2013	Ekiti, Lagos, Ogun, Condo, Osun, and Oyo [SW]	PCR	AMP, AZT, CAZ, CFX, GEN	OXA – 51, intl-1, VIM, IMP	Ike et al. (2020)
HA, CA	ND	Wound biopsy and blood	87	26	Jan–Dec 2016	Oyo [SW]	Vitek 2 system	LEV, CRX, CAZ, AMK, CFX	ND	Dada-Adegbola et al. (2020)
ND	NA	Clinical sample not specified	ND	21	ND	ND	WGS	ESBL	NDM-1, OXA-51, OXA-23	Ogbolu et al. (2020)
CA	≥16	Urine	175	1	Jul.–Dec.2017	Osun [SW]	Multiplex PCR	CTX, CAZ, CRO, AMC, PEN, AMP, STR, TET, F, CHL, ERY	SHV, TEM, CTX – M	Bebe et al. (2020)
HA	ND	Wound swabs	140	18	Nov.2018-Mar.2019	Ogun [SW]	PCR	TET, ERY, MER, CRX, AUG, GEN, CAZ	OXA- 51	Fasuyi et al. (2020)
HA	ND	Urine, blood, and wound swabs	72	69	Apr.2011–May.2013	Ekiti, Lagos, Ogun, Condo, Osun and Oyo [SW]	PCR, 16SrRNASequencing	MER, IMP, AML, AMC, AMP, CPD, CAZ, CFX, CRX, CXC, CPZ, ERY, AZTCPT, KAN, CHL, NIT, OFX, COL	OXA-51, OXA-23, ADC-7	Ike et al. (2020)
HA	≥18	Wound swab, urine catheter, nasal specimen	401	9	Jul.–Dec.2016	Kano [NW]	PCR, Sequencing	AMS, PEF, CIP, AMK	ND	Alkali et al. (2019)
HA	≥16	Urine	660	20	Jul.–Dec.2018	Akwa-Ibom [SS]	PCR	ESBL	SHV, TEM, CTX-M	Uyanga et al. (2019)
CA	ND	Urine, wound, sputum, stool, ear swab, genital specimens, pleural aspirates	1741	16	Nov.2017–Feb.2018	Adamawa [NE]	RT-PCR	AmpC, ESBL	*bla*KPC, *bla*NDM, *bla*VIM, *bla*IMP, and *bla*OXA-48)	Shettima et al. (2020)
CA, CR	25	Blood, sputum, urine, wound biopsy	4	3	Jul.–Dec.2018	Kaduna [NW]	Microbact GNB/24E, 16S rRNA sequences	GEN, CIP, CAZ, CPM, PIP/TAZ, MER	ND	Jimoh et al. (2018)
HA, CA	≥20	Urine	181	1	Apr.2014 & Sep.2015	Ondo [SW]	Conventional method	COT, TET	ND	Oluwafemi et al. (2018)
HA, CA	ND	Wound Swab	142	5	Oct.2016–Mar.2017	Oyo, Ogun [SW]	API 20 E and API 20 NE	GEN, NET, OFX, CHL	ND	Bello et al. (2018)
HA, CA	ND	Wound swab, blood, urine, vagina secretion, sputum	ND	42	ND	Imo state [SE]	Conventional method A	MS, PIP/TAZ, CAZ, CPM, CTX, CFX, IMP, GEN, TOB, AMK, CIP, LEV, SXT	ND	Nsofor and Anyanwu (2015)
HA-ICU	≥1->70	Blood, urine, sputum, wound swab, CSR	150	11	ND	Osun [SW]	API 20NE, PCR	CIP, AMK, CEF, CAZ, AMP, MER, GEN, PIP	OXA, CTX-M, TEM, and SHV	Odewale et al. (2016)
HA-ICU	2-95	Tracheal aspirate, catheter urine, wound biopsies, blood	400	11	Jan.-Sept.2011	Ibadan [SW]	Microbat 20E	AMC, GEN, CIP, CEF, OFX, AMS	ND	Nwadike et al. (2013)
HA, CA	ND	Clinical	550	72	Apr.2011–May.2013	Ekiti, Lagos, Ogun, Condo, Osun, and Oyo [SW]	Microbat 20E	AML, AMC, AMP, CPD, CAZ, CEF, CRX, CXC	ND	Ike et al. (2014)
HA, CA	ND	Clinical	ND	5	March-May 2012	Oyo [SW]	MALDI-TOF, RT-PCR	IMP	OXA-23, OXA-58, OXA-143, OXA-51-like	Olaitan et al. (2013)
	Total		4950	418						

Keys: ND: Not determined; CA: Community-Acquired; HA: Hospital-Acquired, ICU: Intensive Care Unit; CR: Case Report; CIP: Ciprofloxacin; TET: Tetracycline; SXT: Trimethoprim/Sulfamethoxazole; CHL: Chloramphenicol; Gen: Gentamycin; AMK: Amikacin; FF: Florfenicol; STR: Streptomycin; AMC: Amoxicillin/Clavulanic acid; CEF: Ceftiofur; SU: Sulfamethoxazole; PEN: Penicillin; APX: Ampiclox; NAL: Nalidixic acid; PEF: Pefloxacin; CEP: Ceporex; OFX: Ofloxacin; NIT: Nitrofurantoin; CTX: Cefotaxime; CAZ: Ceftazidime; CRO: Ceftriaxone; AMP: Ampicillin; ERY: Erythromycin; CFX: Ceftriaxone; AMS: Ampicillin/Sulbactam; IMP: Imipenem; MER: Meropenem; PIP: Piperacillin; CPD: Cefpodoxime; CRX: Cefuroxime; CXC: Cloxacillin; AUG: Augmentin; AML: Amoxicillin; CPZ: Cephazolin; AZT: Aztreonam; CPT: Cephalothin; KAN: Kanamycin; COL: Colistin; LEV: Levofloxacin; ESBL: Extended Spectrum Beta lactamases. SW: South West; SE: Southeast; NE: North East; NW: North West; SS: South-South, Microbat 20E: Biochemical Identification kits 20E (Oxoid, United Kingdom).

Table 2: Distribution of MDR clinical *A. baumannii* strains in Nigeria as reported in literature published within the last decade (2011-2021).

Source	No. of samples	No. of isolates	Year of sampling	State/zones	Detection method	AMR profile	Genes detected	Reference
Hospital surfaces swabs	220	1	Sept.2011–Jul.2012	Lagos [SW]	Vitek 2 system	ND	ND	Agbalaya et al. (2021)
Soil and lake water	122	3	ND	Oyo [SW], Anambra [SE], Akwa-Ibom [SS], Abuja [NC], Adamawa [NE] and Kana [NW]	PCR	CIP, TET, SXT, CHL, GEN, AMK	*bla*OXA-23, *bla*OXA–40	Le Terrier et al. (2020)
Drinking water	96	4	Dec.2010–Jul.2011	Osun, Oyo, and Ondo [SW]	16SrRNA Sequencing	FF, CHL, SXT AMC, CEF, SU	floR	Adesoji and Call (2020)
Hospital wastewater	60	72	Jan.–Mar.2014	Edo [SS]	Convent. Method.	PEN, GEN, APX, AMC, NAL, CHL, PEF	ND	Igbinosa and Beshiru (2017)
Bird feces	48	5	ND	Kano [NW]	Microbat 20E	STR, SXT, AMP, CEP, OFX, NAL, PEF, GEN, AMC, CPX, STX	ND	Dahiru and Enabulele (2015)

Keys: CIP: Ciprofloxacin; TET: Tetracycline; SXT: Trimethoprim/Sulfamethoxazole; CHL: Chloramphenicol; Gen: Gentamycin; AMK: Amikacin; FF: Florfenicol; STR: Streptomycin; AMC: Amoxicillin/Clavulanic acid; CEF: Ceftiofur; SU: Sulfamethoxazole; PEN: Penicillin; APX: Ampiclox; NAL: Nalidixic acid; PEF: Pefloxacin; CEP: Ceporex; OFX: Ofloxacin; NIT: Nitrofurantoin; CTX: Cefotaxime; CAZ: Ceftazidime; CRO: Ceftriaxone; AMP: Ampicillin; TET: Tetracycline; ERY: Erythromycin; CFX: Ceftriaxone; AMS: Ampicillin/Sulbactam; IMP: Imipenem; MER: Meropenem; PIP: Piperacillin; CPD: Cefpodoxime; CRX: Cefuroxime; CXC: Cloxacillin; AUG: Augmentin; AML: Amoxicillin; CPZ: Cephazolin; AZT: Aztreonam; CPT: Cephalothin; KAN: Kanamycin; COL: Colistin; LEV: Levofloxacin; NR: Not reported; ND: Not determined; ESBL: Extended Spectrum Beta lactamases. Vitek 2 system; Convent. Method. Conventional biochemical routine test.

Le Terrier et al. (2020) reported *bla*OXA-23 and *bla*OXA-40 in three *A. baumannii* isolates recovered from 122 samples (water obtained from lakes and soil sampled from landfills) collected in 2017 from six different locations, i.e., Abuja (North Central), Kano (North West), Yola (North East), Nnewi (South East), Akwa Ibom (South) and Ibadan (South West). Also, Adesoji and Call (2020) reported resistant genes (*FloR*) in 96 drinking water samples from Osun, Oyo, and Ondo in a study conducted between December 2010 and January 2011 using 16SrRNA sequencing for species diagnostics.

Trends of antibiotic resistance in *A. baumannii*

Twenty-three commonly used antibiotics were reported by 95.8% (23/24) of published articles reviewed within the study periods (2010-2021). However, between 2014 and 2021, a fluctuation in the trend of most antibiotics' resistance reported in *A. baumannii* was observed (Figure 4). Interestingly, *A. baumannii* resistance to tetracycline had steadily increased from 91.7% in 2014 to 93.4 in 2017 and 100% from 2018 to 2021. Also, resistance to piperacillin/tazobactam had maintained reduced susceptibility from 80.8% in 2016 to 100% in 2018 through 2019. Furthermore, there is a noticeable steady increase in the trend of *A. baumannii* resistance to imipenem from 56.7% in 2014 to 100% in 2021 (Figure 4).

Discussion

One Health is a concept that acknowledges the connections between the well-being of people, animals, and the environment in which they live. It uses a cooperative, multi-sectoral, and transdisciplinary strategy at the local, regional, national, and international levels to improve health systems and outcomes (Ihekweazu et al., 2021). *A. baumannii* had been isolated from human, animal, and environmental sources. The current study reported the first systematic review of the occurrence of *A. baumannii* in Nigeria.

A total of 24 eligible publications reported *A. baumannii* isolates in clinical, environmental, and animal samples from 14 of 36 states, including Federal Capital Territory (FCT) Abuja. The lack of data from the other 22 states reflects the lack of culture-based studies and poor infrastructure to undertake cultural and molecular identification of *A. baumannii* strains. Also, the challenging differentiation of *A. baumannii* from *A. baumannii-A. calcoaceticus* complex or ABC complex, and the lack of researchers' interest in *A. baumannii* play a significant role in the paucity of information. This study recorded 418, 80, and 5 strains of *A. baumannii* of human, environmental, and animal origin.

Occurrences of 8.4%, 16.06%, and 10.42% of culture-proven *A. baumannii* clinical, environmental, and animal samples collections were clearly showed that *A. baumannii* infections and colonization are public health issues. The studies on humans were done purposefully to determine the occurrence of *A. baumannii* in clinical settings, while samples from animals and the environment were randomly collected. An occurrence of 8.4% in clinical samples may indicate poor prevention and control is inadequate. Healthcare facilities, the lack of a surveillance strategy for epidemiological control, inadequate sewage treatment/disposal systems, and various other associated risk factors had been previously identified by (Odewale et al., 2016). Studies from sub-national investigations in other African countries found considerably varying occurrences of clinical *A. baumannii* infections in their patients. 8.4% occurrence was recorded in Ethiopia from nosocomial infections in a cross-sectional study (Motbainor et al., 2020), 0.54% was recorded by Moyo et al. (2021) in Tanzania (both west Africa), 5.64% in Morocco by Uwingabiye et al. (2016), and in Egypt 3.8% according to Abd El-Baky et al. (2020). This occurrence variation might be connected to the sampling plan, sample sources, study type, or detection methods.

Also, other species of ABC complex were reported in 16.67% (4/24) of published articles between 2014 and 2020 from clinical studies along with *A. baumannii*. These species include *A. iwoffi* (n=22), *A. haemolyticus* (n=20), and *A. calcoaceticus* (n=1). Thus, four ABC species are currently causing community-acquired and nosocomial infections in Nigeria. The majority of studies were single-center studies. This is an important consideration as this reflects the clonal diversity of the *A. baumannii* isolates available for each study.

Interestingly, 75% of the reports were conducted in the Oyo state of South-west Nigeria. In the North-east, North-central (excluding the FCT), and South-east, there was a general lack of published articles and a very low occurrence of clinical *A. baumannii*. These are most likely linked to the security concerns and crises that have plagued those regions over the previous decade, despite international humanitarian support/interventions. There is supposed variability in the spatial distribution/ occurrence of *A. baumannii* across the states/zones if a sample summation of reported clinical data is done. For instance, South-west (SW) recorded the highest occurrence of clinical *A. baumannii*, 14.65% (301/2054), based on data from 12 scientific publications, the zone with the highest number of publications.

In North-west, three scientific articles calculated an occurrence at 3.64% (18/495). The least occurrence of 0.92% (16/1741) was derived from a single scientific publication. Considering environmental and animal studies, no trends can be described due to the lack of data. The need for further research is obvious. No conclusion should be drawn at that time. In this review, 21.1% (4/19) of articles reported *A. baumannii* infections across all age groups, independent of gender. However, age (>49) years and male gender were associated with *A. baumannii* infections (Nwadike et al., 2013; Odewale et al., 2016; Bello et al., 2018; Alkali et al., 2019). Furthermore, sickle cell anemia (Bebe et al., 2020), Intensive Care Unit (ICU) stay (Odewale et al., 2016), and a diabetic ulcer (Bello et al., 2018), among others, are considered predisposing factors. Older people have been reported to be more prone to *A. baumannii* infections due to decline in immu-

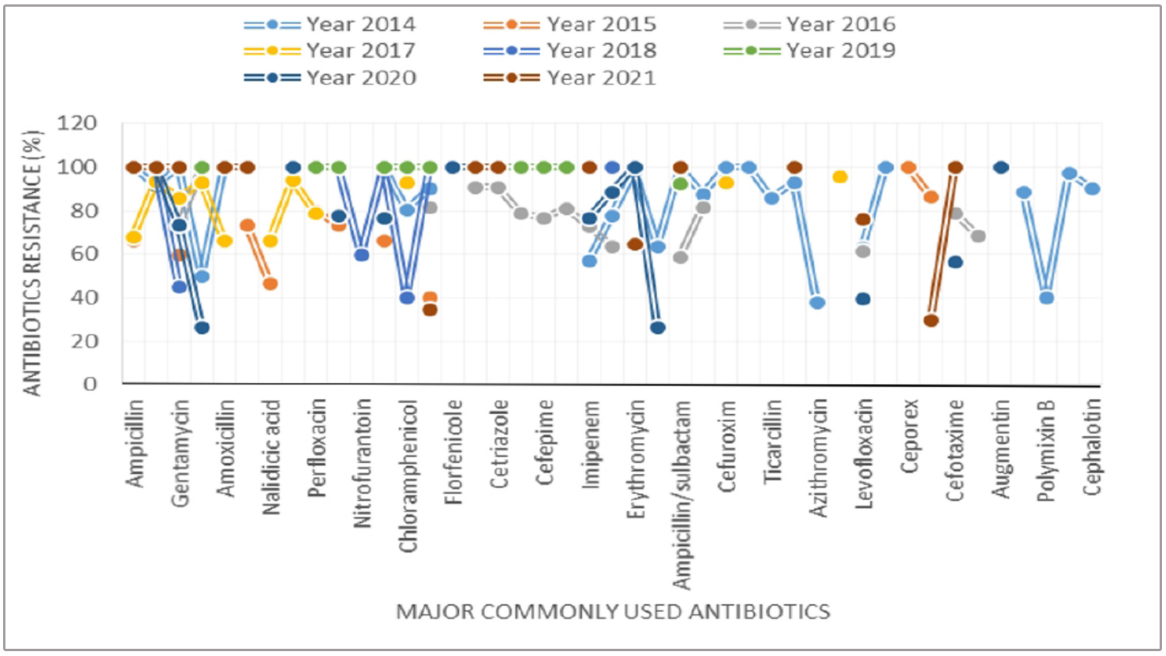

Figure 4: Trend of antibiotics resistance in *A. baumannii* reported in published articles (2014-2021).

nity (Odewale et al., 2016). Also, the isolation of *A. baumannii* strains from males has been traced to the constant shifting of job locations due to job placement which usually makes them exposed to accidental and occupational traumas (Odewale et al., 2016).

Antimicrobial resistance or genes of AMR in *A. baumannii* were reported by 96% (23/24) of articles. More than 90% of *A. baumannii* isolates resisted one or more of the 39 antibiotics tested, especially first-line empirical antibiotics. In addition, meropenem and imipenem resistance in *A. baumannii* were recorded in 54 and 40 isolates from 72 samples (Ike et al., 2020). Infections caused by MDR (=more than 3 classes) *A. baumannii* strains are more severe than those caused by susceptible strains (Jimoh et al., 2018). In Nigeria, efficacies of the first-line empirical antibiotics such as tetracycline, ampicillin, cotrimoxazole, chloramphenicol, amoxicillin, and penicillin against *A. baumannii* are associated with infections that have an unfavorable outcome/prognosis due to loss of efficacy (Alkali et al., 2019; Ike et al., 2021).

This carbapenem resistance is likely due to the widespread replacement of traditional first-line antibiotics with carbapenem. Now carbapenem-resistant *A. baumannii* (CRAB) strains are an emerging public health threat in Nigeria (Ike et al., 2020) and some other African countries such as Morocco (Uwingabiye et al., 2016), Ethiopia (Pritsch et al., 2017), South Africa (Lowe et al., 2018), and Egypt (Abouelfetouh et al., 2022). In this study, *A. baumannii* isolates also had resistance to ceftazidime, cefotaxime, and cefuroxime, indicating that other antibiotics that were used to treat *A. baumannii* infections are becoming less effective. For the time being, in Nigeria and other developing countries where selective pressure on these antibiotics is high, the total suspension of ampicillin, tetracycline, chloramphenicol, and cotrimoxazole in treating bacteria-associated infections is recommended (Akinyemi et al., 2018).

This systematic review revealed the lack of aggregated national data on the epidemiology of *A. baumannii* infection. Research is needed at the state and federal levels to assess Nigeria's genuine burden of *A. baumannii*-associated infections in humans and animals and to assist healthcare policymakers and stakeholders. The wide range of resistance genes found i.e. *bla*OXA-23, *bla*OXA-48, *bla*OXA-58-like, *bla*OXA-143, and the intrinsic *bla*OXA-51-like, most recently discovered *bla*NDM-1 and *intl*-1, *bla*SHV, *bla*TEM, *bla*CTX-M, *bla*ADC, *bla*IMP and *bla*VIM from Nigeria in *A. baumannii* strains within the last decade is alarming. Of these, *bla*OXA-51 and *bla*OXA-23 were the most reported.

In this systematic review, the commonly used assays to investigate *A. baumannii* were conventional PCR, WGS, multiplex-PCR, 16S rRNA Sequencing, MALDI-TOF, and RT-PCR. Indeed, the intrinsic/species-specific OXA-51-like gene can be used as a simple and reliable way to identify *A. baumannii* in a resource-poor setting like Nigeria (Voets et al., 2011; Ghaith et al., 2017; Lowe et al., 2018). The high occurrence of *bla*OXA-23-like genes is an assumed result of hygiene practices in Nigeria which results in advanced resistance towards carbapenems such as imipenem and meropenem. Hence, these findings with other studies from South Africa (Lowe et al., 2018), India (Vijayakumar et al., 2019), China (Lee et al., 2017), Northern Africa, and the Middle East (Higgins et al., 2021). The *bla*NDM-1 was found primarily in *E. coli* and *K. pneumoniae* but not predominant in *Pseudomonas* and *Acinetobacter* in the past. In Nigeria, the first published report of an *A. baumannii* strain with *bla*NDM-

1 was not before 2021, in contrast to Germany, where it was reported in 2007 (Göttig et al., 2010; Wareth et al., 2020). In the past, international travel of colonized patients, particularly from high-occurrence areas such as the Mediterranean and Asian countries, has resulted in the introduction and later spread of MDR *A. baumannii* to Europe and worldwide (Wisplinghoff et al., 2008; Higgins et al., 2010; Jones et al., 2015).

AMR gene detection and characterization have progressed from PCR technology to whole genome sequencing (WGS) and in-silico detection using a variety of databases (Wareth et al., 2021a). The selective power of NGS allows for transmission-chain analysis (the ability to track the route source of infectious agents based on the application of WGS, metagenomics, and other bioinformatics applications), improved surveillance, and choice of appropriate containment measures (Wareth et al., 2021a). It also can be used to spot transmission dynamics (Eigenbrod et al., 2019). However, only one study has used WGS technology in Nigeria so far (Ogbolu et al., 2020). Hence, till now, the majority of WGS-based *A. baumannii* investigations were conducted in outbreak situations, and there is little experience on how to use WGS in surveillance settings in developing countries (Leistner et al., 2015; Willems et al., 2016; Wendel et al., 2018). The high transmissibility and fast acquisition of resistance genes from other bacteria genera urge Nigeria to establish an epidemiological surveillance structure to combat the spread of MDR *A. baumannii*. WGS-based surveillance should be implemented in Nigeria as the best tool for epidemiologists, public health officers, and physicians. In hospital settings, it will help to contain outbreaks and initiate treatment with the right drug at the right time.

Conclusion

Clinical multidrug-resistant *A. baumannii* isolates seriously threaten public health and contribute significantly to high global mortality. In Nigeria, data on the general distribution and antibiotic resistance of *A. baumannii* in animals, food, and the environment is lacking. It is urged that screening and hygiene practices be put in place right away in the Nigerian setting to stop the transmission and spread of *A. baumannii* because it can survive in the environment for extended periods and easily acquire resistance genes.

Despite the fact that carbapenems are efficient medicines for treating *A. baumannii* infections, the number of carbapenem-resistant isolates has been steadily growing in humans and the environment. Several pathways conferring carbapenem resistance in *A. baumannii* have been discovered in clinical samples with poor associating risk factors. Therefore, it is pertinent to establish NGS-based molecular epidemiology at hospitals to combat the spread of and guarantee well-timed on the set of appropriate treatment of infections caused by MDR, XRD, and PDR *A. baumannii* at the current emerging time with trend. The lack of data for the epidemiologic status/situation of *A. baumannii* occurrence and disease burden must be tackled immediately. A spread via the environment or the food production chain must be eliminated if possible.

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References

Abd El-Baky, R.M., Farhan, S.M., Ibrahim, R.A., Mahran, K.M., Hetta, H.F., 2020. Antimicrobial resistance pattern and molecular epidemiology of ESBL and MBL producing *Acinetobacter baumannii* isolated from hospitals in Minia, Egypt. Alexandria Journal of Medicine 56, 4–13. 10.1080/20905068.2019.1707350.

Abouelfetouh, A., Mattock, J., Turner, D., Li, E., Evans, B.A., 2022. Diversity of carbapenem-resistant *Acinetobacter baumannii* and bacteriophage-mediated spread of the Oxa23 carbapenemase. Microbial Genomics 8. 10.1099/mgen.0.000752.

Adesoji, A.T., Call, D.R., 2020. Molecular analysis of florfenicol-resistant bacteria isolated from drinking water distribution systems in Southwestern Nigeria. Journal of Global Antimicrobial Resistance 23, 340–344. 10.1016/j.jgar.2020.10.005.

Agbalaya, O.V., Osuagwu, C., Oduyebo, O., 2021. Environmental reservoirs of healthcare associated infections in the neonatal wards of a university teaching hospital in Lagos, Nigeria. Medical Microbiology & Diagnosis 10, 1–5.

Akinyemi, K.O., Oyefolu, A.O.B., Mutiu, W.B., Iwalokun, B.A., Ayeni, E.S., Ajose, S.O., Obaro, S.K., 2018. Typhoid fever: Tracking the trend in Nigeria. The American Journal of Tropical Medicine and Hygiene 99, 41–47. 10.4269/ajtmh.18-0045.

Al Bayssari, C., Dabboussi, F., Hamze, M., Rolain, J.M., 2015. Emergence of carbapenemase-producing pseudomonas aeruginosa and *Acinetobacter baumannii* in livestock animals in Lebanon. The Journal of Antimicrobial Chemotherapy 70, 950–951. 10.1093/jac/dku469.

Alkali, B., Aliero, A.A., Idris, A.M., Takalmawa, H.U., Faruk, S., Ezera, A., 2019. Molecular characterization of *Acinetobacter baumannii* from patients with prolonged hospital stays in three tertiary hospitals of Kano Metropolis, Northwestern Nigeria. African Journal of Microbiology Research URL: https://academicjournals.org/journal/AJMR/article-abstract/3D4402A61948.

Askari, N., Momtaz, H., Tajbakhsh, E., 2020. Prevalence and phenotypic pattern of antibiotic resistance of *Acinetobacter baumannii* isolated from different types of raw meat samples in isfahan, Iran. Veterinary Medicine and Science 6, 147–153. 10.1002/vms3.199.

Bebe, T., Odetoyin, B., Bolarinwa, R., 2020. Occurrence of multidrug-resistant uropathogens implicated in asymptomatic bacteriuria in adults with sickle cell disease in ile-ife, Southwest Nigeria. Oman Medical Journal 35, e109. 10.5001/omj.2020.27.

Bello, O.O., Oyekanmi, E.O., Kelly, B.A., Mebude, O.O., Bello, T.K., 2018. Antibiotic susceptibility profiles of bacteria from diabetic foot infections in selected teaching hospitals in Southwestern Nigeria. International Annals of Science 4, 1–13. 10.21467/ias.4.1.1-13.

Cho, G.S., Li, B., Rostalsky, A., Fiedler, G., Rösch, N., Igbinosa, E., Kabisch, J., Bockelmann, W., Hammer, P., Huys, G., Franz, C.M.A.P., 2018. Diversity and antibiotic susceptibility of *Acinetobacter* strains from milk powder produced in Germany. Frontiers in Microbiology 9, 536. 10.3389/fmicb.2018.00536.

Dada-Adegbola, H., Brown, B., Sanusi, A., 2020. Antibiotic susceptibility pattern of acinetobacter species isolated in clinical specimens from the university college hospital, Ibadan, Nigeria. African Journal of Health Sciences URL: https://www.ajol.info/index.php/ajhs/article/view/206244.

Dahiru, M., Enabulele, O.I., 2015. *Acinetobacter baumannii* in birds feces: A public health threat to vegetables and irrigation farmers. Advances in Microbiology 05, 693–698. 10.4236/aim.2015.510072.

Dijkshoorn, L., Nemec, A., Seifert, H., 2007. An increasing threat in hospitals: Multidrug-resistant *Acinetobacter baumannii*. Nature Reviews. Microbiology 5, 939–951. 10.1038/nrmicro1789.

Eigenbrod, T., Reuter, S., Gross, A., Kocer, K., Günther, F., Zimmermann, S., Heeg, K., Mutters, N.T., Nurjadi, D., 2019. Molecular characterization of carbapenem-resistant *Acinetobacter baumannii* using WGS revealed missed transmission events in Germany from 2012-15. The Journal of Antimicrobial Chemotherapy 74, 3473–3480. 10.1093/jac/dkz360.

Fasuyi, O., Ike, W., Ojo, D., Adeboye, A., 2020. Plasmid profile of multidrug resistant *Acinetobacter baumannii* strains from wounds of patients attending federal medical centre, Abeokuta, Southwest, Nigeria. Nigerian Journal of Pharmaceutical and Applied Science Research 9, 47–51.

Ghaith, D.M., Zafer, M.M., Al-Agamy, M.H., Alyamani, E.J., Booq, R.Y., Almoazzamy, O., 2017. The emergence of a novel sequence type of MDR *Acinetobacter baumannii* from the intensive care unit of an Egyptian tertiary care hospital. Annals of Clinical Microbiology and Antimicrobials 16, 34. 10.1186/s12941-017-0208-y.

Göttig, S., Pfeifer, Y., Wichelhaus, T.A., Zacharowski, K., Bingold, T., Averhoff, B., Brandt, C., Kempf, V.A., 2010. Global spread of New Delhi metallo-β-lactamase 1. The Lancet Infectious Diseases 10, 828–829. 10.1016/S1473-3099(10)70275-9.

Hamouda, A., Findlay, J., Al Hassan, L., Amyes, S.G.B., 2011. Epidemiology of *Acinetobacter baumannii* of animal origin. International Journal of Antimicrobial Agents 38, 314–318. 10.1016/j.ijantimicag.2011.06.007.

Higgins, P.G., Dammhayn, C., Hackel, M., Seifert, H., 2010. Global spread of carbapenem-resistant *Acinetobacter baumannii*. The Journal of Antimicrobial Chemotherapy 65, 233–238. 10.1093/jac/dkp428.

Higgins, P.G., Hagen, R.M., Kreikemeyer, B., Warnke, P., Podbielski, A., Frickmann, H., Loderstädt, U., 2021. Molecular epidemiology of carbapenem-resistant *Acinetobacter baumannii* isolates from Northern Africa and the Middle East. Antibiotics 10. 10.3390/antibiotics10030291.

Holt, K., Kenyon, J., Hamidian, M., Schultz, M., Pickard, D., Dougan, G., Hall, R., 2016. Five decades of genome evolution in the globally distributed, extensively antibiotic-resistant *Acinetobacter baumannii* global clone 1. Microbial Genomics 2, e000052. 10.1099/mgen.0.000052.

Hrenovic, J., Seruga Music, M., Durn, G., Dekic, S., Hunjak, B., Kisic, I., 2019. Carbapenem-resistant *Acinetobacter baumannii* recovered from swine manure. Microbial Drug Resistance 25, 725–730. URL: http://dx.doi.org/10.1089/mdr.2018.0087, 10.1089/mdr.2018.0087.

Huang, Z.Y., Li, J., Shui, J., Wang, H.C., Hu, Y.M., Zou, M.X., 2019. Co-existence of *bla*oxa-23 and *bla*vim in carbapenem-resistant *Acinetobacter baumannii* isolates belonging to global complex 2 in a chinese teaching hospital. Chinese Medical Journal 132, 1166–1172. 10.1097/CM9.0000000000000193.

Igbinosa, E., Beshiru, A., 2017. Characterization and identification of antibiotic-resistant *Acinetobacter baumannii* from hospital waste waters. Nigerian Journal of Microbiology .

Ihekweazu, C., Michael, C.A., Nguku, P.M., Waziri, N.E., Habib, A.G., Muturi, M., Olufemi, A., Dzikwi-Emennaa, A.A., Balogun, M.S., Visa, T.I., Dalhat, M.M., Atama, N.C., Umeokonkwo, C.D., Mshelbwala, G.M., Vakuru, C.T., Kabir, J., Okolocha, E.C., Umoh, J.U., Olugasa, B., Babalobi, O., Lombin, L., Cadmus, S., Group, N.Z.D.P., 2021. Prioritization of zoonotic diseases of public health significance in nigeria using the one-health approach. One Health 13, 100257. 10.1016/j.onehlt.2021.100257.

Ike, W., Adeniyi, B., Peters, J., 2020. Molecular basis of carbapenem-resistant *Acinetobacter baumannii* from Southwest, Nigeria. Nigerian Journal of Pharmaceutical Sciences URL: https://nijophasr.net/index.php/nijophasr/article/view/340.

Ike, W., Adeniyi, B., Peters, J., 2021. Class 1 integrons and associated gene cassettes in multidrug resistant *Acinetobacter baumannii* from Southwest Nigeria: A tertiary-hospitals study. Nigerian Journal of Pharmaceutical Sciences URL: https://nijophasr.net/index.php/nijophasr/article/view/422.

Ike, W.E., Adeniyi, B.A., Soge, O.O., 2014. Prevalence of multidrug-resistant *Acinetobacter baumannii* in eight tertiary hospitals in Southwestern Nigeria. New York Science Journal 7, 86–93. URL: http://www.sciencepub.net/newyork.

Ilomuanya, M.O., Enwuru, N.V., Adenokun, E., Fatunmbi, A., Adeluola, A., Igwilo, C.I., 2022. Chitosan-based microparticle encapsulated *Acinetobacter baumannii* phage cocktail in hydrogel matrix for the management of multidrug resistant chronic wound infection. Turkish Journal of Pharmaceutical Sciences 19, 187–195. 10.4274/tjps.galenos.2021.72547.

Iregbu, K.C., Ogunsola, F.T., Odugbemi, T.O., 2002. Infections caused by *Acinetobacter* species and their susceptibility to 14 antibiotics in Lagos University Teaching Hospital, Lagos. West African Journal of Medicine 21, 226–229. 10.4314/wajm.v21i3.28036.

Jimoh, O., Ejembi, J., Aliyu, S., Abubakar, M., Ibrahim, M., Olayinka, A., 2018. Postburns sepsis caused by multidrug-resistant *Acinetobacter baumannii*. Annals of Tropical Pathology 9, 172. 10.4103/atp.atp_18_18.

Jones, C.L., Clancy, M., Honnold, C., Singh, S., Snesrud, E., Onmus-Leone, F., McGann, P., Ong, A.C., Kwak, Y., Waterman, P., Zurawski, D.V., Clifford, R.J., Lesho, E., 2015. Fatal outbreak of an emerging clone of extensively drug-resistant *Acinetobacter baumannii* with enhanced virulence. Clinical Infectious Diseases 61, 145–154. 10.1093/cid/civ225.

Kanaan, Ghaffoori, M.H., Al-Shadeedi, S.M.J., Al-Massody, A.J., Ghasemian, A., 2020. Drug resistance and virulence traits of *Acinetobacter baumannii* from turkey and chicken raw meat. Comparative Immunology, Microbiology and Infectious Diseases 70, 101451. 10.1016/j.cimid.2020.101451.

Kim, Y.J., Kim, S.I., Hong, K.W., Kim, Y.R., Park, Y.J., Kang, M.W., 2012. Risk factors for mortality in patients with carbapenem-resistant *Acinetobacter baumannii* bacteremia: Impact of appropriate antimicrobial therapy. Journal of Korean Medical Science 27, 471–475. 10.3346/jkms.2012.27.5.471.

Klotz, P., Higgins, P.G., Schaubmar, A.R., Failing, K., Leidner, U., Seifert, H., Scheufen, S., Semmler, T., Ewers, C., 2019. Seasonal occurrence and carbapenem susceptibility of bovine *Acinetobacter baumannii* in Germany. Frontiers in Microbiology 10, 272. 10.3389/fmicb.2019.00272.

Le Terrier, C., Masseron, A., Uwaezuoke, N.S., Edwin, C.P., Ekuma, A.E., Olugbeminiyi, F., Shettima, S., Ushie, S., Poirel, L., Nordmann, P., 2020. Wide spread of carbapenemase-producing bacterial isolates in a Nigerian environment. Journal of Global Antimicrobial Resistance 21, 321–323. 10.1016/j.jgar.2019.10.014.

Lee, C.R., Lee, J.H., Park, M., Park, K.S., Bae, I.K., Kim, Y.B., Cha, C.J., Jeong, B.C., Lee, S.H., 2017. Biology of *Acinetobacter baumannii*: Pathogenesis, antibiotic resistance mechanisms, and prospective treatment options. Frontiers in Cellular and Infection Microbiology 7, 55. 10.3389/fcimb.2017.00055.

Lee, H.Y., Chen, C.L., Wu, S.R., Huang, C.W., Chiu, C.H., 2014. Risk factors and outcome analysis of *Acinetobacter baumannii* complex bacteremia in critical patients. Critical Care Medicine 42, 1081–1088. 10.1097/CCM.0000000000000125.

Lee, Y.T., Kuo, S.C., Chiang, M.C., Yang, S.P., Chen, C.P., Chen, T.L., Fung, C.P., 2012. Emergence of carbapenem-resistant non-*baumannii* species of *Acinetobacter* harboring a *bla*oxa-51-like gene that is intrinsic to *A. baumannii*. Antimicrobial Agents and Chemotherapy 56, 1124–1127. 10.1128/AAC.00622-11.

Leistner, R., Denkel, L.A., Gastmeier, P., Werner, G., Layer, F., Pfeifer, Y., 2015. Prevalence of MRSA and gram-negative bacteria with ESBLs and carbapenemases in patients from Northern Africa at a German hospital. The Journal of Antimicrobial Chemotherapy 70, 3161–3164. 10.1093/jac/dkv219.

Lowe, M., Ehlers, M.M., Ismail, F., Peirano, G., Becker, P.J., Pitout, J.D.D., Kock, M.M., 2018. *Acinetobacter baumannii*: Epidemiological and beta-lactamase data from two tertiary academic hospitals in Tshwane, South Africa. Frontiers in Microbiology 9, 1280. 10.3389/fmicb.2018.01280.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L.A., PRISMA-P Group, 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-p) 2015 statement. Systematic Reviews 4, 1. 10.1186/2046-4053-4-1.

Motbainor, H., Bereded, F., Mulu, W., 2020. Multi-drug resistance of blood stream, urinary tract and surgical site nosocomial infections of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* among patients hospitalized at Felegehiwot referral hospital, Northwest Ethiopia: A cross-sectional study. BMC Infectious Diseases 20, 92. 10.1186/s12879-020-4811-8.

Moyo, S.J., Manyahi, J., Hubbard, A.T.M., Byrne, R.L., Masoud, N.S., Aboud, S., Manji, K., Blomberg, B., Langeland, N., Roberts, A.P., 2021. Molecular characterisation of the first new delhi metallo−β-lactamase 1-producing *Acinetobacter baumannii* from Tanzania. Transactions of the Royal Society of Tropical Medicine and Hygiene 115, 1080–1085. 10.1093/trstmh/traa173.

Nocera, F.P., Attili, A.R., De Martino, L., 2021. *Acinetobacter baumannii*: Its clinical significance in human and veterinary medicine. Pathogens 10. 10.3390/pathogens10020127.

Nsofor, C., Anyanwu, N., 2015. High antibiotic resistance pattern observed in bacterial isolates from a tertiary hospital in South East Nigeria. International Journal of Research in Pharmacy and Biosciences .

Nwadike, V., Ojide, C., Kalu, E., 2013. Multidrug resistant *Acinetobacter* infection and their antimicrobial susceptibility pattern in a Nigerian tertiary hospital ICU. African Journal of Infectious Diseases 8, 14–18. 10.4314/ajid.v8i1.4.

Odewale, G., Adefioye, O.J., Ojo, J., Adewumi, F.A., Olowe, O.A., 2016. Multidrug resistance of *Acinetobacter baumannii* in Ladoke Akintola University teaching hospital, Osogbo, Nigeria. European Journal of Microbiology & Immunology 6, 238–243. 10.1556/1886.2015.00018.

Ogbolu, D.O., Alli, O.A.T., Oluremi, A.S., Ogunjimi, Y.T., Ojebode, D.I., Dada, V., Alaka, O.O., Foster-Nyarko, E., Webber, M.A., 2020. Contribution of NDM and OXA-type carbapenemases to carbapenem resistance in clinical *Acinetobacter baumannii* from Nigeria. Infectious Diseases 52, 644–650. 10.1080/23744235.2020.1775881.

Olaitan, A.O., Berrazeg, M., Fagade, O.E., Adelowo, O.O., Alli, J.A., Rolain, J.M., 2013. Emergence of multidrug-resistant *Acinetobacter baumannii* producing OXA-23 carbapenemase, Nigeria. International Journal of Infectious Diseases 17, e469–e470. 10.1016/j.ijid.2012.12.008.

Oluwafemi, T., Akinbodewa, A., Ogunleye, A., Adejumo, O., 2018. Urinary tract infections and antibiotic sensitivity pattern of uropathogens in a tertiary hospital in South West, Nigeria. Sahel Medical Journal 21, 18. 10.4103/1118-8561.232779.

Oyegoke, P.I., Olayinka, B.O., Ehinmidu, J.O., Tytler, B.A., 2021. Molecular characterization of multidrug-resistant bacteria isolated from patients with pneumonia at two hospitals in North-West Nigeria. International Journal of Epidemiologic Research 8, 23–30. 10.34172/ijer.2021.05.

Peleg, A.Y., Seifert, H., Paterson, D.L., 2008. *Acinetobacter baumannii*: Emergence of a successful pathogen. Clinical Microbiology Reviews 21, 538–582. 10.1128/CMR.00058-07.

Pritsch, M., Zeynudin, A., Messerer, M., Baumer, S., Liegl, G., Schubert, S., Löscher, T., Hoelscher, M., Belachew, T., Rachow, A., Wieser, A., 2017. First report on bla_{NDM}-1-producing *Acinetobacter baumannii* in three clinical isolates from Ethiopia. BMC Infectious Diseases 17, 180. 10.1186/s12879-017-2289-9.

Scott, H.M., Acuff, G., Bergeron, G., Bourassa, M.W., Simjee, S., Singer, R.S., 2019. Antimicrobial resistance in a one health context: exploring complexities, seeking solutions, and communicating risks. Annals of the New York Academy of Sciences 1441, 3–7. 10.1111/nyas.14057.

Shettima, S.A., Tickler, I.A., Dela Cruz, C.M., Tenover, F.C., 2020. Characterisation of carbapenem-resistant gram-negative organisms from clinical specimens in Yola, Nigeria. Journal of Global Antimicrobial Resistance 21, 42–45. 10.1016/j.jgar.2019.08.017.

Tavakol, M., Momtaz, H., Mohajeri, P., Shokoohizadeh, L., Tajbakhsh, E., 2018. Genotyping and distribution of putative virulence factors and antibiotic resistance genes of *Acinetobacter baumannii* strains isolated from raw meat. Antimicrobial Resistance and Infection Control 7, 120. 10.1186/s13756-018-0405-2.

Uwingabiye, J., Frikh, M., Lemnouer, A., Bssaibis, F., Belefquih, B., Maleb, A., Dahraoui, S., Belyamani, L., Bait, A., Haimeur, C., Louzi, L., Ibrahimi, A., Elouennass, M., 2016. Acinetobacter infections prevalence and frequency of the antibiotics resistance: Comparative study of intensive care units versus other hospital units. The Pan African Medical Journal 23, 191. 10.11604/pamj.2016.23.191.7915.

Uyanga, F., Ekundayo, E., Nwankwo, E., 2019. Extended spectrum beta-lactamase produced by *Acinetobacter baumanii*, *Enterobacter clocae* and *Proteus mirabilis* from pregnant women in three secondary health care facilities in South-West Nigeria. Journal of Advances in Microbiology 18, 1–9.

Vijayakumar, S., Biswas, I., Veeraraghavan, B., 2019. Accurate identification of clinically important *Acinetobacter* spp.: An update. Future Science 5, FSO395. 10.2144/fsoa-2018-0127.

Voets, G.M., Fluit, A.C., Scharringa, J., Cohen Stuart, J., Leverstein-van Hall, M.A., 2011. A set of multiplex PCRs for genotypic detection of extended-spectrum β-lactamases, carbapenemases, plasmid-mediated AmpC β-lactamases and OXA β-lactamases. International Journal of Antimicrobial Agents 37, 356–359. 10.1016/j.ijantimicag.2011.01.005.

Vázquez-López, R., Solano-Gálvez, S.G., Juárez Vignon-Whaley, J.J., Abello Vaamonde, J.A., Padró Alonzo, L.A., Rivera Reséndiz, A., Muleiro Álvarez, M., Vega López, E.N., Franyuti-Kelly, G., Álvarez Hernández, D.A., Moncaleano Guzmán, V., Juárez Bañuelos, J.E., Marcos Felix, J., González Barrios, J.A., Barrientos Fortes, T., 2020. *Acinetobacter baumannii* resistance: A real challenge for clinicians. Antibiotics 9. 10.3390/antibiotics9040205.

Wareth, G., Brandt, C., Sprague, L.D., Neubauer, H., Pletz, M.W., 2020. Spatio-temporal distribution of *Acinetobacter baumannii* in Germany-A comprehensive systematic review of studies on resistance development in humans (2000-2018). Microorganisms 8. 10.3390/microorganisms8030375.

Wareth, G., Brandt, C., Sprague, L.D., Neubauer, H., Pletz, M.W., 2021a. WGS based analysis of acquired antimicrobial resistance in human and non-human *Acinetobacter baumannii* isolates from a german perspective. BMC Microbiology 21, 210. 10.1186/s12866-021-02270-7.

Wareth, G., Neubauer, H., Sprague, L.D., 2019. *Acinetobacter baumannii*: A neglected pathogen in veterinary and environmental health in Germany. Veterinary Research Communications 43, 1–6. 10.1007/s11259-018-9742-0.

Wareth, G., Pletz, M.W., Neubauer, H., Sprague, L.D., 2021b. A rapid method for the detection of motility in *Acinetobacter baumannii* and its association to the existence of the virulence-associated genes *pil*A and *alg*W. German Journal of Microbiology 1, 11–17. 10.51585/gjm.2021.3.0009.

Wendel, A.F., Malecki, M., Otchwemah, R., Tellez-Castillo, C.J., Sakka, S.G., Mattner, F., 2018. One-year molecular surveillance of carbapenem-susceptible *A. baumannii* on a German intensive care unit: diversity or clonality. Antimicrobial Resistance and Infection Control 7, 145. 10.1186/s13756-018-0436-8.

Willems, S., Kampmeier, S., Bletz, S., Kossow, A., Köck, R., Kipp, F., Mellmann, A., 2016. Whole-genome sequencing elucidates epidemiology of nosocomial clusters of *Acinetobacter baumannii*. Journal of Clinical Microbiology 54, 2391–2394. 10.1128/JCM.00721-16.

Wisplinghoff, H., Hippler, C., Bartual, S.G., Haefs, C., Stefanik, D., Higgins, P.G., Seifert, H., 2008. Molecular epidemiology of clinical *Acinetobacter baumannii* and *Acinetobacter* genomic species 13TU isolates using a multilocus sequencing typing scheme. Clinical Microbiology and Infection 14, 708–715. 10.1111/j.1469-0691.2008.02010.x.

Zhang, W.J., Lu, Z., Schwarz, S., Zhang, R.M., Wang, X.M., Si, W., Yu, S., Chen, L., Liu, S., 2013. Complete sequence of the *bla*(NDM-1)-carrying plasmid pNDM-AB from *Acinetobacter baumannii* of food animal origin. The Journal of Antimicrobial Chemotherapy 68, 1681–1682. 10.1093/jac/dkt066.