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Antibiotic resistance genes circulating in Nigeria: a systematic review and meta-analysis from the One Health perspective

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Abstract

Background The misuse of antibiotics in developing countries has created serious threats to public healthcare systems and reduced treatment options. Multidrug-resistant bacteria harbour antibiotic resistance genes that help them subdue the effectiveness of several available antibiotics. This review aimed to assess antimicrobial resistance genes circulating in Nigeria via a systematic review and meta-analysis.

Methods A comprehensive literature search was performed using five electronic databases: PubMed, Web of Science, Scopus, Google Search, and African Journals Online (AJOL). Articles related to antibiotic resistance genes in Nigeria, published between January 1, 2015 and October 31, 2024, were included. The Newcastle-Ottawa scale (NOS) was used to assess the risk of bias. The meta-analysis for random effects was performed to determine the proportions and pooled prevalence of the resistance genes from the various One Health domains, as well as heterogeneity in the data, using R software (Version 4.3.3) and the metaprop package.

Results Of the 762 articles retrieved, 56 (humans [*n* = 33], animals [*n* = 8], environment [*n* = 12], human/animal [*n* = 1], and human/animal/environment [*n* = 2]) from the six geopolitical zones in Nigeria met the inclusion criteria. The extended-spectrum beta-lactamase (ESBL) gene with the highest pooled prevalence was *bla*SHV (24.0% [95% CI: 12.0–44.0]), followed by *bla*CTX-M (23.0% [95% CI: 14.0–37.0]), and the least was *bla*TEM (18.0% [95% CI: 8.0–37.0]). Among the carbapenemase genes, *bla*KPC (33.0% [95% CI: 7.0–76.0]) was the most prevalent, followed by *bla*NDM (21.0% [95% CI: 9.0–41.0]), *bla*OXA (11.0% [95% CI: 2.0–46.0]) and the least was *bla*VIM (9.0% [95% CI: 3.0–26.0]). The *mec*A gene also had a high pooled prevalence (51.0% [95% CI: 14.0–86.0]). The pooled prevalence of the *erm*, *sul*, *tet*, and *qnr* genes ranged from 19.0% (95% CI: 8.0–38.0) to 27.0% (95% CI: 13.0–47.0). Some antibiotic resistance genes were shared among the three domains.

Conclusion This systematic review and meta-analysis has demonstrated the co-existence of antibiotic resistance genes among bacteria causing infection in Nigeria, via the One Health approach. There is a need for future research on the circulation of antibiotic resistance genes in developing countries using internationally approved approaches to track down this menace.

Keywords Antibiotic resistance, Genes, Meta-analysis, One Health, Nigeria

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Introduction

Antimicrobial resistance (AMR) is a major global health threat to humanity, contributing to about seven hundred thousand deaths annually, with this death rate anticipated to rise by as much as ten million by the year 2050 [1–3]. Although a global problem, AMR is more pronounced in low- and middle-income countries, such as Nigeria, where facilitators of the menace abound [4–6]. In a previous systematic review on the global burden of AMR based on One Health, West Africa was reported as one of the regions that had higher death rates attributed to bacterial AMR, with a mortality rate of over 75/100,000 [7]. In Nigeria, in the year 2019, the number of deaths attributable to AMR was 64,500, and the number associated with AMR was 263,400. Nigeria has the 20th highest age-standardised mortality rate per 100,000 populations associated with AMR across African countries [8]. Yet, insights on AMR in Nigeria is poor, and irrational and sub-optimal antimicrobial use is pervasive, further compounding the AMR menace [9, 10]. Moreover, there is limited consolidated data on AMR in the country, which is a cardinal hinderance to tailored surveillance efforts and intervention implementation.

The goal of this systematic review and meta-analysis was to determine the distribution of antimicrobial resistance genes in Nigeria from the One Health perspective. The important One Health triad, which examines human, veterinary, and environmental factors, was of utmost importance in this analysis. Antimicrobial resistance reports from 36 states in Nigeria, which make up the six geopolitical zones of the country were meticulously analysed. The major objectives of this study were to (i) evaluate the antibiotic resistance genes (ARGs) in bacteria isolated in Nigeria within the past ten years, (ii) determine the multidrug resistance (MDR) of bacterial pathogens that are the most frequently reported, and (iii) identify the commonly shared antibiotic resistance genes within the three domains.

Materials and methodology

The systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [11]. It included all research conducted on genotypic antibiotic resistance (AMR) in humans, animals, and the environment. The relevant articles were identified through five electronic databases, including Scopus, PubMed, Google Scholar, Web of Science, and AJOL, using specific search terms for antibacterial resistance detected in Nigeria from January 1, 2015, until October 31, 2024, and limited to studies published in English. To ensure a detailed search of all relevant studies in the selected area, a combination of keywords was used. The search strategies included terms such as "molecular identification of antibiotic resistance", "genotypic antibiotic resistance", "antibiotic resistance genes", "ESBL genes", "beta-lactamase genes", "carbapenemase genes", "tetracycline, sulphonamides, fosfomycin, phenicol resistance genes", "aminoglycoside resistance genes, macrolide resistance genes and quinolone resistance genes", "geo-political zones" and "Nigeria" (Table S3).

Inclusion and exclusion criteria

Freely accessible research articles published in the area of bacterial genotypic antibiotic resistance in humans, animals, and environmental sources in Nigeria were included in the study. Restrictions were not applied to bacterial genera, species, and sample source, whether in humans, animals, or the environment. Studies on antimicrobial resistance genes in fungi, viruses, parasites, and protozoa were excluded. Furthermore, studies that reported antibiotic prescription and not resistance profiles or genes, or those lacking clear identification of antibiotic resistance genes through molecular methods such as PCR or genomic sequencing, were also excluded. In addition, studies that focused on the review of antibiotic resistance and case reports were not included.

Data extraction

The retrieved articles were initially screened by title and abstract. Full texts of those that passed the initial screening were then assessed for eligibility, and the qualifying articles were included in the final review. The data included in this study were meticulously screened and extracted using a Microsoft Office Excel spreadsheet. The data extracted included first author's details, publication year, sample source (animal, human or environment), study period, study location or geopolitical zone, specimen type, bacteria isolated, antibiotic resistance genes, and number of isolates analysed genotypically. Other extracted information included adopted definition of MDR, number of isolates, MDR occurrence, antimicrobial susceptibility testing (AST) methods (disc diffusion, broth microdilution, agar dilution, E-test or automated methods), minimum inhibitory concentration (MIC) breakpoint used, method for identifying resistance genes, specific genes involved, number of each gene, and author references.

Evaluation of bias

The studies included in this review were assessed for risk of bias using the Newcastle-Ottawa scale (NOS) for assessing non-randomised and cross-sectional studies [12]. The NOS method for assessing the risk of bias was grouped into three based on selection, comparability, and outcome in non-randomised, cross-sectional studies. This was further divided into eight parts based on possible bias. This assessment criteria evaluated the following

items: the representativeness of the exposed cohort, the selection of the non-exposed cohort, the ascertainment of exposure, confirmation that the outcome of interest was not present at the start of the study, comparability of cohorts based on study design or analysis, the method of outcome assessment, the follow-up duration being sufficient for outcomes to occur, and the adequacy of cohort follow-up. The included studies were assessed for each of these categories as low, medium, or high risk of bias. Studies that had 7–8 stars were considered to have a low risk of bias, those studies that had six stars were rated as having a moderate risk, and those with 5 stars and below were considered to have a high risk of bias. The results of the quality assessment is presented in Table S2.

Statistical analysis

The meta-analyses for random effects were performed to determine the proportions and pooled prevalence of the bacterial isolates/resistance genes present using R software, Version 4.3.3, and the metaprop package. The pooled prevalence was estimated using a 95% confidence interval. The random-effects model was obtained from the meta-analysis based on the expected heterogeneity among the included studies. The model captured type of study, geographic locations, time periods, sample types, and bacterial species. The funnel plot, Egger's test, and metabias test were used to determine the publication bias and $\chi 2$ test was used to evaluate heterogeneity in the data. Significant studies were recorded to have a p value of less than 0.05 and non-significant a p value of greater than 0.05.

Results

Search result

A comprehensive search was conducted using five electronic databases to generate 762 articles from Scopus ($n = 223$), PubMed ($n = 141$), Web of Science ($n = 108$), Google Scholar ($n = 211$), and AJOL ($n = 79$). The duplicated articles ($n = 172$) were carefully extracted and removed. Qualitative review was performed on 590 studies by screening their titles and abstracts, and 384 studies were excluded for not meeting the inclusion criteria. Further evaluation for eligibility carried out on the remaining 206 studies resulted in the removal of 150 studies for reasons such as not reporting a clear outcome or on the population of interest, not specifying locations, and reporting only on virulence genes. Finally, the 56 studies [13–68] that met the inclusion criteria were thoroughly reviewed, and ARG data were extracted for the meta-analysis (Fig. 1).

Study characteristics

The type of studies reviewed included prospective, retrospective, descriptive, and cross-sectional ones. These studies included data collected from six geo-political zones in Nigeria and generally reported on antibiotic resistance genes in bacteria of the 56 studies included, 33 (58.9%) focused on humans, 8 (14.3%) on animals, 12 (21.4%) on the environment, 1 (1.8%) on both humans and animals, and 2 (3.6%) on all three: humans, animals, and the environment. The frequency of the selected articles based on geo-political zones is as follows: North Central had 13 studies (23.2%), with 7 focused on humans, 2 on humans, animals, and the environment, 2 on animals, and 2 on the environment; North East had 5 studies (8.9%), with 4 on humans, 1 on the environment, and none on animals; North West had 4 studies (7.1%), with 3 on humans, 1 on the environment, and none on animals; South East also had 5 studies (8.9%), with 1 on humans, 1 on animals, 2 on the environment, and 1 on both humans and animals; South South had 9 studies (16.1%), consisting of 5 on humans, 2 on animals, and 2 on the environment; and South West had 20 studies (35.7%), with 13 on humans, 3 on animals, and 4 on the environment. Thus, the highest number of studies included in this review was obtained from the South West zone and the least was from the North East zone. The AMR genes presented from the included studies were reported from bacteria isolated from the following sample sources: humans (faecal matter, blood, urine, wound, biopsy, cerebrospinal fluid, sputum, aspirates, ear, eye swabs, high vaginal swabs, catheter tips, diabetic foot ulcer swabs, nasal swabs, endocervical swabs, ascitic fluid, throat swabs, tracheal swabs, urethral swabs, semen, and pleural fluid), the environment (such as walls, floors, water source, hospital wastewater, sediment samples, abattoir wastewater, and door handle swabs), and animals (such as shellfish, clams, oysters, periwinkles, poultry, cafeteria, cattle, goat, pig, egrets, and sheep) (Table S1).

Antimicrobial susceptibility testing (AST)

Exactly 48 (85.7%) studies reported antibiotic resistance using antimicrobial susceptibility testing. Out of the 48 studies, 42 (87.5%) evaluated antibiotic resistance using the Kirby-Bauer disc diffusion method, 5 (10.4%) studies employed the VITEK-2 system, one (2.1%) study used the broth microdilution method, and eight (14.3%) studies did not specify the method used; 46 (82.1%) studies adhered to the Clinical and Laboratory Standards Institute (CLSI) guidelines, 6 (10.7%) studies used the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations, and four (7.1%) studies did not specify the guidelines relied on (Table S1).

Detection and characterisation of antibiotic resistance genes (ARGs) methods

In the included studies, two main methods were employed in the molecular detection and characterisation

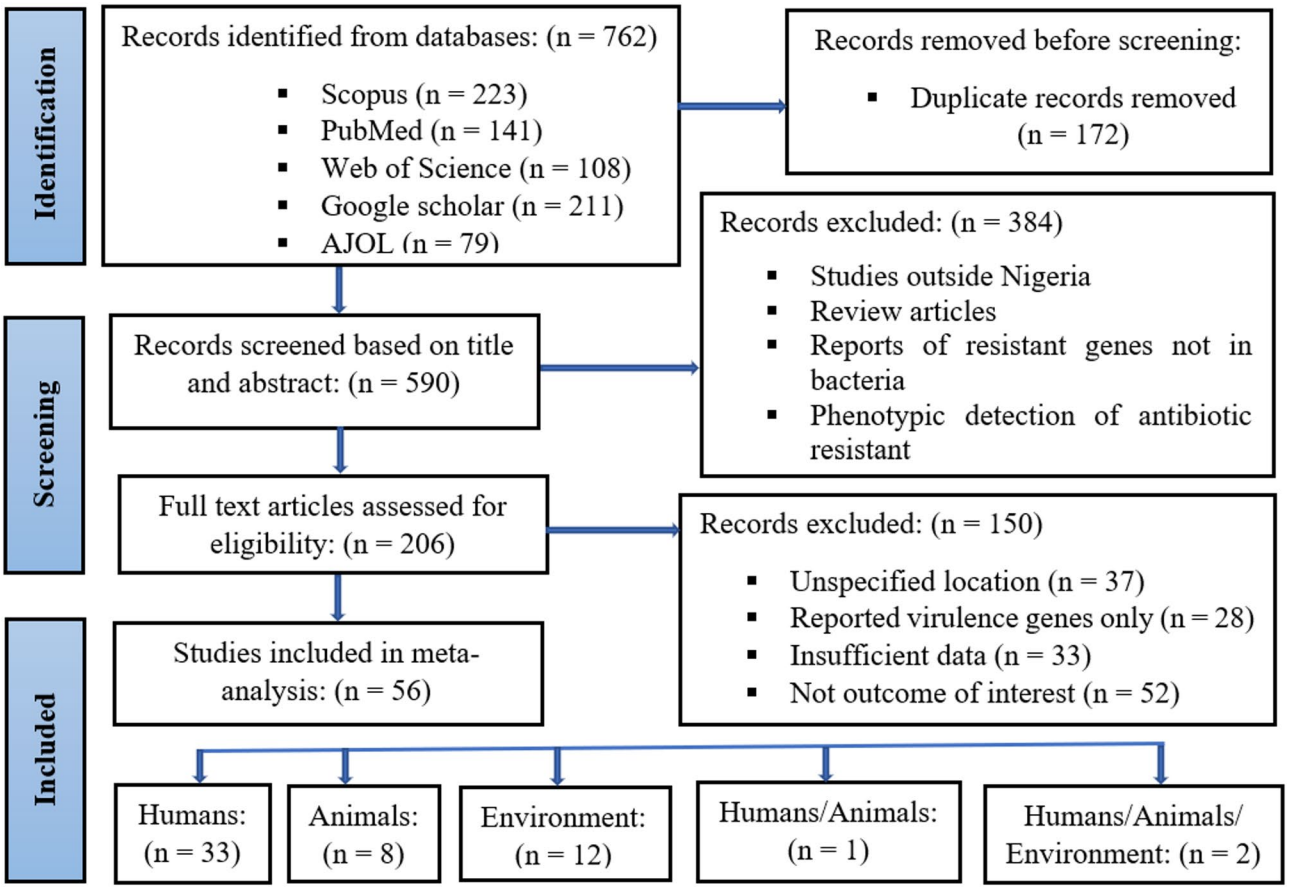

Fig. 1 PRISMA flowchart of identified, screened, and included articles

of ARGs in the various samples (PCR and genome sequencing). The studies that relied on PCR were 34 (60.7%), while those that relied on PCR and genome sequencing techniques were 22 (39.3%). Of these 22 studies, 10 employed whole-genome sequencing (WGS), seven used multi-locus sequences typing (MLST), and five utilised Sanger sequencing (Table S1).

Prevalence of MDR bacteria

In this review, 17 studies identified multidrug-resistant bacteria in humans ($n = 12$), animals ($n = 3$), and the environment ($n = 2$). The MDR bacteria reported by these studies include *Escherichia coli*, *Salmonella enterica*, *Klebsiella quasipneumoniae*, *Salmonella* spp., *Klebsiella pneumoniae*, *Acinetobacter* spp., *Citrobacter* spp., *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Aeromonas* spp., *Alcaligenes* spp., *Bacillus* spp., *C. freundii*, *Pseudomonas* spp., and *Klebsiella* spp. The 17 studies that reported MDR had a pooled prevalence of 56.4% (95% CI: 34.0–76.0) and heterogeneity of 95.0% (Fig. 2).

Prevalence of ARGs circulating in Nigeria

The prevalence of ARGs circulating in Nigeria was determined, and a meta-analysis was conducted on ARGs that were reported in three or more studies. Exactly 12 genes were included in the meta-analysis based on the inclusion criteria, and the included genes were: *bla*CTX-M (including *bla*CTX-M-9, *bla*CTX-M-14, *bla*CTX-M-15, *bla*CTX-M-4, *bla*CTX-M-55 and *bla*CTX-M-2), *bla*TEM (including *bla*TEM-1 and *bla*TEM-191), *bla*SHV, *sul* (including *sul2* and *sul1*), *tet* (*tet(A)*, *tet(B)*, *tet(G)*, *tet(D)*, *tet(E)*, *tet(K)* and *tet(L)*), *qnr* (including *qnr*A, *qnr*S and *qnr*B), *bla*NDM (including *bla*NDM-1 and *bla*NDM-5), *bla*KPC, *bla*VIM (including *bla*VIM-2 and *bla*VIM-5), *bla*OXA (including *bla*OXA-48, *bla*OXA-1 and *bla*OXA-181), *mec*A, and *erm*B (including *erm*A, *erm*B and *erm*C). The genes that did not meet the inclusion criteria because they had one to two frequencies were excluded in the meta-analysis; these were *aad*A1, *aad*A2, *aac*(3)-IIa, *ant*(2")-Ia, *aph*(3')-Ia, *aph*(3")-Ib, *ParC*, *bla*GES-9, *bla*PDC-1, oqxA, oqxB, *bla*IMP, *bla*FOX, *mef*A, *dfrA14*, floR, strB, *bla*CMH-3, *catA1*, *catB4*, *fosA*, dfrG, dfrK, and *bla*CMY-2.

The pooled prevalence of various ARGs, including ESBLs and those conferring resistance to sulphonamides, tetracycline, quinolones, carbapenemase, methicillin, and macrolides, as well as heterogeneity of the included studies were evaluated and recorded. The pooled prevalence

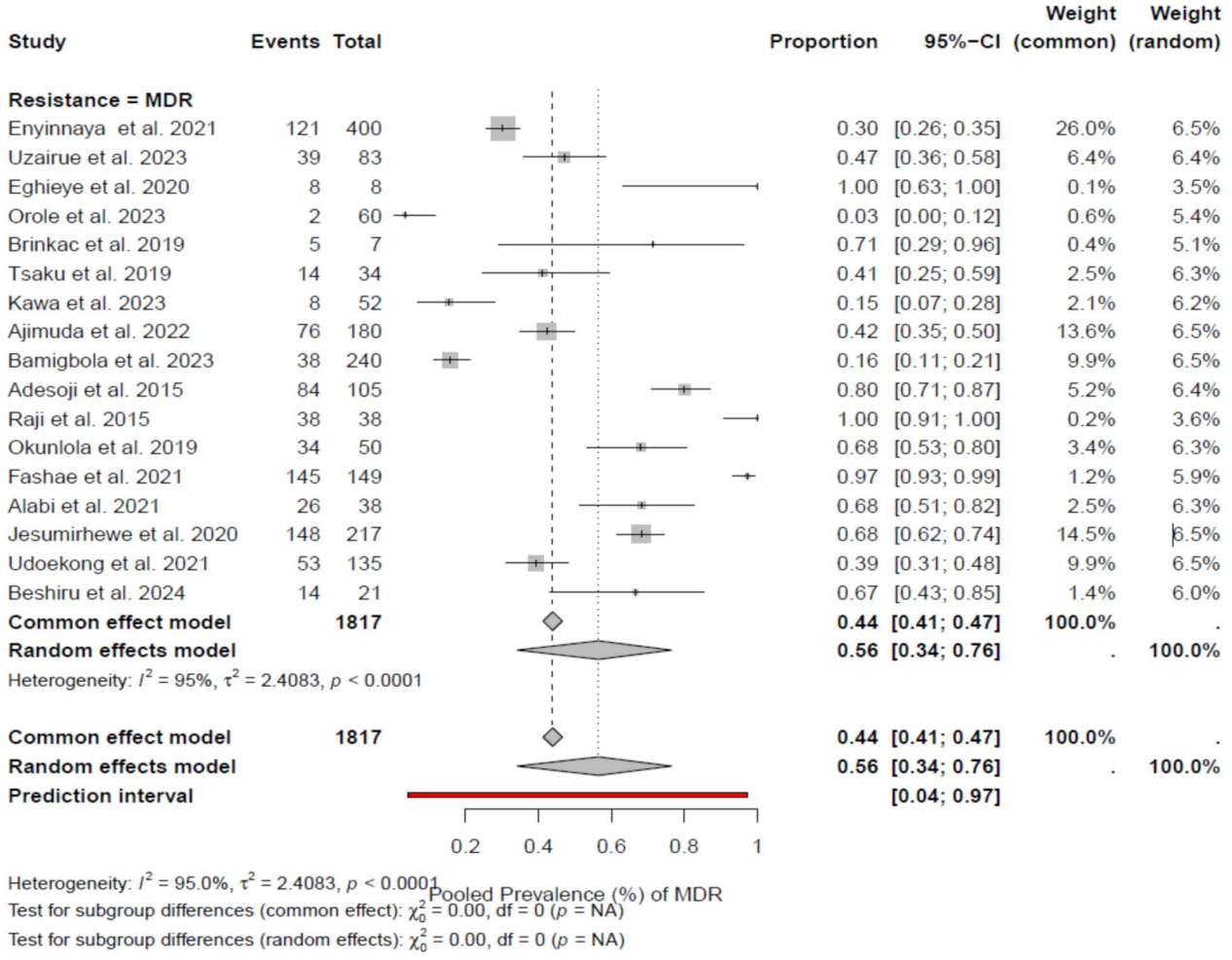

Fig. 2 Pooled prevalence of MDR bacteria

of the ARGs varied widely across different classes, with the highest prevalence observed for *mec*A (51.0%, 95% CI: 14.0–86.0%). Among carbapenemase genes, *bla*KPC showed notably high prevalence (33.0%, 95% CI: 7.0–76.0%), whereas *bla*VIM and *bla*OXA were less common (9.0% and 11.0%, respectively). For ESBL genes, *bla*SHV (24.0%) and *bla*CTX-M (23.0%) were more prevalent than *bla*TEM (18.0%). The quinolone resistance gene *qnr* had the highest prevalence (27%) among non-β-lactam ARGs, followed by *sul* (20.0%) and *tet* (19.0%), which confer sulfonamide and tetracycline resistance, respectively. Overall, the prevalence across all genes ranged from 9% to 51% for *bla*VIM and *mec*A, respectively, with substantial heterogeneity (I^2 > 90% for most genes), suggesting significant variation across studies (Table 1).

The One Health distribution of major antibiotic resistance genes in Nigeria

This study observed that studies from humans, animals, and environmental sources had several ARGs in common (Fig. 3). The ARGs, including *bla*CTX-M, *bla*CTX-M-9, *bla*CTX-M-14, *bla*CTX-M-15, *bla*TEM, *bla*TEM-1, *bla*SHV, *sul*2, *tet*A, *qnr*A, *qnr*S, *bla*NDM-1, *bla*NDM-5, *bla*KPC, *bla*VIM, *bla*OXA-48, *mec*A, and *erm*B, were detected as the most frequently shared genes. The ARGs commonly harboured by human/animal/environment were seven (7), which include *bla*CTX-M, *bla*CTX-M-15, *bla*TEM, *bla*SHV, *tet*A, *qnr*S, and *mec*A. Human/environment shared four (4) different ARGs in common, which include *qnr*A, *bla*NDM-1, *bla*NDM-5, *and bla*KPC, while human/animal had *bla*CTX-M-14, *erm*B, and anminal/environment harboured *bla*TEM-1, *sul*2 in common. However, three (3) ARGs, *bla*CTX-M-9, *bla*VIM, and *bla*OXA-48, were found to be present only in humans and not in animals and the environment.

Risk of bias assessment

The risk of bias was used to determine the quality of the 56 included studies [13–68], and it was classified based on low, moderate, and high risk of bias. Out of these

Table 1 The pooled prevalence summary of ARGs included in the meta-analysis

Gene	Frequency (*n*)	Proportion (%)	Bacteria harbouring the gene(s)	Total number of bacterial isolates	Pooled prevalence of gene among bacterial isolates	I^2 (%)	*p*-value	Sources
*bla*CTX-M (including *bla*CTX-M-9, *bla*CTX-M-14, *bla*CTX-M-15, *bla*CTX-M-4, *bla*CTXM-55, and *bla*CTX-M-2)	859	31.9	*Klebsiella quasipneumoniae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Salmonella* spp., *Enterobacter* spp., *Citrobacter* spp., *Providencia* spp., *Proteus* spp., *Acinetobacter* spp., and *Pseudomonas aeruginosa*	3341	23.0% (95% CI:14.0–37.0)	95.4	0.0001	Human, Animal and Environment
*bla*TEM (including *bla*TEM-1, and *bla*TEM-191)	440	16.4	*K. quasipneumoniae*, *K. pneumoniae*, *E. coli*, *Salmonella* spp., and *P. aeruginosa*	1845	18.0% (95% CI: 8.0–37.0)	94.9	0.0001	Human, Animal and Environment
*bla*SHV	245	9.1	*K. pneumoniae*, *E. coli*, *Salmonella* spp., *Proteus* spp., and *P. aeruginosa*	1311	24.0% (95% CI: 12.0–44.0)	95.4	0.0001	Human, Animal and Environment
sul (including *sul1*, and *sul2*)	33	1.2	*Citrobacter* spp., *Enterobacter* spp., *E. coli*, *K. pneumoniae*, and *P. aeruginosa*	258	20.0% (95% CI: 7.0–45.0)	74.5	0.0015	Animal and Environment
tet (including *tet*A, *tet*B, *tet*D, *tet*G, *tet*E, *tet*K, and *tet*L)	165	6.1	*Aeromonas* spp., *K. pneumoniae*, *E. coli*, *Salmonella enterica*, *Enterobacter* spp., *and Alcaligenes* spp.	802	19.0% (95% CI: 8.0–38.0)	92.5	0.0001	Human, Animal and Environment
qnr (including *qnr*A, *qnr*B, and *qnr*S)	276	10.3	*K. pneumoniae*, *E. coli*, *Salmonella* spp., and *Providencia* spp.	1014	27.0% (95% CI: 13.0–47.0)	92.9	0.0001	Human, Animal and Environment
*bla*NDM (including *bla*NDM-1, and *bla*NDM-5)	201	7.5	*K. quasipneumoniae*, *K. pneumoniae*, *E. coli*, *Enterobacter* spp, *Citrobacter* spp., *Proteus* spp., *Acinetobacter* spp., *P. aeruginosa*, *Serratia marcescens*, and *Morganella morganii*	1353	21.0% (95% CI: 9.0–41.0)	93.7	0.0001	Human and Environment
*bla*KPC	39	1.5	*K. pneumoniae*, *E. coli*, *Proteus mirabilis*, and *Serratia marcescens*	178	33.0% (95% CI: 7.0–76.0)	87.2	0.0001	Human and Environment
*bla*VIM (including *bla*VIM-2, and *bla*VIM-5)	81	3.0	*P. aeruginosa*, *K. pneumoniae*, *E. coli*, and *Proteus mirabilis*	572	9.0% (95% CI: 3.0–26.0)	94.0	0.0001	Human
*bla*OXA (including *bla*OXA-1, *bla*OXA-48, and *bla*OXA-181)	102	3.8	*Salmonella* spp., *K. quasipneumoniae*, *K. pneumoniae*, *E. coli*, and *Acinetobacter baumanii*	629	11.0% (95% CI: 2.0–46.0)	90.1	0.0001	Human
*mec*A	142	5.3	*Staphylococcus aureus*	263	51.0% (95% CI: 14.0–86.0)	93.9	0.0001	Human, Animal and Environment
erm (including *erm*A, *erm*B, and *erm*C)	105	3.9	*Enterococcus faecalis*, *K. pneumoniae*, *Streptococcus* spp., *Enterobacter* spp., *E. coli*, *P. aeruginosa*, *and Staphylococcus* spp.	469	21.0% (95% CI: 4.0–61.0)	92.4	0.0001	Human and Animal

included studies, 42 (75.0%) were found to have a low risk of bias based on the inclusion and exclusion criteria. Additionally, 9 (16.1%) studies that scored six stars had a moderate risk of bias and 5 (8.9%) studies that scored five stars and below were judged to have a high risk of bias (Table S2).

Discussion

The emergence and re-emergence of antibiotic-resistant microorganisms has posed a serious threat to the existing antibiotics, including last-line ones, especially in Africa where the public healthcare system is not functioning at optimum levels. The lack of comprehensive systematic data collection has impeded proper understanding of the circulating antibiotic resistance genes causing treatment failures in the healthcare systems in Africa. The One Health approach was employed in this systematic review to determine the prevalence of circulating ARGs in bacteria within six major geopolitical zones in Nigeria. This review reported the presence of both Gram-negative and Gram-positive bacteria harbouring ARGs from human, animal, and environmental sources in Nigeria. The most common bacteria that were reported by studies to carry ARGs belong to the family of Enterobacteriaceae, which is consistent with findings of one previous study [69]. Noteworthily, the most frequent ARGs observed came from

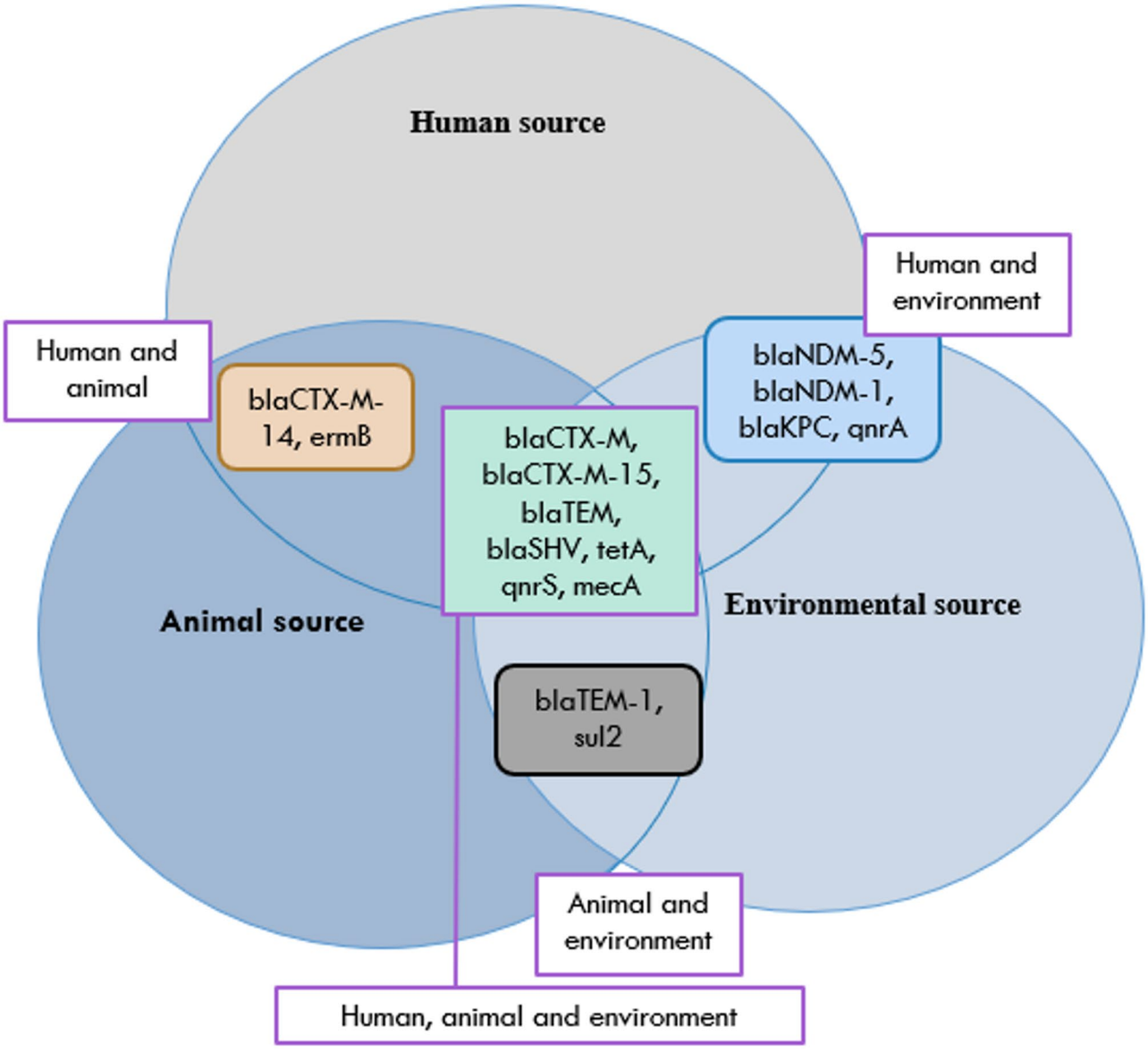

Fig. 3 ARGs shared among human, animal, and environmental sources

the ESBL gene family; this includes *bla*SHV, *bla*CTX-M, and *bla*TEM. Other common ARGs reported are those conferring resistance to sulphonamides, tetracycline, quinolones, carbapenemase, methicillin, and macrolides; there was also co-existence of ARGs in humans, animals, and the environment. This evidence proves the possible interconnected reservoirs facilitating the spread of resistance within the healthcare system and the environment. To curtail further spread of ARGs and their development, it is important to adopt a multi-sectoral stewardship approach. This review serves as a hand note on the use of the One Health approach to employ strategies and generate data for easy management of antibacterial resistance in Africa and worldwide.

Of the 56 studies examined across the six geopolitical zones in Nigeria, various distributions of ARG prevalence were reported. Human studies accounted for the majority of included articles, followed by environmental studies, while animal studies were the least represented. Regionally, the South West contributed the highest number of studies, followed by the North Central region, whereas the North West recorded the fewest.

This review identified the average pooled prevalence of ESBL genes *bla*CTX-M (including *bla*CTX-M-9, *bla*CTX-M-14, *bla*CTX-M-15, *bla*CTX-M-55, *bla*CTX-M-2 and *bla*CTX-M-4), *bla*TEM (including *bla*TEM-1, and *bla*TEM-191) and *bla*SHV found in humans, animals, and the environment. The pooled prevalence reported ranged from 18.0% (95% CI: 8.0–37.0) to 24.0%

(95% CI: 12.0–44.0), and demonstrated a high level of heterogeneity (I^2), ranging from 49.9 to 95.6%. This pooled prevalence is consistent with that previously reported in animal populations, at an estimated rate of 26.6% (95% CI = 18.2 to 37.3) using a random-effects model [70]. The highest pooled prevalence was reported for the *bla*SHV genes at 24.0%, followed by *bla*CTX-M genes at 23.0%, and the least was *bla*TEM genes at 18.0%. By comparison, prevalence of 54.0% and 40.0% have been reported in previous systematic reviews in Nigeria and Pakistan, respectively, as well as 23.9% in one Nepalese study that involved the analysis of over 4000 samples [71–73]. Previous studies have reported *bla*CTX-M-15 and *bla*TEM as the most frequent genes circulating in humans in Nigeria [26]. The *bla*TEM and *bla*SHV genes are also circulating in animals in Nigeria [51] and Indonesia [74]. The *bla*CTX-M and *bla*TEM genes were isolated from environmental sources in Nigeria [24, 25]. The continuous increase in the prevalence of these antibiotic resistance genes is alarming and may pose a serious threat to the therapeutic effectiveness of antibiotics. Nigeria is faced with the burden of poverty, lack of national antibiotic guidelines, poor healthcare systems, and poor environmental conditions, such as lack of potable water, sanitation, and inadequate infection control. These factors are crucial for the spread of microbial strains harbouring resistance genes [75]. Thus, this review provides current data on ESBL genes circulating in different geopolitical zones in Nigeria based on the One Health approach. It is important that the spread of ESBL genes is given serious research attention by national health policy makers to reduce the prevalence, which will aid in preserving the activities of beta-lactam antibiotics. This systematic review identified carbapenem resistance genes, including *bla*NDM (including *bla*NDM-1, and *bla*NDM-5), *bla*KPC, *bla*VIM (including *bla*VIM-2, and *bla*VIM-5) and *bla*OXA (including *bla*OXA-1, *bla*OXA-48, and *bla*OXA-181) from bacterial isolates at a low rate, with pooled prevalence ranging from 9.0 to 33.0%. The most prevalent gene was *bla*KPC at 33.0% (95% CI: 7.0–76.0), followed by *bla*NDM-1 at 21.0% (95% CI: 9.0–41.0), *bla*OXA at 11.0% (95% CI: 2.0–46.0), and the least was *bla*VIM at 9.0% (95% CI: 3.0–26.0). Notably, *bla*NDM-1, *bla*NDM-5, and *bla*KPC were reported in human and environmental studies; *bla*VIM and *bla*OXA-48 were reported in human studies only, and none of the carbapenem resistance genes were reported in animal studies. The prevalence of carbapenem resistance genes has been reported in some West African countries, with *bla*OXA-type (32.7%) being the most frequent gene, which is in contrast with the observations in our review. Prevalence of 17.9% of *bla*OXA-type and 28.6% of *bla*VIM-type has been reported in East Africa [76] and *bla*VIM (29.0%) in the Asia-Pacific region [77]. These prevalence are in consonance with the prevalence of *bla*NDM (up to 29.8%), *bla*VIM (up to 12.5%), and *bla*OXA-48 (up to 3.1%) that were reported in two recent systematic reviews on carbapenem resistance in West Africa [78, 79]. Another study reported the prevalence of *bla*KPC (31%; 94.7%) as being dominant in Canada, Brazil, and *bla*OXA-48 (65.6%) in Russia [80]; these prevalence are higher than that observed in this study. This study revealed that humans and the environment serve as major conduits for microorganisms to circulate carbapenem resistance genes via the presence of plasmids.

Furthermore, the pooled prevalence of other antibiotic resistance genes was computed (sulphonamides, *sul* 20.0% [95% CI: 7.0–45.0]; tetracycline, *tet* 19.0% [95% CI: 8.0–38.0] methicillin, *mec*A 51.0% [95% CI: 14.0–86.0]; macrolides, *erm* 21.0% [95% CI: 4.0–61.0]; quinolones, *qnr* 27.0% [95% CI: 13.0–47.0]). These antibiotic resistance genes were found to co-exist among humans, animals, and the environment. A systematic review in Nigeria identified *sul*2 and *mec*A as having a prevalence of 1.8% [81], which is lower than what was observed in the current systematic review. The rapidly increasing demand for livestock products, driven by human population growth, urbanisation, and animal interaction within the environment, has inadvertently entrenched an uncontrolled use of antimicrobials, which has been associated with an increase in antimicrobial resistance [82, 83]. A few of the included studies reported on the prevalence of genes conferring resistance to trimethoprim, fosfomycin, chloramphenicol, rifampicin, aminoglycosides, streptomycin, lincosamide, colistin, and other antibiotics, but at lower proportions. Previous studies in Africa compared antibiotic resistance genes in humans, animals, and the environment and reported the presence of aac(6′)-Ib-cr, *tet*A, *tet*B, *sul*1, *sul*2, and *qnr* in all three compartments [84, 85]. The prevalence of various antibiotic resistance genes identified through the One Health lens underscores the contribution of mobile genetic elements to the dissemination within the environment and healthcare systems in Nigeria. The transfer of bacteria carrying resistance genes by national/international travellers may have played an important role in the distribution of bacteria in West Africa and worldwide. The major mechanisms of antibiotic resistance identified by some of the studies included in this review were efflux pump upregulation, mutation, virulence gene, inactivating enzyme, detection folate pathway antagonists, ribosomal protection proteins, carbapenemase production, and reduced production of outer membrane porin. Healthcare policymakers need to intensify action on the use of antibiotics, establish collaborative action, and monitor trends in antibiotic resistance.

The pooled prevalence of the MDR bacteria across the three domains was 56.4% (95% CI: 34.0–76.0) with

heterogeneity of 95.0%. *E. coli* was the most frequent MDR bacteria, followed by *Klebsiella* and *Aeromonas* species. In Vietnam, a high prevalence of MDR *E. coli* (81.3%) has been reported, and improper antibiotic use is significantly associated with MDR resistance in bacteria [86]. Indiscriminate antibiotic use in animals for prophylaxis, growth promotion, and metaphylaxis; those used in crops/environment and misuse in humans are important driving factors of antibiotic resistance [87]. MDR bacterial genomes feature mutations or genes that prove advantageous for their survival in the presence of antimicrobial agents, and horizontal gene transfer is believed to take place via mobile genetic elements, such as plasmids, transposons, integrons, and prophages, as reported in identical sequences of multidrug-resistant bacteria from the environment and humans [88]. The major reservoirs and habitats of MDR bacteria include the environment (water, soil, wastewater, sewage, plants [fruit, vegetables, herbs]) [89], animals (raw meat and dairy products), and humans (gastrointestinal tract, the upper respiratory system, and the skin) [90]. The weak antimicrobial resistance surveillance systems in Nigeria are of great concern, and poor usage of antibiotics has led to the introduction of MDR bacteria in humans, animals, and the environment. The circulation of MDR bacteria has strongly contributed to the failure of infectious disease treatment. This challenge is of both medical and veterinary importance. It could jeopardise treatment options for clinicians and veterinary personnel. It is pertinent that urgent action be taken to combat and monitor the regional circulation of antibiotic-resistant bacteria in Nigeria, West Africa, and worldwide.

Strengths and limitations

This systematic review has provided in-depth knowledge and data on antibiotic resistance genes in Nigeria using the One Health approach. It is the first of its kind to assess the prevalence of ARGs in humans, animals, and the environment cutting across the geopolitical zones in Nigeria via systematic review and meta-analysis. The data generated have provided comprehensive information on ARG circulation, which will guide national health policy makers on the best approach to curtailing ARG circulation. One limitation of this systematic review is that the included studies used different phenotypic techniques to detect the bacteria in the samples, which limits insights on the transmission dynamics of the AMR genes. Also, the use of different approaches/protocols or molecular methods in the laboratory by the included studies may account for variations in the levels of ARGs reported, which contributed to the high level of heterogeneity. Limited studies are based on the One Health approach to the surveillance of ARGs in some part of Nigeria. The studies included in the meta-analysis were not equally distributed; animals and the environment had limited data, which may have affected the prediction of the potential circulation of ARGs within the three domains.

Conclusion

This systematic review and meta-analysis provided current data on the ARGs of bacteria circulating between humans, animals, and the environment in Nigeria. The findings of this study provide baseline insights on the connectivity of multidrug resistance genes based on the One Health approach. The pooled prevalence of ESBL genes was highest in *bla*SHV and lowest in *bla*TEM-14. The *bla*KPC gene was identified as the most frequent carbapenemase gene, followed by *bla*NDM. The *mec*A gene was also reported at a high prevalence. Other circulating antibiotic resistance genes, such as those that confer resistance to tetracycline, sulphonamides, macrolides, aminoglycosides, fosfomycin, phenol, and quinolones, were also observed, but at lower prevalence. The factors that drive the spread of ARGs in bacteria within the three domains constitute a serious and difficult problem that cannot be easily addressed. Adopting internationally recommended surveillance measures that take into account data obtained from humans, animals, and the environment could help curtail the menace. Monitoring antibiotic production and usage in humans, animals, and the environment is important through the collaboration of agencies involved in the three domains. This could help clinicians/veterinarians obtain a blueprint on the use of antibiotics and monitor future occurrences of antibiotic resistance.

Recommendations

Routine surveillance programmes

Establishing comprehensive regular surveillance programmes that monitor the spread of multidrug-resistant (MDR) bacteria and resistance genes within the three domains. This should include periodic sampling and testing using both traditional culture-based methods and molecular techniques.

Strengthen antibiotic stewardship, regulation, and capacity building

Health policymakers should tighten the regulation and oversight of antibiotic use. Implement strict guidelines for the therapeutic use of antibiotics, especially in animal husbandry system. Antibiotic stewardship programmes/campaigns should be enforced at both local, state, geopolitical, and national levels. Capacity building should be enhanced by training healthcare workers on recent methods of diagnosis, detection of ARGs and biosecurity measures for animal/environmental health workers.

Future targeted research

Funds should be mapped out for researchers in the area of antibiotic resistance to enable them conduct a long-term national surveys via the One Health approach on both existing multidrug-resistant organisms, yet to be reported organisms, and under-studied organisms across the geopolitical zones. This will inform health policymakers, clinicians, and veterinarians about alternative antibiotics for treating infections caused by such organisms. This will provide national map data on the circulation of antibiotic resistance genes in Nigeria.

Abbreviations

AJOL	African Journals Online
AMR	Antibiotic resistance
AMS	Antimicrobial stewardship
ARGs	Antibiotic resistance genes
AST	Antimicrobial susceptibility testing
CLSI	Clinical and Laboratory Standards Institute
DNA	Deoxyribonucleic Acid
ESBL	Extended-spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
MDR	Multidrug resistance
MIC	Minimum inhibitory concentration
MLST	Multi-locus sequence typing
MRSA	Methicillin-resistant Staphylococcus aureus
NOS	Newcastle-Ottawa Scale
PCR	Polymerase chain reaction
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
WGS	Whole-Genome Sequencing

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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E.N.U., E.S.D. and F.C.N.K wrote the main manuscript text and E.N.U., E.S.D. and F.C.N.K prepared figures. All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

All the authors have given their consent for the publication of this manuscript.

Competing interests

The authors declare no competing interests.

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