## SYSTEMATIC REVIEW

# A systematic review and meta-analysis on antibiotic resistance genes in Ghana

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### Abstract

**Background** Addressing antimicrobial resistance (AMR) poses a complex challenge, primarily because of the limited understanding of bacterial antibiotic resistance genes (ARGs) and the spread of these genes across different domains. To bridge this knowledge gap in Ghana, we undertook a comprehensive systematic review and meta-analysis to quantify and estimate the prevalence of circulating ARGs in bacteria isolated from human, animal, and environmental sources.

**Methods** A thorough literature search was conducted across three major databases—Web of Science, PubMed, and Scopus—to retrieve all relevant articles related to ARGs in Ghana from the inception of the databases to February 25, 2024. A risk-of-bias evaluation was performed using the Newcastle-Ottawa Scale (NOS), and the data analysis involved descriptive statistics and proportional meta-analysis.

**Results** Of the 371 articles initially obtained, 38 met the inclusion criteria. These studies adequately covered Ghana geographically. The most prevalent ESBL gene identified was *bla<sub>CTX-M</sub>*, with a prevalence of 31.6% (95% CI: 17.6–45.7), followed by *bla<sub>TEM</sub>* (19.5% [95% CI: 9.7–29.3]), and *bla<sub>SHV</sub>* (3.5% [95% CI: 0.3–6.6]). The pooled prevalence of carbapenemase genes ranged from 17.2% (95% CI: 6.9–27.6) for *bla<sub>NDM</sub>* to 10.3% (95% CI: 1.9–18.7) for *bla<sub>OXA</sub>*. Additionally, other ARGs, including *sul1*, *qnrS*, *gyrA*, *erm*(*B*), and *mecA*, were detected, with prevalence ranging from 3.9% (95% CI: 0.0–8.5) to 16.4% (95% CI: 3.1–29.8). Several ARGs were shared across human, animal, and environmental sources.

**Conclusion** This review revealed that bacteria obtained from human, animal, and environmental samples in Ghana shared genes associated with AMR. This finding provides evidence on the interconnection of AMR across these three domains. Horizontal gene transfer, which enables the dissemination of ARGs between genetically diverse bacteria, can occur, necessitating a multidisciplinary approach to addressing antimicrobial resistance in Ghana.

**Keywords** Antimicrobial resistance (AMR), Prevalence, Antibiotic resistance genes (ARGs), Ghana, One Health, Multidrug resistance (MDR), Systematic review

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#### Introduction

Antibiotic resistance genes (ARGs) are DNA segments that enable bacteria to withstand the effects of antibiotics. These genes can be naturally present or acquired through mutation or horizontal gene transfer, during which bacteria exchange genetic material [1, 2]. ARGs complicate the treatment of bacterial infections by allowing bacteria to survive antibiotic treatments that typically eliminate them, resulting in persistent infections [3]. Furthermore, ARGs can spread between different bacteria, including those not previously exposed to antibiotics, accelerating the spread of resistance and potentially leading to outbreaks of infections with antibiotic-resistant bacteria [4].

The World Health Organization (WHO) has identified antimicrobial resistance (AMR) as a critical and urgent global public health issue [5]. Infections caused by antibiotic-resistant bacteria lead to increased mortality rates and prolonged illnesses. For example, in 2019, AMR was associated with an estimated 4.95 million deaths worldwide [6]. This alarming figure exceeds the combined annual global mortality rates of tuberculosis (1.5 million), HIV/AIDS (864,000), and malaria (643,000) [7]. Projections suggest that, without intervention, AMR could result in 10 million deaths annually by 2050 [8]. Low- and middle-income regions bear a disproportionate AMR burden [9]. In sub-Saharan Africa, overburdened health systems struggle to combat resistant infections, compounding crisis-level tuberculosis, HIV/AIDS, and malaria mortality [10, 11].

Ghana faces notable AMR challenges. A recent systematic review by Donkor et al. [12] demonstrated a significant presence of multidrug-resistant bacteria in the country, including Escherichia coli, Klebsiella pneumoniae, and methicillin-resistant Staphylococcus aureus (MRSA). The review underscored the widespread resistance among these key pathogens and highlighted the interconnection of human, animal, and environmental health in the spread of AMR in Ghana. It also pointed out the critical concern of environmental bacteria that are potentially transmitting ARGs to human pathogens. While detailed molecular studies have identified specific resistance genes and their mechanisms, there remains a significant gap in comprehensive data on the molecular determinants of AMR and spread of ARGs across different sectors in Ghana, hindering the ability to track trends over time. Consequently, this review aimed to quantify and estimate the prevalence of circulating ARGs in bacteria isolated from human, animal, and environmental sources in Ghana.

#### Methodology

This systematic review used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology [13]. A comprehensive search was conducted across three databases: Web of Science, PubMed, and Scopus. The search terms used were predetermined and focused on gathering research articles related to ARGs in Ghana published from the inception of the databases until February 25, 2024. The search was limited to studies published in English. To ensure a comprehensive search encompassing all relevant studies in the chosen area, a combination of keywords (including terms such as "antibiotic resistance genes", OR "ESBL genes", OR "beta-lactamase genes", OR "carbapenemase genes" AND "Ghana") was employed.

#### Inclusion and exclusion criteria

This comprehensive review encompassed all studies examining bacterial resistance genes in three distinct settings: humans (clinical contexts), animals (farms), and the environment (hospital surroundings, wastewater, and drinking water). No restrictions related to bacterial species, sample source (human, animal, environment), or study design, were placed on the search. Both observational and interventional study designs were included. To ensure relevance, studies conducted outside of Ghana and review articles were excluded from the analysis. Furthermore, studies that reported on only AMR without the use of molecular tests to characterise ARGs were also excluded, as accurate identification of ARGs requires confirmation at the DNA level. Additionally, studies focusing only on virulence genes or reporting on resistance genes in viruses and parasites were not included in the review, since ARG transmission dynamics differ.

#### **Data extraction**

Once ineligible studies were excluded and duplicates were removed, a meticulous analysis of each selected article was undertaken. Two researchers, A.O. and E.S.D., extracted the data using Microsoft Excel. To circumvent the potential for bias, an essential database was created during this process, and this included information such as the study setting and period, sample source, adopted definition of multidrug resistance (MDR), microorganism isolated, number of isolates, MDR occurrence, antimicrobial susceptibility testing (AST) method, minimum inhibitory concentration (MIC) breakpoint used, method for identifying resistance genes, specific genes involved, number of each gene, and author references. Any discrepancies in data extraction between the two reviewers were identified and resolved through discussion and consensus building. In instances when an agreement could not be reached, a third reviewer was consulted to arrive at a final decision.

#### **Evaluation of bias**

Risk of bias in individual studies was evaluated using the Newcastle-Ottawa Scale (NOS) for assessing non-randomised studies [14]. The NOS evaluates selection, comparability, and outcome for cross-sectional studies. Each study received a star rating for the selection of study populations (four stars maximum), comparability of groups (two stars maximum), and ascertainment of outcome of interest (three stars maximum). Studies that achieved a rating of six stars or more were considered to be at a low risk of bias; those that achieved four to five stars were deemed to have a moderate risk, and those that had less than four stars were adjudged to have a high risk of bias. Two reviewers independently applied the NOS, resolving disagreements through consensus building. Results of the quality assessment are presented in Supplementary Table S2.

#### Statistical analysis

The data analysis involved descriptive statistics and proportional meta-analysis. For the meta-analysis, studies that reported the number of isolates and the number that harboured a resistance gene were included. Using R software, Version 4.3.3 (2024-02-29), and the "metaprop" package, a random-effects meta-analysis was performed to determine the pooled prevalence of resistance genes. The pooled prevalence was estimated in this analysis using a 95% confidence interval. A random-effects metaanalysis was also used to calculate the pooled prevalence ratios (PRs). The random-effects model was chosen for the meta-analysis given the expected heterogeneity between included studies with regard to factors such as geographic locations, time periods, sample types, and bacterial species. Compared to a fixed-effects model, the random-effects approach provides a more conservative estimate by incorporating between-study variability in the pooled prevalence calculation. Using a funnel plot and the "metabias" command, publication bias was examined, and heterogeneity in the data was measured using the  $\chi^2$  test.

Publication bias was assessed visually using funnel plots to detect asymmetry that could arise from non-publication of small or non-significant studies. The funnel plots revealed a slight asymmetry (Supplementary Figures S13-S25). However, the Egger linear regression test did not yield statistically significant results, suggesting that small study effects were unlikely to be present. In contrast, the regression-based Egger test indicated potential reporting bias, as evidenced by a p value less than 0.05.

#### Results

#### Search result

The search yielded 371 articles from PubMed (n = 113), Scopus (n = 170), and Web of Science (n = 88), with 78 duplicates removed. After the abstracts of the remaining articles were reviewed (n = 293), 243 articles were excluded for not meeting the eligibility criteria. These exclusions included studies conducted outside Ghana, review articles, studies lacking molecular or genetic detection of resistance genes, and reports focusing on resistance genes in viruses and parasites. Of the 50 remaining articles, 12 were excluded because they were from unspecified locations and reported only on virulence genes. The remaining 38 articles [15–52] were included in this systematic review and underwent a thorough review to extract data on ARGs (Fig. 1).

#### Study characteristics

The reviewed studies geographically covered seven of the then ten administrative regions of Ghana (the existing regional demarcation at the time most of the included studies were conducted). However, no study describing the detection and characterisation of ARGs in antibioticresistant bacteria (ARB) has been reported for the Upper East, Upper West, and Brong-Ahafo Regions. Among the included studies, 13 involved the Ashanti Region, followed by nine involving the Greater Accra Region. The Northern and Volta Regions had four studies each, whereas the Central and Western Regions had three and two studies, respectively. Three studies provided data on ARGs for two or more regions, indicating the use of a multicentre approach (Table S1).

The studies collected samples from various sources, including humans (urine, blood, stool, sputum, wounds, high vaginal swabs, nasal swabs, ear swabs, endocervical swabs, cerebrospinal fluid oropharynx), animals (poultry meat, poultry litter, cockroaches, sheep, goats, pigs, fresh milk, and fish farms), and the environment (water sources, surroundings of patient beds, latrines, tables, soil, sewage, and latrines). Of the 38 included studies, 25 were conducted in humans only, whereas three focused on environmental sources only. Seven identified ARGs in animals only. Two studies detected ARGs in both human and animal sources, and one identified ARGs across human, animal, and environmental sources (Table S1).

#### Antimicrobial susceptibility testing (AST)

A total of 27 studies conducted antimicrobial susceptibility testing. Among these, 19 utilised the Kirby-Bauer disk diffusion method, whereas eight employed the VITEK-2 system. Twelve studies followed the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), fifteen adhered to the guidelines of the Clinical and Laboratory Standards Institute (CLSI), and three combined the two recommendations for antimicrobial susceptibility testing (Table S1).

## Methods for the detection and characterisation of antibiotic resistance genes (ARGs)

The genetic detection and characterisation of ARGs in various sample matrices were primarily performed using three main methods. In 21 studies, PCR coupled with DNA sequencing was employed. Twelve studies utilised





Fig. 1 PRISMA flowchart for article evaluation, screening, and record identification.

a combination of PCR, DNA, and genome sequencing techniques (such as whole-genome sequencing [WGS], multilocus sequence typing [MLST], and Sanger sequencing). Three studies relied solely on DNA and genome sequencing, whereas two studies exclusively employed genome sequencing (Table S1).

#### **Risk of bias**

Based on the risk of bias assessment, the quality of included studies [15–52] was generally good. Of the 38 studies, 33 (87%) were adjudged to have a low risk of bias, and five (13%), a moderate risk. No "high-risk" study was found. For selection of study populations, most scores were high (3 or 4), as the studies included were representative of bacterial isolates from defined populations or included all eligible specimens within the study period. However, one study scored lower (2), as its eligibility criteria were not clearly defined. Comparability of groups was commonly moderate risk due to a lack of consistent

control for location and year of sample collection, which may influence outcomes. Outcome ascertainment was typically low-risk as ARGs were detected using validated molecular techniques such PCR in certified laboratories.

#### Prevalence of Multidrug-resistant bacteria

Multidrug-resistant bacteria, including *Staphylococcus* aureus, *Escherichia coli*, *Campylobacter* spp., *Salmonella* spp., *Arcobacter butzleri*, *Staphylococus sciuri*, *Strepto-coccus pneumoniae*, *Pseudomonas aeruginosa*, *Acineto-bacter* spp., and *Pseudomonas putida*, were identified in 12 studies across human, animal, and environmental sources, with a pooled prevalence of 40.8% (95% CI: 21.5–60.2) (Fig. 2).

#### Prevalence of circulating ARGs

ARGs that were identified in three or more studies were included in the meta-analysis. Twelve genes met this requirement, including *ermB*,  $bla_{SHV}$  mecA,



#### Fig. 2 Pooled prevalence of multidrug-resistant bacteria

 $bla_{OXA}$  (including  $bla_{OXA-48}$ ,  $bla_{OXA-61}$ , and  $bla_{OXA-1}$ ), *bla<sub>NDM</sub>* (including *bla<sub>NDM-1</sub>*), *qnr* (including *qnrS*, qnrS1, qnrB, qnrS1, qnrB2, qnrB19, qnrB1, qnrA, qnrC, and qnrD), gyrA, gepA, sul (including sul1, sul2, and sul3),  $bla_{TEM}$  (including  $bla_{TEM-1h}$  and  $bla_{TEM-24}$ ), tet (including tet(W), tet (K), tet (L), tet (G), tet (A), tet (O), tet (M) and tet (B)), and  $bla_{CTX-M}$  (including  $bla_{CTX-M-15}$ ,  $bla_{CTX-M-914}$ ,  $bla_{CTX-M-825}$ ,  $bla_{CTX-M-28}$ ,  $bla_{CTX-M-1}$ ,  $bla_{CTX-M-9}$ ,  $bla_{CTX-M-3}$ ,  $bla_{CTX-M-27}$  and  $bla_{CTX-M-14}$ ). In contrast, genes identified in fewer than three studies were excluded from the meta-analysis. These genes included cat1, cat 4, bla<sub>EBC</sub>, cmIA, fosA, mcr-1, mcr-2, TOHO-1, oqxA, oqxB, fosB, bla<sub>CMY</sub>, bla<sub>VIM</sub>, bla<sub>DIM-1</sub>, bla<sub>CARB</sub>, aac(6")-Iy, mdtK, mdsA, mdsB, mdsC, golS, rssB+, sdiA, dfrA14, ant(9), mdf(A), aph(3'')-Ib, aph(6)-Id, aadA5, fosA7, catA1, catA2, strA, strB, str, aac(3)-II, aadD, aadB, mexB, bla<sub>VIM-1</sub>, bla<sub>FOX-M</sub>, bla<sub>EBC-M</sub>, bla<sub>DHA-M</sub>, aac(6')-Ib-cr, parC, mefA, sal(A), cat(pC221), dfrG, dfrK, aac(6')-aph(2"), cmeB, aadE, oprD, and aacA4.

The most predominant ESBL gene identified was *bla<sub>CTX-M</sub>*, with a prevalence of 31.6% (95% CI: 17.6–45.7), followed by *bla<sub>TEM</sub>* (19.5% [95% CI: 9.7–29.3]), and  $bla_{SHV}$  (3.5% [95% CI: 0.3–6.6]). The pooled prevalence of carbapenemase genes ranged from 17.2% (95% CI: 6.9-27.6) for  $bla_{NDM}$  (including  $bla_{NDM-1}$ ) to 10.3% (95% CI: 1.9-18.7) for *bla<sub>OXA</sub>* (including *bla<sub>OXA-48</sub>*, *bla<sub>OXA-61</sub>*, and  $bla_{OXA-1}$ ). In addition to resistance genes for beta-lactam and carbapenem resistance, other ARGs were detected. These included genes conferring resistance to sulfonamides (including sul1, sul2, and sul3), fluoroquinolones and quinolones (including qnrS, qnrS1, qnrB, qnrS1, qnrB2, qnrB19, qnrB1, qnrA, qnrC, qnrD, qepA and gyrA), tetracycline (including tet(W), tet(K), tet(L), tet(G), tet(A), tet (O), tet (M), and tet (B)), macrolides (ermB), and methicillin (mecA). The pooled prevalence of these genes ranged from 3.9% (95% CI: 0.0-8.5) to 16.4% (95% CI: 3.1-29.8) (Table 1).

# Genes shared across human, animal, and environmental sources

Several ARGs were shared across human, animal, and environmental sources (Fig. 3). These genes were  $bla_{CTX-M-15}$ ,  $bla_{CTX-M}$ ,  $bla_{TEM-1b}$ ,  $bla_{SHV}$ ,  $bla_{NDM}$  (including  $bla_{NDM-1}$ ),  $bla_{OXA-48}$ , sul1, gyrA, ermB, qnrS, and gyrA. The  $bla_{CTX-M-15}$ ,  $bla_{NDM-1}$ ,  $bla_{OXA-48}$ , and sul1 genes were detected in human, animal, and environmental sources. Shared genes between humans and animals included gyrA, ermB, mecA,  $bla_{SHV}$ ,  $bla_{CTX-M}$  and  $bla_{TEM-1b}$ . Animals and the environment shared the  $bla_{OXA-48}$  gene. Additionally, the  $bla_{NDM}$  gene was found to be shared between humans and environmental sources.

#### Discussion

This systematic review adopted a comprehensive "One Health" approach to investigate the available literature on the prevalence of ARGs in bacteria isolated from human, animal, and environmental sources in Ghana. The findings carry significance for public health policies and programmes, as well as future research efforts. Notably, the high prevalence of ESBL genes observed, particularly *bla<sub>CTX-M-15</sub>*, underscores the need for strengthened containment measures. Though the prevalence of carbapenem resistance genes currently appears relatively low, ongoing vigilance is prudent given its potential negative implications for treatment outcomes. The extensive gene sharing revealed reinforces interconnected reservoirs facilitating resistance spread. Coordinated multi-sectoral stewardship is imperative to curtail further development and dissemination. By establishing an evidence base integrating human, animal, and environmental data, this review facilitates strategic planning. The One Health nature of resistance underscores the importance of collaborative surveillance and containment support across sectors.

A total of 38 studies that adequately covered Ghana identified several prevalent ARGs. Although data for the Upper East, Upper West, and Brong-Ahafo Regions were

#### Table 1 Summary of the pooled prevalence of ARGs included in the meta-analysis

Gene	Fre- quen- cy (n)	Pro- por- tion (%)	Bacteria harbouring the gene(s)	Total number of bacterial isolates	Pooled preva- lence of gene among bacte- rial isolates	l <sup>2</sup> (%)	<i>p</i> -value	Sources
$bla_{OXA}$ (including $bla_{OXA-48}$ , $bla_{OXA-61}$ , and $bla_{OXA-1}$ )	75	3.6	Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii, and Proteus mirabilis	965	10.3% (95% Cl: 1.9–18.7)	89	< 0.01	Human, animal and environment
$bla_{NDM}$ (including $bla_{NDM-1}$ )	137	6.5	P. mirabilis, Acinetobacter spp., Pseudo- monas aeruginosa, E. coli, Cronobacter sakazakii, and Providencia stuartii	873	17.2% (95% Cl: 6.9–27.6)	96	< 0.01	Human, animal and environment
$bla_{SHV}$ (including $bla_{SHV-3}$ and $bla_{SHV-73}$ )	36	1.7	K. pneumoniae, E. coli, Enterobacter spp., P. mirabilis, P. aeruginosa, and Salmonella spp.	1051	3.5% (95% Cl: 0.3–6.6)	78	< 0.01	Human and animal
$bla_{TEM}$ ( $bla_{TEM-1b}$ , $bla_{TEM-14}$ , and $bla_{TEM-24}$ )	311	14.8	Staphylococcus aureus, Streptococcus spp., Micrococcus spp., Cellobiococcus spp., Ath- robacter spp., E. coli, Klebsiella spp., Citrobac- ter spp., Enterobacter spp., Proteus spp., and Acinetobacter spp.	1613	19.5% (95% Cl: 9.7–29.3)	97	< 0.01	Human and animal
bla <sub>CTX-M</sub> (including bla <sub>CTX-M-15</sub> , bla <sub>CTX-M-914</sub> , bla <sub>CTX-M-825</sub> , bla <sub>CTX-M-28</sub> , bla <sub>CTX-M-1</sub> , bla <sub>CTX-M-9</sub> , bla <sub>CTX-M-3</sub> , bla <sub>CTX-M-27</sub> , and bla <sub>CTX-M-14</sub> )	969	46.2	E. coli, K. pneumoniae, Enterobacter spp., Salmonella spp., Citrobacter spp., P. mirabilis, Acinetobacter spp., Citrobacter spp., and Providentia spp.	3379	31.6% (95% Cl: 17.6–45.7)	100	< 0.001	Human, animal and environment
<i>tet</i> (including <i>tet(W), tetK,</i> <i>tetL, tetG, tetA, tetO, tetM,</i> and <i>tetB</i> )	89	4.2	S. aureus, A. butzleri, Campylobacter spp., E. coli, P. aeruginosa, K. pneumoniae, and S. pneumoniae	1621	6.4% (95% Cl: 1.9–11.0)	86	< 0.01	Human, animal and environment
qepA	20	1.0	E. coli, Klebsiella spp., Citrobacter spp., and Enterobacter spp.	700	4.7% (95% CI: 0.0–11.1)	83	< 0.01	Human
qnr (including qnrS, qnrS1, qnrB, qnrS1, qnrB2, qnrB19, qnrB1, qnrA, qnrC, and qnrD)	173	8.2	Campylobacter spp., Arcobacter butzleri, Sal- monella spp., E. coli, S. aureus, K. pneumoni- ae, Citrobacter spp., and Enterobacter spp.	3049	6.3% (95% Cl: 3.4–9.1)	89	< 0.01	Human
gyrA	66	3.1	C. freundii, Campylobacter spp., A. butzleri, and Salmonella spp.	638	10.0% (95% Cl: 1.1–19.0)	96	< 0.01	Human and animal
ermB	13	0.6	A. butzleri, Campylobacter spp., Staphylococ- cus spp., and Streptococcus pneumoniae	351	3.9% (95% Cl: 0.0–8.5)	78	0.01	Human and animal
<i>sul</i> (including <i>sul1</i> , <i>sul2</i> , and <i>sul3</i> )	144	6.9	C. freundii, Klebsiella spp., Enterobacter spp., Salmonella spp., E. coli, and P. aeruginosa	1066	16.4% (95% Cl: 3.1–29.8)	96	< 0.01	Human, animal and environment
mecA	65	3.1	S. aureus and Staphylococcus hominis	320	17.2% (95% Cl: 0.0–34.8)	96	< 0.01	Human and animal

unavailable, ARGs were found to be widespread across the country. The majority of these studies focused on human populations. The  $bla_{CTX-M-15}$  gene was found to be the most prevalent  $\beta$ -lactamase gene in humans, animals, and the environment in Ghana. This observation aligns with similar studies conducted in other countries. For example, a study in the Philippines examined the prevalence of the  $bla_{CTX-M-15}$ ,  $bla_{TEM}$  and  $bla_{SHV}$  genes in *E. coli* isolates from broiler farms and revealed  $bla_{CTX-M-15}$ as the predominant  $\beta$ -lactamase gene [53]. Similarly, another study conducted in Bangladesh reported that the  $bla_{CTX-M-15}$  gene was highly prevalent in *E. coli* isolates that cause extraintestinal infections [54]. Furthermore, a study in India revealed a significant prevalence of the  $bla_{CTX-M-15}$  gene in *E. coli* strains obtained from an urban aquatic environment [55]. These data demonstrate the global dissemination of  $bla_{CTX-M-15}$ . Given its high regional circulation, vigorous monitoring of this ESBL gene is important for Ghana to prevent local spread and limit its prevalence from increasing within high-risk settings such as hospitals and farms.

Although the prevalence of the carbapenem resistance genes in Ghana seemed generally lower than those observed for the ESBL genes, their prevalence, which ranged from 10.3% (95% CI: 1.9-18.7) for  $bla_{OXA-48}$  to 17.2% (95% CI: 6.9-27.6) for  $bla_{NDM-1}$ , are arguably high, given their superior public health significance. In other African settings as well, carbapenem resistance has been



Fig. 3 Shared ARGs from human, animal and environmental sources

demonstrated as a rising threat to public health. To illustrate, in Egypt [56] and Cameroon [57] where  $bla_{NDM}$ and  $bla_{OXA}$  (or related genes thereof) have been detected, carbapenem-resistant pathogen prevalence of 28% and 25% have been respectively reported. Besides, especially in Asia, dissemination of the  $bla_{NDM}$  gene has been observed in animals, particularly livestock. For example, He et al. [58] demonstrated the persistence of  $bla_{NDM}$ positive bacteria in chickens and farm environments in China. This study revealed the transmission of bla<sub>NDM</sub>positive bacteria and *bla<sub>NDM</sub>*-bearing plasmids between different farms and locations, indicating that poultry could act as reservoirs for the spread of *bla<sub>NDM</sub>*. The bla<sub>NDM</sub> gene is known to confer resistance to carbapenem antibiotics, which are crucial last-resort treatments for various bacterial infections [59–61].

In addition to carbapenemase and  $\beta$ -lactamase genes, other ARGs that confer resistance to a wide range of antibiotics, such as trimethoprim, fosfomycin, chloramphenicol, rifampicin, aminoglycosides, fluoroquinolones, quinolones, tetracycline, streptomycin, lincosamide, sulfonamides, and colistin, were identified. A major concern is the potential transfer of these resistance genes from environmental bacteria to human pathogens. The *sul1* gene, which confers sulfonamide resistance, was found in isolates from animal, human, and environmental sources, implying that horizontal gene transfer is taking place. Notably, the availability of molecular surveillance data on ARGs in various environmental reservoirs in Ghana is scarce. The limited use of longitudinal investigations introduces uncertainties regarding the seasonal

and temporal dynamics of resistance gene abundance and identities as they move through environmental reservoirs such as soil, waterways, and air. To address this issue, incorporating environmental monitoring into disease treatment and advocacy efforts is essential for public health.

We identified E. coli and S. aureus as the predominant multidrug-resistant bacterial species in Ghana, with an overall prevalence of 40.8% (95% CI: 21.5-60.2). This is lower than the prevalence reported in Bangladesh, where S. aureus and E. coli exhibited high MDR rates in chickens [62]. The mechanisms of  $\beta$ -lactam resistance in S. aureus include target modification, drug inactivation, biofilm formation, and efflux pump expression [63]. Coagulase-negative staphylococci (CoNS) serve as reservoirs for transferable resistance genes that support the survival of specific S. aureus strains [64]. The widespread use of last-resort antibiotics in agriculture, such as tetracyclines, sulfonamides, and streptomycin-penicillin combinations, has contributed to the emergence and spread of MRSA strains with increased resistance to non- $\beta$ -lactam antibiotics [65, 66]. Similarly, *E. coli*, a common gut bacterium in humans and animals, has developed resistance to cephalosporins due to the production of ESBLs [67, 68]. This MDR phenotype in E. coli poses a significant therapeutic challenge, as it limits the available treatment options. The declining efficacy of multiple antibiotic classes highlights the urgent need for continued monitoring of resistance gene profiles and the implementation of antimicrobial stewardship measures to address the growing threat of AMR in Ghana.

#### Strength and limitation

Our systematic review is the first to comprehensively examine the prevalence of ARGs in Ghana. It adopted a One Health approach, considering ARGs across human, animal, and environmental settings to provide a holistic understanding of the country's AMR landscape. However, the findings are limited by some deficiencies in the available data. Some of the studies had incomplete or missing information on the number of resistance genes detected, precluding their inclusion in the final analysis. Methodological heterogeneity, such as the use of varying resistance gene detection methods (culture-based vs. molecular techniques), may have affected the reliability of the quantitative estimates. Furthermore, the reliance on convenience sampling from single hospitals or regions limits the generalisability of the resistance profiles, especially to underrepresented rural areas. The scarcity of data from animal agriculture and environmental settings also hinders the understanding of potential transmission dynamics between these sectors.

#### Conclusion

According to this review, bacteria isolated from human, animal, and environmental sources in Ghana harbour genes linked to antibiotic resistance. AMR is interconnected, as evidenced by the detection of multiple resistance genes in diverse sectors. The high prevalence of carbapenemase genes such as  $bla_{NDM-1}$  and  $bla_{OXA-48}$ , as well as ESBL genes such as *bla<sub>CTX-M-15</sub>*, highlights the urgent need for focused public health interventions. Since horizontal gene transfer allows ARGs to spread resistance between bacteria in different domains, it is clear that the problem of AMR cannot be solved in isolation. Fostering interdisciplinary collaborations between public health, veterinary, and environmental agencies will be important to designing integrated surveillance systems, conducting joint field studies, and coordinating response initiatives attuned to AMR's complex drivers.

#### Recommendations

It is important to strengthen integrated AMR surveillance systems and conduct longitudinal, multi-sector studies to better understand AMR transmission dynamics across human, animal, and environmental domains in Ghana.

#### Abbreviations

AMR	Antimicrobial resistance
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
LMICs	Low- and middle-income countries
MDR	Multidrug resistance
MIC	Minimum inhibitory concentration

MLST	Multilocus sequence typing
MRSA	Methicillin-resistant Staphylococcus aureus
PCR	Polymerase chain reaction
PRISMA	Preferred Reporting Items for Systematic Reviews and
	Meta-Analyses

WGS Whole-Genome Sequencing

#### Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12920-024-02050-y.

Supplementary Material 1 Supplementary Material 2 Supplementary Material 3

#### Acknowledgements

Not applicable

#### Author contributions

E.S.D. and A. O wrote the main manuscript. A.O., E.S.D., A.-H.O., S.D. and F.C.N.K. revised the manuscript. E.S.D. supervised the work. All authors read and approved the final version.

#### Funding

This systematic review was supported by the Fogarty International Center of the National Institutes of Health through the Research and Capacity Building in Antimicrobial Resistance in West Africa (RECABAW) Training Programme hosted at the Department of Medical Microbiology, University of Ghana Medical School (Award Number: D43TW012487). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

#### Data availability

Data is provided within the manuscript or supplementary information files.

#### 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.

Received: 26 August 2024 / Accepted: 12 November 2024 Published online: 12 March 2025

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