

SYSTEMATIC REVIEW

Antimicrobial resistance in *Escherichia coli* at the human–pig interface: A One Health systematic review of genotypic and phenotypic evidence (2019–2024)



Dinda Iryawati^{1,2} , Aisyah Amanda Hanif³ , Fauziyatul Munawaroh⁴ , Sulpiana Sulpiana³ , Chaerul Basri⁵ , Srihadi Agungpriyono^{6,7} , and Hadri Latif⁵

1. Animal Biomedical Study Program, IPB Postgraduate School, School of Veterinary Medicine and Biomedical Sciences, IPB University, Bogor, 16680, Indonesia.
2. Division of Public Health and Ethicomedicolegal, Faculty of Medicine, IPB University, Bogor, 16680, Indonesia.
3. Division of Biomedical Sciences and Medical Education, Faculty of Medicine, IPB University, Bogor, 16680, Indonesia.
4. Division of Pharmacology, Graduate School of Medicine, Kobe University, Kobe, Hyogo, 650-0017, Japan.
5. Division of Veterinary Public Health and Epidemiology, School of Veterinary Medicine and Biomedical Sciences, IPB University, Bogor, 16680, Indonesia.
6. Division of Anatomy, Histology, and Embryology, School of Veterinary Medicine and Biomedical Sciences, IPB University, Bogor, 16680, Indonesia.
7. Global Health Agromaritime–One Health Collaborating Center, IPB University, Bogor, 16680, Indonesia.

ABSTRACT

Background and Aim: Antimicrobial resistance (AMR) presents a major global health threat, particularly at the interface of human and animal health. *Escherichia coli* is a key indicator organism for AMR surveillance and is commonly found in both humans and pigs. Pigs are recognized as significant reservoirs of antibiotic resistance genes (ARGs), facilitating the potential transmission of resistant bacteria to humans. This study aimed to systematically review ARG profiles and associated phenotypic resistance in *E. coli* isolates from human and pig sources using whole-genome sequencing (WGS) data.

Materials and Methods: A systematic search was conducted across PubMed, Scopus, Web of Science, and Wiley Online Library for English-language studies published from January 1, 2019, to October 21, 2024. Studies were included if they reported WGS-based ARG profiles and corresponding phenotypic resistance data for *E. coli* isolates from either humans or pigs. Data extraction and synthesis followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Gene nomenclature was standardized using the National Center for Biotechnology Information and the Comprehensive Antibiotic Resistance Databases.

Results: Of 3,550 records screened, 13 studies met inclusion criteria, comprising 7 on human isolates, 5 on pig isolates, and 1 covering both. Ampicillin resistance was the most prevalent overall (71.4%), with rates of 75% in humans and 100% in pigs. A total of 80 ARGs spanning 11 antibiotic classes were identified, with 58 appearing in multiple studies. The most frequently reported ARGs were *blaTEM*, *sul1*, *sul2*, *dfrA17*, *tet(A)*, and *tet(B)*. Notably, the *qnrS* gene, conferring quinolone resistance, was consistently detected in pig isolates. Geographic variation was observed, with a dominance of Chinese studies and variable resistance patterns across continents.

Conclusion: This review highlights a high prevalence of multidrug-resistant *E. coli* in both human and pig sectors, underscoring the misuse of antibiotics in medical and agricultural settings. The consistent detection of ARGs, particularly *blaTEM* and *qnrS*, calls for urgent cross-sectoral action. A One Health approach is essential to strengthen AMR surveillance, promote prudent antibiotic use, and implement coordinated interventions across human, veterinary, and environmental domains. Future research should integrate metagenomics and environmental monitoring to capture broader resistance dynamics.

Keywords: antibiotic resistance, antimicrobial resistance, *Escherichia coli*, One Health, pigs, resistance genes, surveillance, whole genome sequencing.

Corresponding Author: Dinda Iryawati

E-mail: dindairyawati@apps.ipb.ac.id

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Co-authors: AAH: aisyahsiregar@apps.ipb.ac.id, FM: 242m919m@gsuite.kobe-u.ac.jp, SS: sulpianaupia@apps.ipb.ac.id, CB: chaerul@apps.ipb.ac.id, SA: ysrihadi@apps.ipb.ac.id, HL: hadrilatif@apps.ipb.ac.id

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INTRODUCTION

Antimicrobial resistance (AMR) is recognized as one of the top ten global health threats, posing serious risks to human and animal health, livelihoods, and food security. In 2019 alone, an estimated 4.95 million deaths were associated with bacterial AMR, with 1.27 million deaths directly attributed to resistant infections. These figures underscore the widespread impact of AMR and its significant challenge to achieving the Sustainable Development Goals [1–3]. As a quintessential One Health concern, AMR stems from interconnected factors across human, animal, and environmental systems. The indiscriminate and excessive use of antibiotics in healthcare, veterinary medicine, and agriculture has accelerated the emergence and dissemination of resistance genes, driving AMR toward crisis levels [4, 5].

Escherichia coli serves as a sentinel organism for AMR monitoring due to its prevalence in the gut microbiota of both humans and animals, its remarkable ability to acquire a broad range of antibiotic resistance genes (ARGs), and its role in facilitating horizontal gene transfer [6]. One notable example is the *bla*_{TEM} gene, which confers resistance to beta-lactamase antibiotics and is commonly identified in both clinical and livestock-associated *E. coli* isolates [7]. Pigs, in particular, are key reservoirs of ARGs due to the intensive use of antibiotics, high-density farming practices, and the elevated potential for horizontal gene exchange within their gastrointestinal microbiota. These factors enable the potential transmission of resistant bacteria to humans through direct contact, environmental exposure, or foodborne pathways [8–11].

Beyond their agricultural significance, pigs are also valued as biomedical models for studying human physiology, developmental processes, and responses to pathogens [12]. Comparative genomic analyses of *E. coli* isolates from humans and pigs offer valuable insights into shared resistance mechanisms, cross-species gene flow, and overarching AMR trends, informing more effective control strategies [13, 14]. Whole-genome sequencing (WGS), with its high resolution, enables precise detection and characterization of resistance determinants and their transmission dynamics. When combined with clinical and epidemiological data, WGS serves as a powerful tool to enhance AMR surveillance and inform targeted public health interventions [15].

Despite the growing body of literature on AMR in both human and animal health, integrated, high-resolution analyses comparing resistance gene profiles in *E. coli* across the human–pig interface remain limited. While individual studies have documented the prevalence of ARGs and phenotypic resistance patterns in clinical and agricultural settings, these are often reported in isolation, without cross-sectoral comparison or standardization of methods. Moreover, the use of WGS – a powerful tool for detecting ARGs, mobile genetic elements, and transmission dynamics – has

not been systematically applied to explore the overlap in resistomes between human and pig-derived *E. coli*. Few reviews have attempted to synthesize such genomic and phenotypic data concurrently, particularly under a One Health framework that accounts for the complex interactions between antibiotic use, resistance development, and interspecies gene flow. In addition, regional disparities in AMR surveillance data – especially from low- and middle-income countries – create blind spots in global risk assessments and hinder the development of unified mitigation strategies.

This study aims to systematically review and synthesize published evidence on AMR gene profiles and corresponding phenotypic resistance patterns in *E. coli* isolates from human and pig sources between January 2019 and October 2024. By focusing on studies utilizing WGS and phenotypic antimicrobial susceptibility testing (AST), the review seeks to (i) identify and compare dominant ARGs and resistance patterns across sectors, (ii) evaluate sector-specific and geographic trends in resistance gene distribution, and (iii) highlight key ARGs indicative of potential cross-species transmission. Through this comparative One Health analysis, the study endeavors to provide actionable insights for AMR surveillance, stewardship, and policy development aimed at minimizing resistance spread between humans and animals.

MATERIALS AND METHODS

Ethical approval

This study did not require ethical approval as it was based exclusively on the analysis of previously published literature and did not involve any human or animal subjects.

Study period and location

The study was conducted from July to October 2024 in Bogor, West Java, Indonesia.

International Prospective Register of Systematic Reviews (PROSPERO) registration

The systematic review protocol was prospectively registered in PROSPERO under the registration number CRD42025646668 (<https://www.crd.york.ac.uk/PROSPERO/view/CRD42025646668>). The protocol outlines the objectives, eligibility criteria, and methodological approach, ensuring transparency and reproducibility in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines [16].

Eligibility criteria based on PICOS framework

The inclusion and exclusion criteria were developed using the PICOS framework:

- Population (P): *E. coli* isolates obtained from human and pig sources
- Intervention (I): WGS for the identification of AMR genes (ARGs)
- Comparison (C): Comparative analysis between human-derived and pig-derived *E. coli* isolates

- Outcomes (O): Prevalence and distribution of genotypic ARGs and corresponding phenotypic resistance profiles
- Study design (S): Original research articles reporting both genotypic and phenotypic resistance data; only peer-reviewed studies published in English were included.

Studies were excluded if they:

- Did not include both WGS and phenotypic AST data
- Focused solely on antibiotic use patterns or surveillance
- Were review articles, commentaries, or conference abstracts
- Lacked English full-text availability.

Literature search strategy

A comprehensive and systematic literature search was conducted across four major scientific databases: PubMed, Scopus, Web of Science, and Wiley Online Library. The search included articles published between January 01, 2019, and October 21, 2024, and was limited to studies written in English.

Search terms were grouped into four categories related to *E. coli*, AMR, human and pig sources, and genomic methods. Terms within each category were combined using the Boolean operator “OR” and across categories using “AND.” The search was applied to titles, abstracts, and keywords. The software and platforms supporting the review process are summarized in Table 1, and the full search strategy is provided in Table S1.

Study selection process

The study selection followed a two-stage screening protocol:

1. Initial screening: After deduplication, 3,071 unique articles were screened based on titles and abstracts by four independent reviewers using Rayyan software

2. Full-text review: Articles passing the initial screen were assessed for eligibility against the inclusion and exclusion criteria. Discrepancies were resolved through discussion and consensus.

Following this process, 13 studies met the criteria and were included in the final review.

Data extraction and management

Key information was extracted from each included study and compiled into a standardized Excel spreadsheet. Extracted variables included (Table S2):

- First author and publication year
- Country/region of study
- Sample source (human, pig, or both)
- Number of *E. coli* isolates
- AST method and WGS platform used
- Identified ARGs and associated antibiotic resistance profiles.

The data extraction was independently cross-checked by two reviewers to ensure accuracy.

ARG classification and nomenclature standardization

ARGs were categorized into functional classes and standardized using the National Center for Biotechnology Information (NCBI) and the Comprehensive Antibiotic Resistance Database (CARD). Harmonization of gene names was performed using accepted synonyms, e.g., *strA* was reclassified as *aph(3'')-Ib* and *strB* as *aph(6)-Id* [17–20].

Only ARGs reported in at least two separate studies and validated by NCBI or CARD were included in the final analysis. Genes such as *aac(3)-Ia*, *aac(6)-Ib*, *aadA23*, *cmlA*, *dfrA25*, *mcr-3*, and *qnrD*, which were either reported in a single study or not validated by these databases, were excluded.

Data synthesis and analysis

Descriptive statistics were used to summarize the prevalence of phenotypic resistance and the distribution of ARGs across the included studies. Resistance proportions were calculated for each antibiotic class and ARG, stratified by source (human or pig). Comparative assessments were made to identify sector-specific trends and regional patterns.

All analyses were conducted using Microsoft Excel (Version 2505 Build 16.0.18827.20102). Due to the heterogeneity of study designs, sampling methods, and antimicrobial susceptibility testing protocols, a meta-analytical approach was not undertaken. No formal statistical tests were applied to compare prevalence values between groups. Future iterations may benefit from using inferential methods or graphical assessments (e.g., funnel plots) to examine potential publication bias or regional clustering of results.

RESULTS

Study selection and characteristics

A total of 3,550 records were retrieved from four databases: Scopus (n = 2,923), Web of Science (n = 490),

Table 1: Software and platforms supporting the review process.

Tool/Software	Function	Version/Source
Rayyan	Aggregated records from multiple databases, removed duplicates, and facilitated article screening	Web-based (https://www.rayyan.ai)
Microsoft® Excel® for Microsoft 365	Extracted, managed, and organized data from included studies	Version 2505 Build 16.0.18827.20102
Mendeley Cite MapChart	Managed references and citations Generated geographical visualizations	Version 1.67.0 Version 6.7.3 (https://www.mapchart.net)
Canva	Designed visual materials and figures	Web-based (https://www.canva.com)

PubMed (n = 129), and Wiley Online Library (n = 8). After the removal of 479 duplicates, 3,071 unique articles were subjected to title and abstract screening, which excluded 2,718 irrelevant studies. Full-text assessment of the remaining 353 articles led to the exclusion of 240 papers that did not meet the inclusion criteria. Ultimately, 13 studies were included in the final analysis (Figure 1).

These 13 studies comprised 7 focused on human-derived *E. coli* isolates [21–27], 5 on pig-derived isolates [28–32], and 1 study including isolates from both sources [33], resulting in 14 data points for analysis. The selected studies were published between January 01, 2019, and October 21, 2024, and were geographically distributed across Asia, Europe, and North America (Figure 2 and Table S3).

Antibiotic resistance patterns

A total of 39 antibiotics were investigated across all included studies (Table S3). Ampicillin showed the highest overall resistance rate at 71.4%, with 75% prevalence in human isolates and 100% in pig isolates. Tetracycline resistance was especially high in pigs, with one study reporting a 100% resistance rate. Resistance to sulfonamides, trimethoprim, and fluoroquinolones was also frequently observed in both sectors (Figure 3 and Table S4).

Distribution of AMR genes (ARGs)

Across the 13 studies, a total of 80 distinct ARGs conferring resistance to 11 antibiotic classes were identified (Table S3). Of these, 58 ARGs were

reported in at least two studies and were included in the comparative analysis (Figure 4 and Table S5). These genes included:

- Aminoglycosides: 18 ARGs
- Beta-lactamase: 9 ARGs
- Trimethoprim: 10 ARGs
- Tetracyclines: 6 ARGs
- Chloramphenicol: 4 ARGs
- Sulfonamides: 3 ARGs
- Quinolones: 2 ARGs
- Fosfomycin: 2 ARGs
- Others: 1 ARG each for colistin, macrolides, rifampin, and multidrug resistance.

The most frequently reported genes were *blaTEM*, *sul1*, *sul2*, *dfrA17*, *tet(A)*, and *tet(B)*, reflecting resistance to beta-lactamase, sulfonamides, trimethoprim, and tetracyclines.

Geographic distribution of ARGs

Regional patterns in ARG profiles were observed:

- Europe (e.g., Spain, Ireland, and Portugal): Frequent detection of *blaTEM-1A*, *blaTEM-1B*, *blaCTX-M-14*, *aac(6')-Ib-cr5*, and *aph(6)-Id*.
- Asia (particularly China and India): Higher diversity of beta-lactamase genes such as *blaNDM-4*, *blaNDM-5*, *blaCTX-M-55*, *blaCTX-M-65*, and *blaCTX-M-15*, along with aminoglycoside resistance genes such as *aac(3)-IIa*, *aadA1*, *aadA5*, *aph(6)-Id*, and *aph(3')-Ia*.
- Africa (Uganda, Malawi, South Africa): Dominated by *blaTEM-1A*, *blaTEM-1B*, *blaCTX-M-15*, *blaCTX-M-27*, *aac(3)-IIa*, *aph(6)-Id*, and *aph(3')-Ib*.

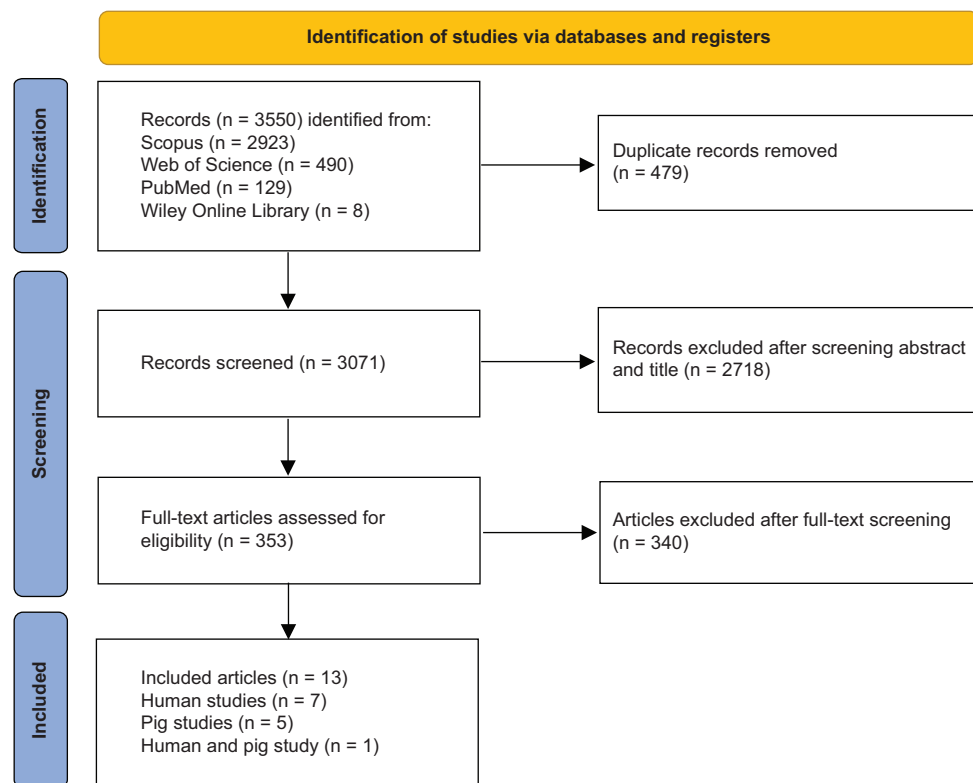


Figure 1: The Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart illustrating the study selection process, showing inclusion of 13 studies across human, pig, and combined sources.

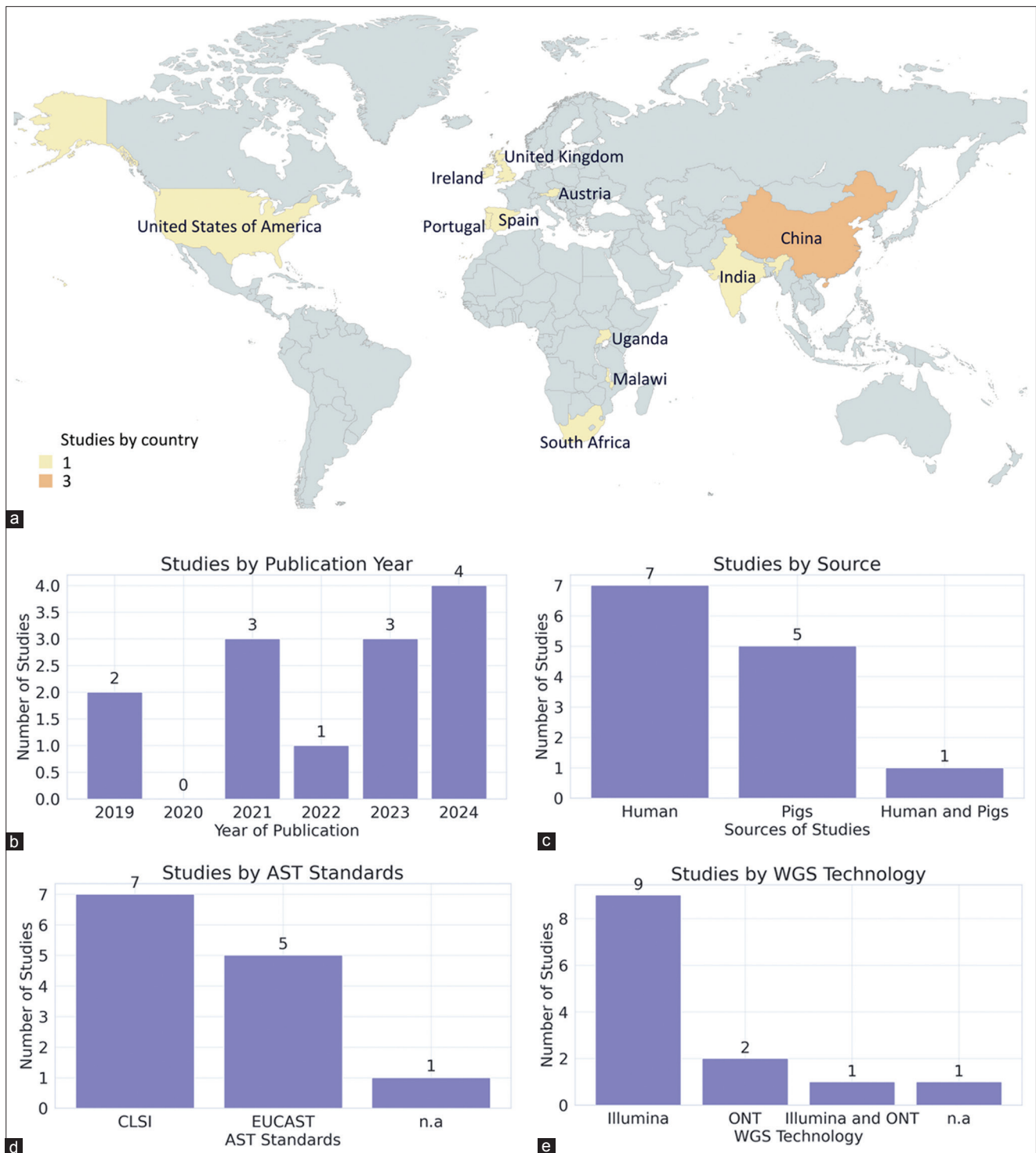


Figure 2: Characteristics of included studies: (a) Geographic distribution; (b) year of publication; (c) sample source (human, pig, and both); (d) aspartate transaminase methodology (Clinical and Laboratory Standards Institute [CLSI] vs. European Committee on Antimicrobial Susceptibility Testing); (e) Whole-genome sequencing platform (e.g., Illumina, Oxford Nanopore Technologies). Notably, China accounted for the largest number of studies, and most studies employed CLSI guidelines and Illumina sequencing.

- Americas: Commonly reported ARGs included *aac(3)-IIa*, *aac(3)-IIId*, *aac(6')-Ib-cr5*, *aph(6)-Id*, *blaCTX-M-14*, *blaCTX-M-15*, and *blaTEM-1B*.

Distinct ARGs in human versus pig isolates

Notable differences were observed between human and pig-derived *E. coli* isolates:

- Pig-specific ARGs: The *qnrS* gene, associated with quinolone resistance, was consistently detected in all pig studies. Other genes – *aac(3)-VIa*, *aadA22*, *aadA24*, *blaSHV*, *tet(C)*, *tet(D)*, *tet(X4)*, and *dfrA21* – were exclusively found in pig isolates.
- Human-specific ARGs: The *blaEC* gene was detected only in human isolates.

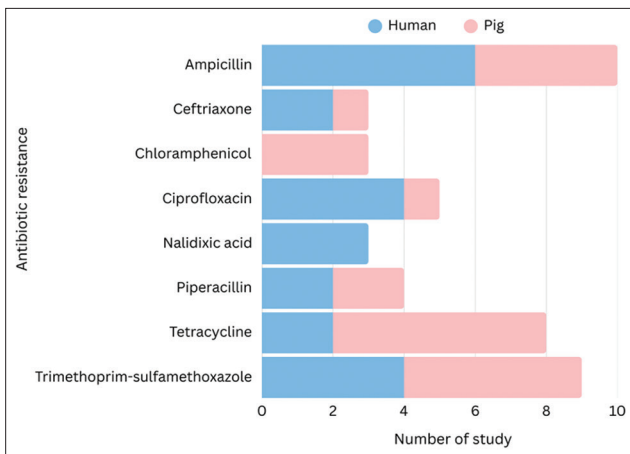


Figure 3: Prevalence of antibiotic resistance in *Escherichia coli* isolates from humans and pigs. Ampicillin had the highest resistance rate in both groups, while tetracycline resistance was most pronounced in pig isolates.

The co-occurrence of multiple ARGs within individual isolates was frequently reported, particularly in multidrug-resistant (MDR) *E. coli* strains. This highlights the complexity of resistance mechanisms and the importance of integrated surveillance across both sectors (Table S4).

DISCUSSION

Global implications of AMR

AMR is a critical global health threat with far-reaching implications for human and animal health, healthcare infrastructure, food safety, and environmental sustainability [34]. The findings of this review affirm these concerns, particularly the high levels of resistance observed in *E. coli* from food-producing animals such as pigs. These results are consistent with global AMR patterns and underscore the urgent need for coordinated, cross-sectoral mitigation strategies [33]. Although this review focuses specifically on human and pig sectors, it reinforces the One Health paradigm, emphasizing the interconnectedness of human, animal, and environmental health. Notably, MDR was highly prevalent in isolates from both sources, with ampicillin resistance being particularly dominant (Figure 3).

Sector-specific resistance trends

Resistance profiles varied across regions and host populations, reflecting differences in antibiotic usage patterns, regulatory frameworks, and genetic determinants of resistance [35].

Beta-lactamase resistance

Extensive resistance to ampicillin, a widely used beta-lactamase antibiotic, is evident across both human and pig isolates. In human medicine, ampicillin is commonly prescribed for urinary tract infections (UTIs) [21–24], biliary tract infections, and various community-acquired infections [23, 26]. In the veterinary sector, it is frequently used

to treat gastrointestinal and respiratory diseases in pigs [36, 37]. Overuse in both domains has led to the proliferation of ampicillin-resistant *E. coli*, contributing to prolonged illnesses, increased treatment costs, and higher mortality rates [38].

The predominant resistance mechanism is mediated by the *bla*TEM gene [39], which encodes extended-spectrum beta-lactamase commonly found on plasmids and transposons [40]. Its widespread presence in both human and pig isolates illustrates the potential for horizontal gene transfer and highlights pigs as key reservoirs for resistant strains that can be transmitted to humans [7, 41].

Tetracycline resistance

Tetracycline resistance was particularly high in pig isolates, consistent with its long-standing use in livestock for disease prevention and growth promotion [28, 42–44]. Its broad-spectrum activity and affordability, combined with lax regulations, have contributed to the widespread use in animal husbandry [33]. Environmental contamination from slaughterhouse waste has further facilitated the dissemination of tetracycline-resistant bacteria [44–46]. Tetracycline is also frequently prescribed in human medicine for infections such as respiratory tract infections, acne, and some sexually transmitted infections [47].

Key resistance genes – *tet(A)* and *tet(B)* – were identified in both human and pig isolates. *tet(A)* is typically plasmid-encoded, promoting rapid horizontal transfer, while *tet(B)* is often associated with transposons and integrative mobile elements, enhancing its dissemination potential [45, 48].

Sulfonamide resistance

Resistance to sulfonamides was also widespread. *sul1* was identified in all included studies and *sul2* in the majority. In pig production, sulfonamides such as sulfamethazine and sulfamethoxazole are commonly administered with trimethoprim to treat respiratory and gastrointestinal infections [49, 50]. In human medicine, co-trimoxazole remains essential, particularly for immunocompromised populations [51].

sul1 is frequently linked with class 1 integrons, which promote the co-transfer of multiple resistance genes [52]. While *sul2* is also mobile, its lower frequency may reflect variations in genetic context or antimicrobial selection pressures [23, 53].

Trimethoprim resistance

Trimethoprim resistance – largely attributed to the *dfrA17* gene – was common across both sectors, but more prevalent in pig isolates. *dfrA17* encodes dihydrofolate reductase, reducing trimethoprim's therapeutic efficacy [54]. Its integration within class 1 integrons enhances its mobility and spread [55–57].

Given the presence of *E. coli* in meat products, resistant strains from livestock pose a tangible risk to public health through foodborne transmission,

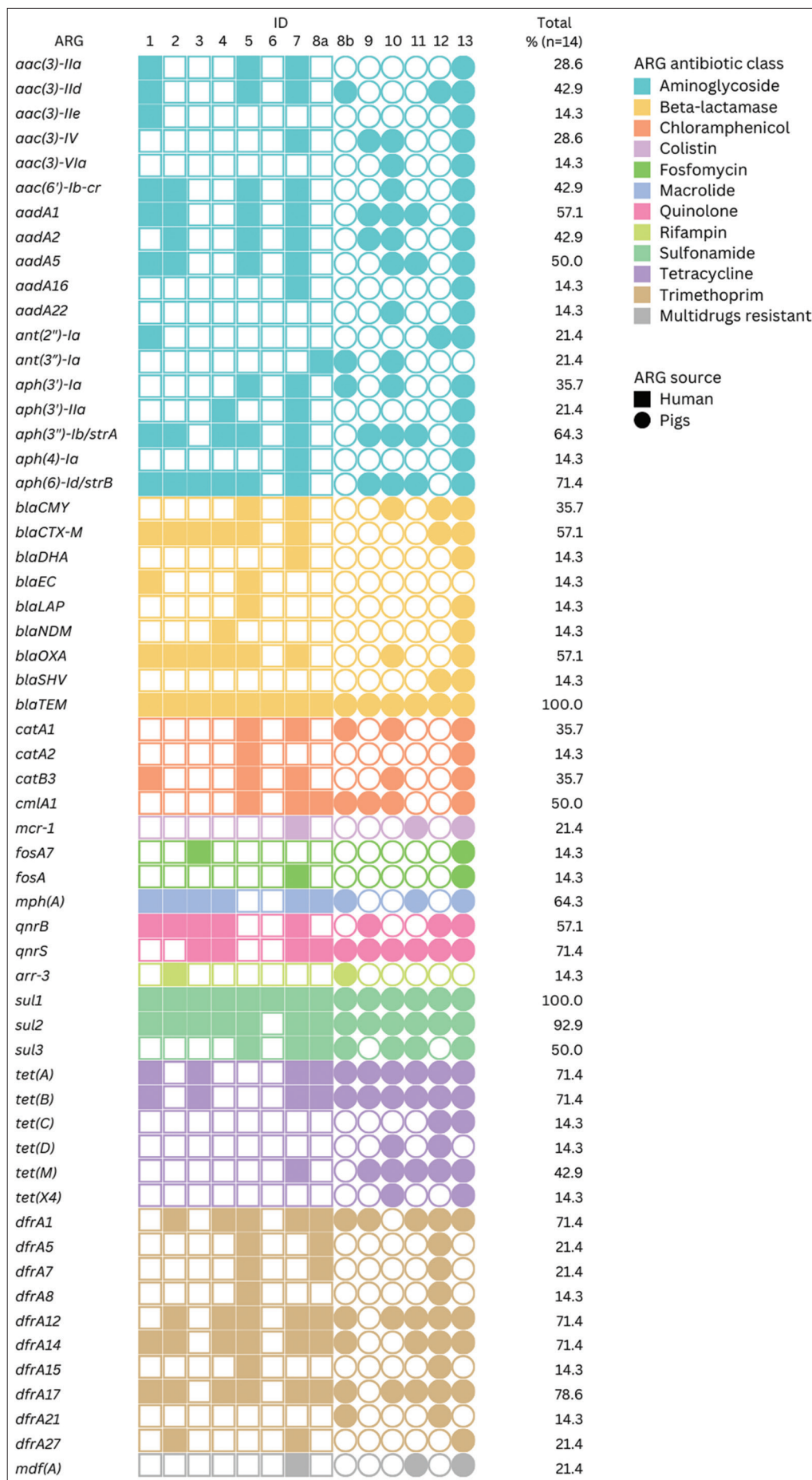


Figure 4: Distribution of the 58 most frequently detected antibiotic resistance genes across studies, highlighting *blaTEM*, *sul1*, *sul2*, *dfrA17*, *tet(A)*, and *tet(B)* as dominant markers.

potentially leading to UTIs or bacteremia in humans [58]. Conversely, human-origin resistant strains may re-enter animal populations through environmental contamination [59].

Aminoglycoside resistance

Among aminoglycoside resistance determinants, *aph(6)-Id* was the most frequently reported. This gene encodes a phosphotransferase enzyme that inactivates aminoglycosides such as kanamycin and neomycin [60]. In pig farming, aminoglycosides such as gentamicin and apramycin are used to treat post-weaning diarrhea [60], whereas in human medicine, they are reserved for severe infections due to potential nephrotoxicity and ototoxicity [61].

The recurrent detection of *aph(6)-Id* in pig-derived *E. coli*, particularly enterotoxigenic strains, highlights its veterinary and zoonotic relevance [62].

Quinolone resistance

The *qnrS* gene, a plasmid-mediated quinolone resistance marker [63], was consistently reported in pig isolates and less frequently in human samples. *qnrS* often coexists with other resistance genes on mobile plasmids, facilitating its spread [64].

Quinolones are widely used in both veterinary and clinical settings due to their broad-spectrum efficacy and oral bioavailability [9, 65, 66]. However, their extensive use in animal production has led to selective pressure that enhances resistance development, raising concerns about transmission through meat, water, or direct contact [8, 67, 68].

Cross-sectoral use of critical antimicrobials

All major antibiotic classes discussed in this review are utilized in both human and veterinary medicine. Their dual use emphasizes the shared responsibility in the emergence and propagation of resistance:

- Quinolones are classified as highest priority critically important antimicrobials and should be restricted to essential uses in animals
- Aminoglycosides are critically important antimicrobials recommended for treatment purposes only
- Ampicillin, tetracyclines, sulfonamides, and trimethoprim are highly important antimicrobials and require stringent regulation to prevent misuse [37, 69].

Policy implications and recommendations

The concurrent detection of resistance to multiple antibiotic classes in *E. coli* from both human and pig sectors highlights the need for comprehensive, cross-sectoral AMR mitigation. The findings of this review strongly support the implementation of One Health strategies, which include:

- Enforcing strict prescription regulations for antimicrobials in the human and veterinary sectors
- Promoting non-antibiotic alternatives in livestock production
- Strengthening surveillance systems to monitor emerging resistance trends.

Furthermore, the identification of sector-specific resistance patterns and ARGs may inform the design of risk-based, integrated AMR surveillance frameworks. These frameworks should facilitate data sharing, harmonize testing protocols, and guide evidence-based interventions to preserve antimicrobial efficacy across the human-animal-environment continuum [70, 71].

Strengths and limitations

A key strength of this review is the dual synthesis of genotypic and phenotypic resistance data from *E. coli* isolates across two interconnected sectors. This integrative approach offers a more comprehensive understanding of resistance dynamics and aids in policy development.

However, several limitations must be acknowledged:

- The small number of eligible studies (n = 13) limits the generalizability of the findings.
- Geographic bias exists, with a disproportionate number of studies originating from China and a notable absence of data from South America.
- The exclusion of non-English language studies and gray literature may contribute to publication bias.
- Variability in AST methods (e.g., CLSI vs. EUCAST) and WGS platforms across studies may affect cross-comparability.
- Due to study heterogeneity, a meta-analytical approach was not feasible.
- Nonetheless, the use of standardized selection criteria and meticulous data curation helped ensure methodological consistency and reduce potential bias.

CONCLUSION

This systematic review highlights the widespread presence of AMR in *E. coli* isolates from both human and pig sources, reinforcing the urgent need for coordinated action under the One Health framework. A total of 80 ARGs across 11 antibiotic classes were identified, with *blaTEM*, *sul1*, *sul2*, *dfrA17*, *tet(A)*, *tet(B)*, and *qnrS* emerging as the most frequently detected and epidemiologically significant. Ampicillin exhibited the highest overall resistance rate (71.4%), with 100% resistance reported in pig isolates, while tetracycline and sulfonamide resistance were also markedly prevalent across both sectors. Notably, the *qnrS* gene was consistently reported in pig isolates, indicating selective pressure from veterinary quinolone use and highlighting potential foodborne and environmental transmission routes. Sector-specific ARG patterns and regional disparities – especially the predominance of studies from China – further underscore the uneven global distribution of AMR surveillance data and the need for harmonized monitoring systems.

To address the limitations of current surveillance and research, the future studies should integrate metagenomic approaches to capture ARGs from unculturable and environmental microbiomes, expand

geographic representation in underreported regions, and develop interoperable AMR databases to enhance cross-sectoral data sharing. Investigations into the role of mobile genetic elements in horizontal gene transfer and evaluations of antimicrobial policy interventions using longitudinal surveillance data are also crucial. Additionally, exploring environmental reservoirs and tracking ARG dissemination through the food chain could provide critical insights into indirect transmission pathways and inform upstream mitigation strategies.

This review reinforces that AMR in *E. coli* is a shared burden across human and animal health domains, driven by overlapping antibiotic use and facilitated by environmental connectivity. The consistent detection of high-risk ARGs in pigs and their genetic overlap with human isolates call for immediate, unified interventions. Strengthening antibiotic stewardship, regulatory oversight, and genomic surveillance through One Health collaboration is essential to preserve the efficacy of critical antimicrobials and mitigate the global AMR threat. Coordinated, evidence-based policies and proactive investment in surveillance infrastructure are not only desirable but also imperative for global health security.

DATA AVAILABILITY

The supplementary data can be made available from the corresponding author upon request.

AUTHORS' CONTRIBUTIONS

DI: Conceptualization, screening and selection of studies, formal analysis, investigation, methodology, project administration, writing original draft, artwork, and review and editing. HL, SA, and CB: Data interpretation and critically revised the manuscript for important intellectual content. AAH, FM, and SS: Screening and selection of studies and revised the manuscript. All authors have read and approved the final manuscript.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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