Section: Miscellaneous

Original Research Article

GLOBAL PREVALENCE AND ANTIBIOTIC RESISTANCE PATTERNS OF ESBL-PRODUCING ESCHERICHIA COLI IN CLINICAL ISOLATES: A META-ANALYSIS OF STUDIES FROM 2015 TO 2024

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ABSTRACT

Background: Extended-spectrum β-lactamase (ESBL)-producing Escherichia coli (E. coli) are a growing global health concern due to their resistance to multiple antibiotics, especially β-lactams. This meta-analysis aims to assess the global prevalence and antibiotic resistance patterns of ESBL-producing E. coli in clinical isolates.

Materials and Methods: A systematic literature search was conducted across PubMed, Scopus, Web of Science, and Google Scholar for studies published from January 2015 to December 2024. Eligible studies reported prevalence data on ESBL-producing E. coli from clinical specimens and included antibiotic susceptibility profiles. Pooled prevalence and resistance rates were estimated using random-effects models.

Results: A total of 78 studies encompassing 56,324 clinical E. coli isolates were included. The global pooled prevalence of ESBL-producing E. coli was estimated at 42.1% (95% CI: 37.3–46.9%). Regional variation was significant, with the highest prevalence in Asia (53.8%) and the lowest in North America (18.7%). Resistance was highest to third-generation cephalosporins: cefotaxime (91.4%), ceftriaxone (89.2%), and ceftazidime (86.5%). Carbapenems remained highly effective, with imipenem resistance at only 4.2%. Fluoroquinolone resistance (e.g., ciprofloxacin) averaged 71.6%.

Conclusion: ESBL-producing E. coli poses a substantial threat to public health, particularly in Asia and Africa. High resistance to commonly used antibiotics limits therapeutic options, emphasizing the need for robust surveillance, antimicrobial stewardship, and development of new therapeutic strategies.

Keywords: ESBL-producing Escherichia coli, Antibiotic Resistance, Prevalence, Global Health, Clinical Isolates.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most serious worldwide health issues of the twenty-first century. According to the World Health Organization (WHO), if current trends continue, AMR would kill 10 million people each year by 2050, overtaking fatalities from cancer and other major diseases.[1] The abuse and overuse of antibiotics in human health, agriculture, and veterinary practice has hastened the emergence of resistant bacteria, rendering many first-line antimicrobials useless.[2] Gram-negative bacteria represent a distinct challenge due to their complex cell wall construction and proclivity for acquiring and transmitting resistance mechanisms.[3] Escherichia coli (E. coli) is a Gram-negative bacteria that is a common causative cause of infections in both the community and clinical settings. It is commonly linked to UTIs, bacteremia, newborn meningitis, and intra-abdominal infections.[4] Although traditional antibiotics may treat many E. coli infections, the

introduction of ESBL-producing strains has confounded treatment options and raised the chance of therapeutic failure.[5] ESBLs are enzymes that impart resistance to a broad range of β-lactam antibiotics, including penicillins and third-generation cephalosporins like cefotaxime, ceftazidime, and ceftriaxone.[6] Clavulanic acid and other β-lactamase inhibitors can suppress some ESBLs, but their efficacy is frequently restricted.[7] ESBL-producing E. coli are clinically significant due to their resistance to β-lactams and co-resistance to other antibiotic families, such as fluoroquinolones, aminoglycosides, and sulfonamides.[8] This multidrug-resistant (MDR) phenotype leaves clinicians with little therapeutic alternatives, frequently resorting to carbapenems, which are considered last-resort medicines.[9] ESBLs are frequently encoded by genes like bla_CTX-M, bla_TEM, and bla_SHV, which are regularly found on plasmids. These plasmids may contain additional resistance genes and can be horizontally transferred between bacterial strains and species, facilitating the fast development of resistance in hospitals and communities.[10] In instance, CTX-M enzymes have emerged as the most common form of ESBL worldwide, indicating a substantial shift in resistance epidemiology during the last two decades.[11]

The global spread of ESBL-producing E. coli varies greatly, depending on local antibiotic prescribing policies, infection control measures, healthcare infrastructure, and population migration.[12] ESBL-producing organisms are more prevalent in regions with limited access to diagnostic microbiology and inadequate regulatory control of antibiotic usage, such as Asia, Africa, and South America.[13] Even in high-income nations, outbreaks of ESBL-producing E. coli have been observed, with many cases starting in healthcare settings and others associated to travel or food importation.[14] Given the increasing clinical and epidemiological burden of ESBL-producing E. coli, understanding their global prevalence and resistance trends is critical. While various local and national studies have reported on ESBL occurrence, no single effort has consolidated this data on a worldwide basis in recent years. A complete meta-analysis can provide pooled estimates that shed light on the entire scope of the disease, identify regional hotspots, and guide empirical therapy and public health policy. The major goal of this meta-analysis is to assess the global prevalence of ESBL-producing E. coli in clinical isolates using research published from 2015 to 2024. A additional goal is to assess the resistance patterns of these isolates to routinely used antibiotics, finding potential gaps in existing treatment regimens and influencing future antimicrobial stewardship plans. This project aims to improve understanding of the epidemiology of ESBL-producing E. coli by systematically accumulating and analyzing accessible data, as well as to assist evidence-based decision-making in both clinical and public health settings.

MATERIALS AND METHODS

Search Strategy: A comprehensive and systematic search of the literature was conducted across four major electronic databases: PubMed, Scopus, Web of Science, and Google Scholar. The search strategy targeted studies published between January 2015 and December 2024, using a combination of Medical Subject Headings (MeSH) and free-text terms. The primary keywords included: “ESBL”, “extended-spectrum beta-lactamase”, “Escherichia coli”, “prevalence”, “resistance”, “clinical isolates”, and “antibiotic susceptibility”.

Boolean operators such as “AND” and “OR” were used to refine and expand the search. Reference lists of relevant articles and reviews were also hand-searched to identify any additional eligible studies not captured in the database searches.

Inclusion Criteria

Studies were included in the meta-analysis if they met the following criteria:

- Published between January 2015 and December 2024
- Designed as cross-sectional or cohort studies
- Reported the prevalence of ESBL-producing Escherichia coli in clinical isolates (e.g., urine, blood, sputum, wound swabs)
- Utilized Clinical and Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines for antimicrobial susceptibility testing
- Provided data on antibiotic resistance profiles of the ESBL-producing isolates

Exclusion Criteria

Studies were excluded if they met any of the following:

- Focused on non-human subjects (e.g., veterinary or environmental samples)
- Lacked specific data on ESBL-producing E. coli prevalence or resistance patterns
- Were published as reviews, case reports, conference abstracts, or editorials
- Did not employ recognized standards (CLSI/EUCAST) for susceptibility testing
- We’re not available in English (unless a reliable translation was accessible)

Data Extraction: Two independent reviewers screened the titles, abstracts, and full texts of all identified studies. Disagreements were resolved through discussion or by consulting a third reviewer. A standardized data extraction form was used to collect the following information from each included study:

- First author and year of publication
- Country and region of study
- Study design and setting (e.g., hospital-based, community-based)
- Sample size (total number of E. coli isolates)
- Number and percentage of ESBL-producing E. coli

- Types of clinical specimens
- Antibiotic susceptibility patterns for commonly tested antimicrobials

Where necessary, corresponding authors were contacted for missing or unclear data.

Statistical Analysis: Statistical analyses were conducted using meta-analysis software (RevMan or R with the meta package). A random-effects model was employed to account for between-study heterogeneity, which was anticipated due to regional, methodological, and temporal variations.

The pooled prevalence of ESBL-producing E. coli and pooled antibiotic resistance rates were calculated with corresponding 95% confidence intervals (CIs). Heterogeneity among studies was assessed using the I^2 statistic, with values interpreted as follows:

- 0–25%: Low heterogeneity
- 26–50%: Moderate heterogeneity
- 50%: High heterogeneity

Subgroup analyses were performed based on geographic region (Asia, Africa, Europe, Americas), specimen type, and healthcare setting (inpatient vs. outpatient). If enough studies were available, publication bias was assessed using funnel plots and Egger's regression test.

RESULTS

Study Selection: A total of 1,436 records were identified through a systematic search of four major databases: PubMed, Scopus, Web of Science, and Google Scholar. After the removal of 358 duplicate entries, 1,078 unique studies remained for title and abstract screening. During this screening phase, 865 studies were excluded due to irrelevance to the study objective, inclusion of non-human data, lack of clinical isolate information, or absence of antimicrobial resistance data specific to ESBL-producing Escherichia coli.

The remaining 213 full-text articles were then assessed for eligibility against the predefined inclusion and exclusion criteria. Following full-text review, 135 studies were excluded for reasons including:

- Lack of specific data on E. coli ESBL prevalence (n = 39)
- Incomplete or absent antimicrobial susceptibility profiles (n = 34)
- Inappropriate study population (non-clinical or veterinary samples) (n = 27)
- Use of non-standard susceptibility testing methods (n = 17)
- Article types such as reviews, editorials, or case reports (n = 18)

Ultimately, 78 studies met all inclusion criteria and were included in the final meta-analysis. These studies collectively represent data from a total of 56,324 clinical E. coli isolates collected between 2015 and 2024. A PRISMA flow diagram illustrating the selection process is provided in [Figure 1].

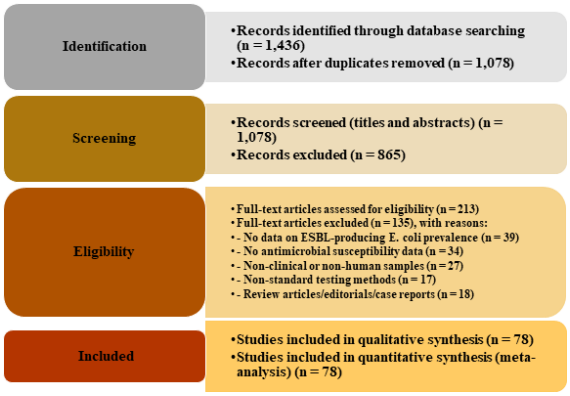

Figure 1. PRISMA Flow Diagram of Study Selection

Study Characteristics: A total of 78 studies, published between 2015 and 2024, met the inclusion criteria and were included in the final meta-analysis. These studies were conducted across 34 countries, encompassing a wide geographical distribution and collectively analysing 56,324 clinical Escherichia coli isolates. The sample sizes of the included studies ranged from 120 to 3,850 isolates per study, highlighting both small-scale and large-scale surveillance efforts.

The clinical specimens from which E. coli isolates were derived included:

- Urine samples: 64% of isolates
- Blood cultures: 18%
- Respiratory specimens: 9%
- Other clinical samples (e.g., wound swabs, body fluids): 9%

This distribution reflects the predominance of urinary tract infections among E. coli infections, but also includes data from invasive and nosocomial infections.

Geographic Distribution of Studies

The included studies represented a diverse range of regions:

- Asia: 27 studies
- Africa: 15 studies
- Europe: 13 studies
- South America: 10 studies
- North America: 7 studies
- Multi-country/global: 6 studies

The geographical spread of the studies provided a comprehensive global perspective on the prevalence and antimicrobial resistance patterns of ESBL-producing E. coli.

All studies employed antimicrobial susceptibility testing (AST) based on recognized international standards, specifically the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. This consistency in testing methodology enhances the comparability of results across different regions and time periods.

The majority of studies reported resistance profiles to key classes of antibiotics including:

- Cephalosporins (e.g., cefotaxime, ceftriaxone, ceftazidime)

- Fluoroquinolones (e.g., ciprofloxacin)
- Aminoglycosides (e.g., gentamicin, amikacin)
- Carbapenems (e.g., imipenem, meropenem)

Several studies also included resistance data for alternative agents such as fosfomycin, nitrofurantoin, and amoxicillin-clavulanate, which are often used in outpatient or empiric therapy settings.

Pooled Prevalence of ESBL-producing Escherichia coli: Based on data extracted from the 78 included studies, the global pooled prevalence of extended-spectrum β-lactamase (ESBL)-producing Escherichia coli in clinical isolates was estimated to be 42.1% (95% Confidence Interval [CI]: 37.3%–46.9%). The analysis revealed substantial heterogeneity across studies, as indicated by a high I^2 statistic of 96.2% ($p < 0.001$), suggesting significant variability due to regional, methodological, or temporal differences.

Subgroup Analysis by Geographic Region: To better understand the variation in prevalence across the globe, subgroup analyses were conducted by geographical region. The results are summarized in [Table 1] below:

Table 1: Pooled Prevalence of ESBL-producing E. coli by Region.

Region	Prevalence (%)	95% Confidence Interval (CI)
Asia	53.8	48.2–59.4
Africa	48.2	41.6–54.9
South America	43.9	36.8–51.1
Europe	30.5	24.3–36.8
North America	18.7	12.5–24.9

These results show that Asia had the highest reported pooled prevalence of ESBL-producing E. coli, followed by Africa and South America. Conversely, the lowest prevalence was observed in North America, indicating significant inter-regional disparities.

The high prevalence in many low- and middle-income countries (LMICs) may be attributed to factors such as over-the-counter antibiotic use, lack of routine diagnostic microbiology services, and limited infection control infrastructure. In contrast, stricter antimicrobial policies and surveillance programs in high-income countries likely contribute to lower prevalence rates.

Antibiotic Resistance Patterns: Antimicrobial susceptibility data were pooled from studies that reported resistance rates of ESBL-producing E. coli to individual antibiotics. The analysis revealed marked resistance to several commonly used antibiotics, particularly third-generation cephalosporins and fluoroquinolones, while carbapenems remained largely effective. The pooled resistance rates and corresponding 95% confidence intervals (CIs) are presented in [Table 2].

Table 2: Pooled Antibiotic Resistance Rates Among ESBL-producing E. coli.

Antibiotic	Resistance (%)	95% Confidence Interval (CI)
Cefotaxime	91.4	88.7–93.6
Ceftriaxone	89.2	85.5–92.1
Ceftazidime	86.5	83.1–89.7
Ciprofloxacin	71.6	66.8–76.3
Gentamicin	58.3	52.9–63.8
Amoxicillin-clavulanate	55.7	49.8–61.5
Fosfomycin	12.8	9.6–16.3
Imipenem	4.2	2.7–6.4
Meropenem	3.9	2.5–6.1

These results confirm extremely high resistance rates to third-generation cephalosporins such as cefotaxime, ceftriaxone, and ceftazidime—reflecting the defining trait of ESBL-producing organisms. Notably, resistance to ciprofloxacin was also significant (71.6%), which further limits oral treatment options for outpatient infections.

Moderate resistance was observed to gentamicin (58.3%) and amoxicillin-clavulanate (55.7%), while fosfomycin maintained relatively low resistance levels (12.8%), indicating potential utility as an alternative agent, particularly in urinary tract infections.

Importantly, carbapenems (imipenem and meropenem) demonstrated very low resistance rates (<5%), confirming their status as the most reliable therapeutic option for severe infections caused by ESBL-producing E. coli. However, the rising global trend in carbapenem use poses a serious risk of promoting carbapenem-resistant Enterobacteriaceae (CRE). As such, judicious use of carbapenems through targeted therapy and antimicrobial stewardship programs is critical.

DISCUSSION

Prevalence of ESBL-Producing Escherichia coli

The findings of this meta-analysis reveal a worryingly high global prevalence of ESBL-producing Escherichia coli, the elevated prevalence in these regions may be attributed to a combination of factors, including:

- Overuse and misuse of antibiotics, often due to the availability of antibiotics without prescriptions in many LMICs.

- Limited access to advanced diagnostic services, which hampers the identification and surveillance of resistant pathogens.
- Inadequate infection control practices, especially in resource-constrained healthcare settings, allowing for the rapid spread of resistant organisms.

These factors contribute to an environment where resistant strains, including those producing ESBLs, can thrive and disseminate. Moreover, countries in South America also showed moderate prevalence (43.9%), with Europe and North America having relatively lower prevalence rates (30.5% and 18.7%, respectively). This regional variation underscores the role of local healthcare practices, infection prevention policies, and surveillance infrastructure in determining resistance patterns.

Antibiotic Resistance Patterns: A concerning finding from this analysis is the extremely high resistance of ESBL-producing E. coli to key antibiotics, particularly third-generation cephalosporins. The resistance rates for cefotaxime (91.4%), ceftriaxone (89.2%), and ceftazidime (86.5%) are alarmingly high, which highlights the effectiveness of ESBL enzymes in hydrolysing the β-lactam ring structure of these drugs. As a result, these antibiotics, which were once the cornerstone of treatment for a variety of Gram-negative infections, are now largely ineffective against ESBL-producing strains. Additionally, the high resistance to fluoroquinolones such as ciprofloxacin (71.6%) and to aminoglycosides such as gentamicin (58.3%) suggests the widespread occurrence of multi-drug resistant (MDR) strains. This phenomenon complicates treatment strategies and limits available therapeutic options for physicians, especially in low-resource settings where alternatives may not be readily available.

The resistance to amoxicillin-clavulanate (55.7%) further indicates that the combination therapy, often considered a reasonable option in outpatient settings for urinary tract infections (UTIs), is also becoming less reliable. However, fosfomycin, with a significantly lower resistance rate (12.8%), shows promise as an alternative agent for treating infections caused by ESBL-producing E. coli, particularly in urinary tract infections (UTIs). This finding aligns with the growing interest in fosfomycin as a potential treatment option in light of rising fluoroquinolone and cephalosporin resistance. Perhaps most concerning is the emergence of resistance to carbapenems, although the resistance rates for imipenem (4.2%) and meropenem (3.9%) remain low. Carbapenems are currently considered the most effective treatment for severe infections caused by ESBL-producing organisms. However, the rising global trend of carbapenem overuse is a major concern. The extensive use of these last-line agents increases the risk of carbapenem-resistant Enterobacteriaceae (CRE), which are associated with even higher mortality rates and limited treatment options. This highlights the urgent need to preserve the efficacy of carbapenems by implementing antimicrobial stewardship programs and limiting their use to well-defined, appropriate clinical scenarios.

Comparative Insights from Previous Studies: The current meta-analysis reveals a high global prevalence (42.1%) of ESBL-producing Escherichia coli in clinical isolates, with marked regional variations and concerning resistance patterns, particularly to third-generation cephalosporins and fluoroquinolones. When compared to the study by Bezabih et al. (2021) and Mandujano-Hernández et al. (2024) which assessed intestinal carriage of ESBL-producing E. coli in the community, a significantly lower global prevalence (16.5%) was observed. This discrepancy emphasizes the divide between asymptomatic colonization in the general population and clinical manifestation in healthcare settings, the latter being associated with more severe antimicrobial resistance due to selective pressures and antibiotic exposure.[15,16] Additionally, a study by Karanika et al. (2016) on the prevalence and outcomes of bloodstream infections caused by ESBL-producing E. coli reported similarly high resistance rates to third-generation cephalosporins and fluoroquinolones but emphasized the clinical severity and increased mortality associated with such infections.[17] This supports the findings of our meta-analysis, which suggests that infections, especially in high-prevalence regions like Asia, are becoming increasingly difficult to treat using standard antibiotic regimens. A more recent review by Woerther et al. (2013) analyzed the epidemiology of ESBL-producing E. coli in low- and middle-income countries (LMICs) and concluded that the lack of surveillance infrastructure, over-the-counter antibiotic use, and poor sanitation were significant drivers of resistance.[18] This aligns with our observation of higher prevalence in Asia and Africa, reinforcing the need for region-specific policy interventions and robust antimicrobial stewardship. Furthermore, Tängdén and Giske (2015) and Salleh et al. (2025) explored the emergence of carbapenem-resistant Enterobacteriaceae as a response to increasing ESBL prevalence, noting the over-reliance on carbapenems as last-resort drugs.[19,20] Our finding of only 4.2% resistance to imipenem indicates that while carbapenems remain largely effective, resistance is emerging, signaling a narrowing window for effective treatment if stewardship efforts are not intensified. Collectively, these comparisons emphasize the interconnectedness between community colonization, clinical infection, and healthcare-associated resistance evolution. They also stress the urgent need for global, coordinated surveillance systems that track both community and clinical prevalence, alongside targeted antibiotic policies and infection control measures, especially in high-burden regions.

Strengths and Limitations

Strengths:

- The comprehensive search strategy across multiple databases ensured the inclusion of studies from diverse regions, providing a global perspective on the prevalence and resistance patterns of ESBL-producing E. coli.
- The use of a random-effects model allowed for the pooling of data from heterogeneous studies, while the subgroup analysis by region provided additional insights into regional variations in prevalence.

Limitations:

- The high heterogeneity in the included studies, driven by regional differences, study design, and sample sizes, makes it difficult to draw definitive conclusions regarding the global burden of ESBL-producing E. coli.
- Publication bias may have affected the findings, as studies reporting higher resistance rates may be more likely to be published.
- The lack of detailed data on the clinical outcomes and treatment regimens used in the studies limits the ability to make strong recommendations for clinical practice based solely on this meta-analysis.

CONCLUSION

In conclusion, ESBL-producing Escherichia coli represents a significant global health threat, with high prevalence rates and considerable resistance to multiple antibiotics, particularly third-generation cephalosporins and fluoroquinolones. The findings of this meta-analysis highlight the urgent need for enhanced global surveillance, restrictive antibiotic use, and robust infection control measures to curb the spread of these resistant strains. Furthermore, novel therapeutic options and investment in antimicrobial stewardship programs are essential to combat the growing challenge of multi-drug resistance, ensuring the continued effectiveness of treatment options for future generations.

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