



REVIEW ARTICLE

Antibiotic Resistance in Enterobacteriaceae: Mechanisms, Prevalence, and Public Health Impact: A Review

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ABSTRACT

Antibiotic resistance (AR) has emerged as a critical global health challenge, threatening the effectiveness of modern medicine, food security, and sustainable development. This review explores the underlying mechanisms, current trends, and regional distributions of antibiotic resistance, with a focus on Enterobacteriaceae—a major family of gram-negative bacteria responsible for a wide range of hospital- and community-acquired infections. The misuse and overuse of antibiotics in human and veterinary medicine, coupled with poor infection control practices and environmental dissemination, have accelerated the emergence of resistant strains such as extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*, as well as carbapenem-resistant Enterobacteriaceae (CRE). Globally, resistance rates to third-generation cephalosporins, fluoroquinolones, and aminoglycosides are alarmingly high, with MDR strains increasingly reported in clinical settings. The situation in the Middle East is particularly concerning, where high resistance rates are documented across Iraq, Iran, Saudi Arabia, Egypt, Turkey, and conflict-affected regions like Syria and Yemen. Factors such as political instability, unregulated antibiotic access, and under-resourced healthcare systems contribute significantly to the problem. Additionally, environmental reservoirs and zoonotic transmission play an emerging role in the spread of resistance genes. Addressing antibiotic resistance requires coordinated international action, enhanced surveillance, antimicrobial stewardship, investment in novel therapeutics, and a one health approach that integrates human, animal, and environmental health. This review underscores the urgent need for comprehensive interventions to curb the rising tide of antibiotic resistance in Enterobacteriaceae and safeguard global health.

Keywords: Antibiotic resistance; Enterobacteriaceae; Antimicrobial stewardship.

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INTRODUCTION

Antibiotic Resistance

Antibiotic resistance (AR) has emerged as one of the most pressing challenges to public health, food security, and sustainable development in the 21st century. The phenomenon occurs when bacteria evolve mechanisms to withstand the drugs that are designed to kill them, rendering standard treatments ineffective and leading to persistent infections, increased medical costs, prolonged hospital stays, and higher mortality rates (World Health Organization [WHO], 2020).

The discovery of antibiotics in the early 20th century revolutionized modern medicine, saving millions of lives and making previously fatal infections treatable. However, over the past decades, the misuse and overuse of antibiotics in human medicine, veterinary practices, agriculture, and aquaculture have accelerated the emergence and spread of resistant bacteria (Ventola, 2015; Alaa *et al.*, 2020). The widespread availability of antibiotics without prescription,

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especially in low- and middle-income countries, further exacerbates the issue (Laxminarayan *et al.*, 2013). Alarmingly, resistance has been observed not only in hospital settings but also in community-acquired infections and environmental reservoirs such as wastewater and soil (Berendonk *et al.*, 2015).

Antibiotic-resistant bacteria such as Methicillin-resistant *Staphylococcus aureus* (MRSA), Carbapenem-resistant Enterobacteriaceae (CRE), and multidrug-resistant (MDR) strains of *Escherichia coli* and *Klebsiella pneumoniae* have become increasingly prevalent worldwide (Centers for Disease Control and Prevention [CDC], 2019). Infections caused by these “superbugs” are difficult to treat and often require last-resort antibiotics like colistin, which themselves are now facing diminishing efficacy (Falagas *et al.*, 2010).

The genetic mechanisms underlying antibiotic resistance are diverse and complex. They include chromosomal mutations, acquisition of resistance genes via horizontal gene transfer (HGT), and the presence of mobile genetic elements such as plasmids, transposons, and integrons (Davies & Davies, 2010). These genetic adaptations can confer resistance to multiple antibiotic classes simultaneously, complicating therapeutic strategies.

In addition to clinical implications, antibiotic resistance poses a significant threat to global development. The World Bank estimates that by 2050, antimicrobial resistance could cause a 3.8% reduction in global GDP and push up to 28 million people into extreme poverty if no action is taken (World Bank, 2017). The COVID-19 pandemic further compounded the issue as increased antibiotic use during the crisis likely contributed to resistance, although data is still emerging (Rawson *et al.*, 2020).

Addressing antibiotic resistance requires a multifaceted and global approach. Key strategies include improving surveillance of resistance patterns, promoting responsible antibiotic use through stewardship programs, enhancing infection prevention and control measures, and investing in the development of new antibiotics and alternative therapies such as bacteriophage therapy and antimicrobial peptides (O'Neill, 2016). International collaborations, such as the Global Action Plan on Antimicrobial Resistance coordinated by the WHO, underscore the need for a “One Health” approach that integrates human, animal, and environmental health efforts.

In conclusion, antibiotic resistance is a dynamic and rapidly evolving threat that transcends national borders and disciplines. Urgent and coordinated action is essential to preserve the effectiveness of antibiotics for current and future generations.

Rate of Antibiotic Resistance in Enterobacteriaceae

Enterobacteriaceae is a large family of Gram-negative bacteria that includes clinically important pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp.,

Proteus spp., and *Serratia* spp. These organisms are a major cause of healthcare- and community-acquired infections, including urinary tract infections (UTIs), bloodstream infections, pneumonia, and intra-abdominal infections. The rise in antibiotic resistance among Enterobacteriaceae is a serious global concern, particularly due to the emergence of multidrug-resistant (MDR) and extended-spectrum β -lactamase (ESBL)-producing strains (Salih *et al.*, 2019).

Globally, the prevalence of resistance to commonly used antibiotics such as cephalosporins, fluoroquinolones, and aminoglycosides among Enterobacteriaceae has increased significantly in recent years. According to the World Health Organization (2020), resistance to third-generation cephalosporins in *E. coli* and *K. pneumoniae* exceeds 50% in many low- and middle-income countries. In some regions, particularly in South Asia and parts of Africa, resistance rates can reach 70 to 80%, severely limiting treatment options.

A notable concern is the widespread production of extended-spectrum β -lactamases (ESBLs), enzymes that hydrolyze and inactivate β -lactam antibiotics, including penicillins and third-generation cephalosporins. ESBL-producing *E. coli* and *K. pneumoniae* are increasingly reported worldwide. For example, a study by Jean *et al.* (2022) found that more than 60% of *K. pneumoniae* bloodstream isolates in Southeast Asia were ESBL producers. Similarly, in the United States, approximately 14% of *E. coli* and 22% of *K. pneumoniae* isolates from healthcare settings were ESBL-positive (CDC, 2019).

Carbapenem resistance among Enterobacteriaceae is another alarming trend, especially in *K. pneumoniae*. Carbapenem-resistant *K. pneumoniae* (CRKP) is associated with high mortality due to limited treatment options. In 2019, the CDC classified carbapenem-resistant Enterobacteriaceae (CRE) as an urgent public health threat. Globally, CRE rates vary, but some countries report resistance levels as high as 40% in hospital settings (Tamma *et al.*, 2021).

Resistance to fluoroquinolones, such as ciprofloxacin and levofloxacin, is also widespread. In many regions, over 50% of *E. coli* isolates are resistant to these agents, particularly among isolates causing urinary tract infections (WHO, 2020). Aminoglycoside resistance, particularly to gentamicin and amikacin, is also increasing among multidrug-resistant Enterobacteriaceae strains.

The rising trend of multidrug resistance (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) phenotypes further complicates clinical management. MDR strains, defined as resistant to at least one agent in

three or more antibiotic categories, have been found in up to 70% of *K. pneumoniae* and *E. coli* isolates in some tertiary care hospitals globally (Liu *et al.*, 2020).

Distribution of Antibiotic Resistance in Enterobacteriaceae in the Middle East

The Middle East has emerged as one of the global hotspots for antibiotic resistance, particularly among members of the Enterobacteriaceae family such as *E. coli*, *K. pneumoniae*, *Enterobacter* spp., and *Proteus* spp. (Rahim *et al.*, 2021). The region faces unique challenges due to a combination of factors, including the overuse and misuse of antibiotics in healthcare and agriculture, limited antimicrobial stewardship programs, poor infection control practices, political instability, and widespread availability of antibiotics without prescription (Abbas *et al.*, 2022).

Numerous studies have reported high rates of multidrug resistance (MDR) and extended-spectrum β -lactamase (ESBL)-producing strains of Enterobacteriaceae across the Middle East. In Iraq, for example, ESBL-producing *E. coli* and *K. pneumoniae* have been detected in more than 50 to 70% of clinical isolates from hospitals, particularly in urinary tract and bloodstream infections (Al-Mayahie, 2021; Hama Soor *et al.*, 2021). Similar findings have been reported in Iran, where ESBL production was observed in up to 64% of *K. pneumoniae* isolates, with a high resistance rate to third-generation cephalosporins and fluoroquinolones (Moein *et al.*, 2020).

In Saudi Arabia, studies have identified *E. coli* resistance rates of over 50% to ciprofloxacin and ampicillin, and more than 40% resistance to third-generation cephalosporins (Al Yousef *et al.*, 2019). *K. pneumoniae* strains isolated from ICU settings in Riyadh have also shown high resistance to carbapenems, with a growing prevalence of carbapenemase-producing strains such as those harboring the *blaKPC* and *blaNDM* genes.

In Egypt, the situation is equally alarming. Surveillance studies have found that over 70% of Enterobacteriaceae isolates from hospitals are ESBL producers. *E. coli* and *K. pneumoniae* strains frequently exhibit resistance to cefotaxime, ceftazidime, and fluoroquinolones, and colistin resistance is also emerging, raising serious concerns about the availability of effective last-line treatment options (Shaaban *et al.*, 2021).

Turkey, situated at the crossroads of Europe and the Middle East, has been identified as a key hub for the dissemination of antibiotic resistance genes, particularly those encoding ESBLs and carbapenemases. A national report indicated that 64% of *K. pneumoniae* and 48% of *E. coli* isolates were ESBL-positive, with increasing detection

of carbapenem-resistant Enterobacteriaceae (CRE) strains harboring *OXA-48* and *NDM-1* genes (Gundogdu *et al.*, 2020).

Furthermore, refugee populations and conflict zones such as Syria and Yemen face significant barriers to infection control and laboratory diagnostics. Studies have reported exceptionally high resistance rates in these areas, including CRE prevalence exceeding 20% among Enterobacteriaceae isolates, largely driven by unregulated antibiotic use in both hospitals and the community (Alrahmany *et al.*, 2023).

Environmental and zoonotic pathways also contribute to the dissemination of resistant Enterobacteriaceae in the Middle East. Resistance genes have been identified in wastewater, food products, livestock, and poultry, indicating a complex and interconnected chain of transmission that aligns with the One Health perspective (Yezli & Li, 2022).

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