

A Comprehensive Review of the Global Distribution of Antibiotic Resistance Genes in Bacteria

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Abstract: Antibiotic resistance is a global problem and is a cause of million death yearly worldwide. Bacteria resist antibiotic through many ways and used different strategies to fight antimicrobial for survival. Health sectors loss millions of Unites States Dollars yearly for using non useful antibiotics due to antibiotic resistance. Proper management of treatment and proper utilization of antimicrobial is necessary to avoid emergence of drug resistance and assisting patients to have better treatments. There are several drug resistance genes made by bacteria and all of them work to deactivate chemical structure of antibiotics. Each group of bacteria can produce different resistance gene; however, some of them work in all species of bacteria, gram positive and gram-negative bacteria. Gathering data about resistance genes in necessary in a short review to provide detailed information about this issue. This review aims to provide a comprehensive overview of the global distribution of antibiotic resistance genes, emphasizing their impact on public health and the necessity for coordinated global efforts to combat this growing threat. Understanding the global distribution of antibiotic resistance genes is crucial for developing effective strategies to mitigate their spread and ensure the continued efficacy of antibiotics in treating bacterial infections. In conclusion, the global spread of antibiotic resistance genes poses a significant threat to public health. Immediate action is required to monitor and control this phenomenon, with a focus on responsible antibiotic use, global collaboration, and continued research into alternative treatments.

Keywords: Antibiotic resistance, resistance genes, Global distribution, Bacterial Resistance, Antimicrobial resistance

1. Introduction

1.1 Antimicrobial resistance (AMR)

It occurs when bacteria evolve the way that protect them from the action of antimicrobials (antibiotics used to treat infections) (Magiorakos et al., 2012). All groups of bacteria can become resistance to one or more antibacterial drugs, making them no longer effective. In Fungi called antifungal resistance, and in bacteria it called antibiotic resistance. Together all of these come under the umbrella of antimicrobial resistance (Magiorakos et al., 2012).

Microbes resistant to multiple antimicrobials are called multidrug resistant (MDR) and are sometimes referred to as superbugs. Although antimicrobial resistance is a naturally occurring process, it is often the result of improper usage of the drugs and management of the infections (Saha & Sarkar, 2021; Tanwar et al., 2014; Bhat et al., 2023).

Antibiotic resistance is a major subset of AMR, that applies specifically to bacteria that become resistant to antibiotics. Resistance in bacteria can arise naturally by genetic mutation, or by one species acquiring resistance from another. Resistance can appear spontaneously because of random mutations, but also arises through spreading of resistant genes through horizontal gene transfer. However, extended use of antibiotics seems to encourage the selection of mutations which can render antibiotics ineffective (Dabour et al., 2016; Fisher et al., 2022). Antifungal resistance is a subset of AMR, that specifically applies to fungi that have become resistant to antifungals. Resistance to antifungals can arise naturally, for example by genetic mutation or through aneuploidy. Extended use of antifungals leads to development of antifungal

resistance through various mechanisms (Fisher et al., 2022). it will pose a problem in some bacteria that is difficult to treat such as helicopter pylori and its shown that the prevalence is very high especially in the Middle East (Hussein Ali, 2022).

Several studies showed the danger and prevalence of resistance genes in bacteria and the rate is high in alarming level. This study rings the bell of threat in health sector that hinder the treatment in hospitals. In addition, it tells us the pace of spreading the issue globally. In middle east and Asia, rate of resistance genes and antibiotic resistance is alarmingly high in different types of bacteria (mm3). In some studies, the information in gathered how the phenomenon is common in all countries of middle east (Rahim et al., 2020).

1.2 Reasons of antibacterial resistance:

Antibiotic resistance occurs when bacteria evolve mechanisms to resist the effects of drugs that once killed them or inhibited their growth. This resistance means that standard treatments become ineffective, and infections persist or worsen (Lee Ventola, 2015). Here's a brief overview of the key aspects:

1.2.1 Causes

- 1) **Overuse and Misuse:** Frequent and inappropriate use of antibiotics, including in agriculture, contributes significantly to resistance. This includes taking antibiotics for viral infections (where they're ineffective) or not completing prescribed courses.
- 2) **Natural Selection:** Bacteria can develop resistance through mutations or by acquiring resistance genes from other bacteria. These resistant strains survive and proliferate when exposed to antibiotics.

- 3) **Inadequate Infection Control:** Poor hygiene and infection control practices can spread resistant bacteria in healthcare settings and communities.

1.3.2 Consequences

- 1) **Treatment Failures:** Infections that were once easily treatable can become severe or even untreatable, leading to longer hospital stays, higher medical costs, and increased mortality.
- 2) **Limited Treatment Options:** Resistance reduces the effectiveness of antibiotics, making it more difficult to treat common infections and increasing the reliance on more expensive or toxic alternatives.
- 3) **Increased Spread:** Resistant bacteria can spread more easily, leading to outbreaks that are harder to control (Frieri et al., 2017; Lee Ventola, 2015).

1.4 Prevention and Mitigation

- 1) **Responsible Antibiotic Use:** Only use antibiotics when prescribed by a healthcare professional, and complete the full course as directed.
- 2) **Infection Control Practices:** Good hygiene, vaccination, and infection control measures in healthcare settings help prevent the spread of resistant bacteria.
- 3) **Research and Development:** Investing in the development of new antibiotics and alternative treatments is crucial to staying ahead of resistance trends.
- 4) **Global Collaboration:** Tackling antibiotic resistance requires coordinated efforts across countries and sectors, including public health initiatives, regulatory measures, and education (Frieri et al., 2017; Lee Ventola, 2015).

Addressing antibiotic resistance is a complex challenge that involves the cooperation of healthcare professionals, policymakers, and the public to ensure antibiotics remain effective for future generations. It also hinders the benefits of some bacteria that used for the probiotic treatment of infections because bacteria are known for its probiotic importance in treatment of some wounds and burns (Ahmed et al., 2021).

1.5 Risks of Antibiotic resistance:

Antibiotic resistance poses several significant risks to public health and well-being. Here's a detailed look at some of the key risks:

1.5.1. Treatment Failures

- **Ineffective Treatments:** Antibiotic-resistant infections are harder to treat because standard antibiotics are no longer effective. This can lead to prolonged illnesses and complications.
- **Need for Alternative Drugs:** Treating resistant infections may require using more expensive or toxic drugs, which might not be as effective or have more severe side effects.

1.5.2. Increased Mortality and Morbidity

- **Higher Death Rates:** Infections that cannot be treated effectively can lead to higher mortality rates. This is particularly concerning for vulnerable populations such as the elderly, infants, and those with weakened immune systems.

- **Severe Complications:** Untreated or inadequately treated infections can lead to severe health complications and increased hospitalization.

1.5.3. Extended Hospital Stays

- **Longer Recovery:** Patients with resistant infections often require longer hospital stays, which can increase the risk of acquiring other infections and lead to higher healthcare costs.
- **Increased Healthcare Burden:** Extended treatment periods place additional strain on healthcare resources and systems.

1.5.4. Spread of Resistant Strains

- **Community Spread:** Resistant bacteria can spread from person to person, potentially causing outbreaks in communities and healthcare settings.
- **Environmental Contamination:** Resistant bacteria can be released into the environment through various means, including wastewater from hospitals and farms, which can contribute to the spread of resistance.

1.5.5. Limited Treatment Options

- **Diminished Choices:** The effectiveness of existing antibiotics diminishes as resistance spreads, limiting treatment options for common infections and complicating the management of more complex cases.
- **Increased Reliance on Last-Resort Antibiotics:** More critical and less frequently used antibiotics may be used as last-resort options, which can further promote resistance if they are overused.

1.5.6. Economic Impact

- **Higher Costs:** Treating resistant infections often involves more expensive drugs, longer hospitalizations, and more intensive care, which can significantly increase healthcare costs.
- **Economic Burden on Families:** The financial strain of extended illness and treatment can impact patients and their families, potentially leading to financial hardship.

1.5.7. Impact on Medical Procedures

- **Complications with Surgery and Treatments:** Many medical procedures, including surgeries and cancer treatments, rely on effective antibiotics to prevent infections. Resistance can increase the risk of complications and reduce the safety of these procedures.

1.5.8. Global Health Threat

- **Cross-Border Challenges:** Antibiotic resistance is a global issue, and resistant strains can spread across borders, affecting international health and complicating global public health efforts. Addressing these risks requires a comprehensive approach, including responsible antibiotic use, improved infection control practices, investment in new treatments, and global collaboration to mitigate the impact of antibiotic resistance (Cassini et al., 2019; Piri et al., 2018).

1.6 Distribution of antibiotic resistance genes in Asia and middle east

several researches had conducted about the prevalence and distribution of bacteria carrying antibiotic resistance genes in Asia such as China, Pakistan, India and Bangladesh and also in middle east such as Iran, Iraq, Egypt, and turkey. In all areas the level of antibiotic resistance genes is very high and all types of resistance genes have been reported.

1.6.1 Pakistan:

In one study, it was found that the rate of ESBL, MBL and AmpC in clinical isolates of *P. aeruginosa* was found to be 23.94%, 40.84% and 35.21% respectively. Co-production of ESBL and AmpC were also was found. There were 14 (19.71%) CTX-M-15 harboring bacteria which were ESBL (64.28%), MBL (21.42%) and AmpC (14.28%) producer (Ullah et al., 2017). In another study betalactamase was found in Enterobacteriaceae in Pakistan and the results and rates was as follow. Notably, 15% of ESBL producing strains harbored blaSHV gene while 43% were positive for blaOXA gene (Waheed et al., 2019).

1.6.2 China:

Out of 224 *K. pneumoniae* strains, 5 (2.2%) were identified to carry inactivated ESBL blaSHV genes. Interestingly, three of the five antibiotic-sensitive *K. pneumoniae* strains containing ESBL blaSHV genes still exhibited mRNA transcription of blaSHV, while the other two exhibited no mRNA transcription (Xu et al., 2014). In another study was found that bacteria isolate in clinical samples. The isolates mainly harbored bla_{CTX-M} ($n = 51$, 70.8%) and bla_{SHV} ($n = 46$, 63.9%) genes. High prevalence of PMQR genes *qnrA1* ($n = 24$, 33.3%), *qnrB* ($n = 4$, 5.6%), *qnrS1* ($n = 2$, 2.8%), and *aac(6)-Ib-cr* ($n = 21$, 29.2%) was observed. Furthermore, CHβLs IMP-4 ($n = 6$, 8.3%) and IMP-8 ($n = 4$, 5.6%), as well as class I integrons ($n = 29$, 40.3%), were found in the ESBL-producing *E. cloacae* (Cao et al., 2017).

1.6.3 Bangladesh

There are several studies in Bangladesh showing the prevalence of resistance genes, in this stud the rate was as follow. blaTEM-type and blaOXA-1-type genes were detected in 33 (82.5%) and 19 (47.5%) isolates, respectively. Virulence genes that are present in diarrhoeagenic *E. coli* were not found. Class-1 integron was present in 20 (50%) isolates (Lina et al., 2014). Genes encoding resistance to tetracycline [tetA, 100% (35/35); tetB, 31.43% (11/35)], fluoroquinolone [qnrA, 35.71% (10/28); qnrB, 25% (7/28)], and streptomycin [aadA1, 90.24% (37/41)] were detected in the isolated *E. coli* (Islam et al., 2022).

1.6.4 Iraq

Several studies were carried out in Iraq showing the rate of beta lactamase is very high in all species of Enterobacteriaceae. In *E. coli* isolate from animal and human the rate was as follow: 18 (20.6%) isolates were positive with blaCTX-M and blaTEM and 17 (19.5%) of them were found in heavy antibiotic users, but only one blaCTX-M gene (Alaa et al., 2020). blaTEM-1 and blaShv were found in five isolate. 21 isolates (17.2%) of Proteus. Three isolates (10.3%) were positive to blaTEM-1 resistance gene and two isolates (6.8%) were positive to blaShv in proteus (Hama-Soor et al., 2021;

Salih et al., n.d.). blaOXAgene (57.5%) was the predominant resistance genes among *E. coli* isolates of diarrhea (Ali et al., 2022). SHV gene, 22.3%, and OXA gene showed the lowest rate 11.7% was found in *E. coli* in different study (Ghafour et al., 2021a; Hama Soor, 2022). The rate was also observed in pseudomonas, s (7.4%) was found to carry blaOXA resistance gene, and two isolates (3.7 %) were positive to blaCMY (Ghafour et al., 2021a, 2021b).

1.6.5 Iran

In Iran the rate is also high and there many studies about resistance genes (Ghasemian et al., 2018; Leylabadlo et al., 2017). Out of 1275 isolates resistant to one of the 3rd-generation cephalosporins, 475 were ESBL strains (12%). TEM was the most common ESBL gene found in phenotypic positive strains (Armin et al., 2020). Out of 100 *Acinetobacter baumannii* isolates, 59% were ESBL positive according to the phenotypic method. The PCR assay could not detect the blaSHV and blaVEB genes in the studied isolates, but the presence of blaTEM gene was demonstrated in 42% of the strains (detektiert werden, n.d.).

2. Conclusion

In conclusion, the global spread of antibiotic resistance genes poses a significant threat to public health. Immediate action is required to monitor and control this phenomenon, with a focus on responsible antibiotic use, global collaboration, and continued research into alternative treatments. Antibiotic resistant is increasing globally and it causes treatment failure. This leads to high morbidity and mortality. Most of antibiotic resistance in bacteria is due to harboring drug resistance gene on bacterial DNA. Bacterial DNA contain many types of antibiotic resistance genes such blaOXA and blaSHV and quinolone resistance genes, qnrB. These genes can be exchanged between bacteria and spread in the world. If authorities will not take steps to contain appearing new resistance bacteria, the consequences will be problematic.

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