# Global Antibiotic Resistance Patterns in Clinical Isolates: Mechanisms, Implications, and Therapeutic Approaches

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Abstract: Antibiotic resistance (AR) is an escalating global health crisis that undermines the efficacy of modern medicine, complicating infection treatment and increasing morbidity and mortality rates. This study critically examines global trends in AR, with a particular focus on key pathogens, including Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Acinetobacter baumannii, which are responsible for healthcare - associated infections and are increasingly resistant to multiple antibiotic classes. The alarming rise in resistance to fluoroquinolones, carbapenems, and third - generation cephalosporins is driven by factors such as antibiotic misuse, weak regulations, and insufficient surveillance. The genetic adaptation of bacteria through mutation and horizontal gene transfer further exacerbates the spread of multidrug - resistant (MDR) and extensively drug - resistant (XDR) strains. Addressing this crisis necessitates a multi - faceted approach, including robust antibiotic stewardship programs, enhanced global surveillance, stringent infection control measures, and the development of alternative therapies such as bacteriophage therapy and novel antibiotics. Coordinated global efforts and innovative solutions are imperative to mitigating the AR threat and preserving antibiotic efficacy for future generations.

Keywords: efficacy, surveillance, exacerbates. Stringent, resistant

## 1. Introduction

Antibiotic resistance (AR) has emerged as one of the most pressing global health challenges, threatening the efficacy of antibiotics that have revolutionized modern medicine. AR occurs when bacteria develop adaptive mechanisms that enable them to survive and proliferate despite the presence of antibiotics designed to kill or inhibit their growth. This phenomenon has led to the rise of multidrug - resistant (MDR) and extensively drug - resistant (XDR) bacterial strains, making infections increasingly difficult to treat and significantly straining healthcare systems worldwide.

Among the most concerning antibiotic - resistant pathogens is methicillin - resistant *Staphylococcus aureus* (MRSA), which resists methicillin and other beta - lactam antibiotics, as well as penicillin - resistant *Enterococcus* species. Another particularly alarming example is multidrug - resistant *Mycobacterium tuberculosis* (MDR - TB), which is resistant to at least two of the most potent first - line tuberculosis drugs, isoniazid and rifampicin. The escalation of MDR - TB into extensively drug - resistant tuberculosis (XDR - TB), which demonstrates resistance to a broader spectrum of antibiotics, further complicates disease management, requiring prolonged treatment regimens with limited success rates. The rise of such resistant strains poses a severe challenge to global public health, necessitating urgent and concerted efforts to mitigate the crisis.

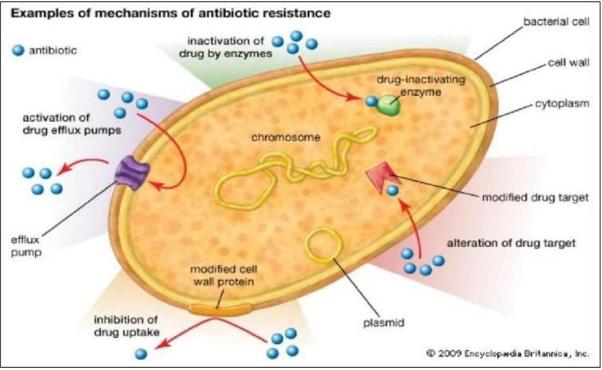
The underlying genetic mechanisms of antibiotic resistance are diverse and involve either spontaneous mutations or the acquisition of resistance genes through horizontal gene transfer (HGT). Key mechanisms include genetic mutations that alter bacterial targets, reducing antibiotic efficacy; HGT, which enables bacteria to rapidly acquire resistance traits through plasmids, transposons, or integrins; efflux pumps that actively expel antibiotics from bacterial cells, lowering their intracellular concentrations; and enzymatic inactivation, where bacteria produce enzymes that degrade or modify antibiotics, rendering them ineffective. The combination of these genetic adaptations has facilitated the emergence of superbugs—bacteria resistant to multiple or even all available antibiotics—making infections increasingly difficult to manage.

Addressing antibiotic resistance requires a multifaceted approach incorporating preventive and therapeutic strategies. Antibiotic stewardship programs aim to optimize the use of antibiotics by ensuring appropriate prescriptions, minimizing misuse, and promoting targeted therapies based on susceptibility testing. Enhanced surveillance and reporting systems are essential for tracking resistance patterns and informing public health decisions. Infection prevention and control measures, including improved hygiene practices, sterilization protocols, and public health campaigns, play a crucial role in limiting the spread of resistant bacteria. Additionally, emerging therapeutic approaches, such as bacteriophage therapy, antimicrobial peptides (AMPs), CRISPR - Cas systems, and combination therapies, hold promise in countering antibiotic resistance and restoring the effectiveness of antimicrobial treatments.

This research paper explores the genetic basis of antibiotic resistance, the factors driving its emergence, and the strategies being developed to combat this growing threat. By understanding the complex interplay between bacterial evolution, antibiotic usage, and public health interventions, this study aims to contribute to the ongoing global efforts to curb antibiotic resistance and safeguard the future of antimicrobial therapies.

## 2. Mechanism of Resistance

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Bacteria can develop antibiotic resistance through several genetic mechanisms. These mechanisms give rise to resistance because they result in biochemical modifications that alter certain bacterial cell properties, which normally render the cell sensitive to an antibiotic. Examples of biochemical modifications that lead to resistance include the production of enzymes that inactivate the drug, the alteration of the protein, enzyme, or receptor targeted by the drug, the activation of drug efflux pumps that actively remove the drug from the cell, and the modification of cell - wall proteins that inhibit drug uptake.

#### **Global Trends in Antibiotic Resistance**

This section examines the rise of antibiotic resistance on a global scale, including regional variations and the factors contributing to this issue, such as the overuse of antibiotics in healthcare, agriculture, and the environment.

#### Underlying Genetic Mechanisms

This section explores the genetic basis of resistance in clinical isolates, including the role of horizontal gene transfer, mutations, and the contribution of mobile genetic elements like plasmids, transposons, and integrons in spreading resistance.

#### **Mitigation Strategies and Emerging Therapies**

This part focuses on current strategies to combat resistance, such as antibiotic stewardship programs, alternative therapies (including phage therapy, antimicrobial peptides, and CRISPR - Cas systems), and the development of novel antibiotics. Understanding antibiotic resistance trends is crucial for guiding effective treatment strategies, shaping public health policies, and developing novel therapeutic approaches to combat resistant infections.

#### **Genetic Basis of Resistance**

#### a) Mutation

Mutations in chromosomal DNA can lead to antibiotic resistance. The rate at which resistance develops depends on the rate of bacterial mutations. Mutations occur naturally during cell division, and bacteria are particularly prone to mutation due to their single - chromosome genome and high replication rate.

#### b) Horizontal Gene Transfer

Horizontal gene transfer involves the uptake of free DNA from the environment through a process known as transformation. Additionally, efforts to combat bacterial infections using bacteriophages were largely abandoned following the discovery of penicillin and broad - spectrum antibiotics in the early 1940s.

The importance of antibiotic resistance lies in its direct threat to global health, as it diminishes the effectiveness of standard treatments, leading to prolonged illnesses, higher mortality rates, and an increased spread of resistant infections.

## Impact of Antibiotic Resistance on Public Health and Healthcare

Antibiotic resistance poses a severe threat to public health and healthcare systems worldwide. It occurs when bacteria and other microorganisms develop the ability to withstand the effects of antibiotics, making infections more difficult to treat. This growing problem has far - reaching consequences, including increased disease transmission, prolonged hospital stays, rising healthcare costs, and elevated mortality rates. The following are the key impacts of antibiotic resistance on public health and healthcare:

1) **Increased Spread of Diseases:** Antibiotic resistance leads to the increased transmission of infectious diseases. When bacteria become resistant to antibiotics, common infections that were once easily treatable become harder to cure. This results in prolonged illnesses, allowing infections to spread more rapidly

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within communities, hospitals, and healthcare facilities. The inability to effectively treat infections can lead to outbreaks, putting vulnerable populations such as children, the elderly, and immunocompromised individuals at higher risk.

- 2) Prolonged Hospital Stays and Increased Medical Visits: Patients suffering from antibiotic - resistant infections often require extended hospital stays, frequent medical follow - ups, and more intensive care. Infections that could have been treated with a short course of antibiotics now demand longer and more complex treatment regimens. This not only places a burden on patients and their families but also puts excessive strain on healthcare infrastructure, leading to overcrowding in hospitals and clinics.
- 3) Rising Healthcare Costs: Antibiotic resistance significantly increases healthcare expenses due to the need for more advanced and costly treatments. Patients with resistant infections may require expensive second line or third line antibiotics, prolonged hospitalizations, additional diagnostic tests, and specialized care. These escalating costs place financial pressure on both individuals and healthcare systems, making quality treatment less accessible to lower income populations.
- 4) Increased Mortality Rates: The inability to treat infections effectively leads to a higher risk of death. Antibiotic - resistant infections can cause severe complications, septicemia, organ failure, and other life - threatening conditions. According to global health reports, antibiotic resistance is responsible for hundreds of thousands of deaths annually, with the number expected to rise if urgent measures are not taken to control its spread.
- 5) Untreatable Infections and Long Term Health Consequences: Some infections caused by antibiotic resistant bacteria become entirely untreatable, leading to chronic illnesses and severe complications. For example, antibiotic resistance can contribute to reproductive tract infections that may result in infertility. Additionally, resistant infections increase the risk of co - infections and the spread of other diseases, further endangering public health.

#### **Global Trends in Antibiotic Resistance**

Antibiotic resistance is a growing global health crisis, with significant regional variations in its prevalence and impact. While developed regions such as North America and Europe face challenges related to multi - drug - resistant pathogens in healthcare settings, the situation is far more critical in Africa and parts of Asia. Factors such as high rates of antibiotic misuse, inadequate healthcare infrastructure, and limited access to clean water exacerbate the problem in these regions. Global Trends in Antibiotic Resistance

- High Resistance in Low and Middle Income Countries (LMICs): Countries in Africa and parts of Asia experience the highest resistance rates due to the widespread misuse of antibiotics and lack of stringent regulations.
- Multi Drug Resistance in Developed Regions: While resistance levels in North America and Europe are generally lower, they still face major challenges with

multi - drug - resistant pathogens, particularly in hospitals and long - term care facilities.

- 3) Emerging Resistance to Last Resort Antibiotics: The rise of resistance to carbapenems and colistin— antibiotics used as a last resort—poses a severe global threat, especially in healthcare settings.
- 4) Limited New Antibiotics: The development of new antibiotics has slowed, leading to a reliance on existing drugs that are becoming less effective against resistant bacteria.
- 5) Global Spread of Resistant Strains: Increased international travel and trade facilitate the spread of resistant pathogens across borders, making antibiotic resistance a truly global challenge.

#### Antibiotic Resistance in Africa

Africa faces unique challenges in controlling antibiotic resistance due to a combination of structural, economic, and health - related factors. While resistance prevalence in some cases may be lower than in other regions, the continent suffers the highest mortality rates due to infectious diseases, exacerbated by inadequate healthcare systems.

- Highest Mortality Rate: Despite having lower overall prevalence of resistant bacteria compared to some regions, Africa experiences the highest mortality rates due to infectious diseases. Countries such as Somalia, Malawi, Zimbabwe, and the Democratic Republic of the Congo (DRC) are particularly affected. The ongoing conflicts in the DRC further contribute to poor healthcare access and antibiotic resistance.
- 2) High Resistance to Common Antibiotics: Many African nations report high resistance rates to essential antibiotics, including fluoroquinolones. This resistance leads to complications such as nervous system disorders, musculoskeletal problems, and sensory impairments, reducing treatment options for bacterial infections.
- 3) Challenges in Surveillance: Africa struggles with inadequate surveillance systems, making it difficult to track resistance trends accurately. Many countries lack the infrastructure to monitor antibiotic use and resistance patterns effectively, leading to unregulated antibiotic consumption and further resistance development.

## Factors Contributing to Antibiotic Resistance in Africa

Several key factors contribute to the rising resistance problem across Africa:

- Poor Sanitation: The lack of proper waste management and sanitation systems promotes the spread of resistant bacteria.
- Limited Access to Clean Water: Contaminated water sources facilitate the transmission of resistant bacteria, especially in rural communities.
- Self Medication: The widespread practice of self medicating with antibiotics without prescriptions leads to misuse and increased resistance.
- Inadequate Healthcare Infrastructure: Many African healthcare systems suffer from a lack of trained professionals, insufficient medical supplies, and poor regulatory frameworks for antibiotic distribution.

#### Asia

Antibiotic resistance is a growing global crisis, and Asia plays a crucial role in shaping its trajectory. Several factors in the

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region contribute to the worldwide trends in antimicrobial resistance (AMR), influencing healthcare outcomes far beyond national borders.

1) Diverse Resistance Patterns

Asia exhibits significant variation in resistance levels, with densely populated countries like India and China experiencing particularly high resistance rates. These regions often serve as hotspots for resistant bacterial strains due to high population density, inadequate sanitation, and inconsistent regulatory frameworks for antibiotic use. The spread of resistant bacteria from Asia to other parts of the world occurs through global travel and trade, making AMR a transnational challenge.

- 2) Hospital Acquired Infections and Multidrug Resistance The high burden of hospital - acquired infections (HAIs) in many Asian countries exacerbates the AMR crisis. Infections caused by multidrug - resistant organisms (MDROs), such as Methicillin - resistant *Staphylococcus aureus* (MRSA) and Carbapenem - resistant *Enterobacteriaceae* (CRE), are particularly prevalent in hospitals. Limited infection control measures, overcrowding in healthcare facilities, and insufficient antibiotic stewardship programs contribute to the persistence and spread of resistant strains, ultimately impacting global healthcare systems.
- Overuse and Misuse of Antibiotics
   Asia is a major contributor to the overuse and misuse of
   antibiotics, driven by factors such as easy over the counter access, self medication, and excessive antibiotic
   prescriptions. In many countries, antibiotics are readily

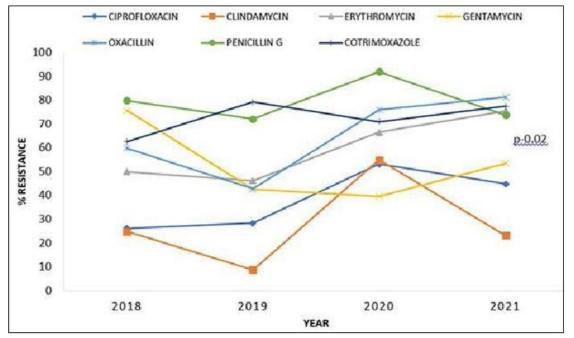
available without prescriptions, leading to inappropriate usage. Additionally, the widespread use of antibiotics in livestock and aquaculture for growth promotion further accelerates resistance. The global repercussions of this practice include the emergence of antibiotic - resistant bacteria that can spread through food chains, water systems, and international travel.

4) Impact on Global Public Health

The rise of antibiotic resistance in Asia has global implications. Resistant bacterial strains originating in Asia have been detected in other continents, demonstrating how AMR transcends national boundaries. The inefficacy of last - resort antibiotics threatens global health security, complicating treatment options for infectious diseases worldwide. Furthermore, medical tourism in Asia, where patients travel for healthcare services, has facilitated the spread of resistant pathogens across international borders.

5) Efforts to Mitigate Resistance

Recognizing the severity of AMR, several Asian countries have implemented national action plans in alignment with the World Health Organization's (WHO) Global Action Plan on AMR. Initiatives include stricter antibiotic regulations, improved infection control in healthcare settings, and awareness campaigns to educate both healthcare professionals and the public. However, stronger international collaboration, surveillance, and policy enforcement are needed to curb the growing resistance crisis.



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## Europe

Antibiotic resistance is a growing global health threat, with significant regional variations in prevalence and control measures. Europe plays a crucial role in setting benchmarks for antibiotic stewardship and surveillance efforts.

1) Rising Global Resistance: Across the world, antibiotic resistance is escalating, especially in regions with high antibiotic misuse, weak healthcare systems, and limited

regulatory enforcement. South Asia, Africa, and parts of Latin America face higher resistance rates due to widespread over - the - counter antibiotic use and poor sanitation.

 Europe's Lower Resistance Rates: Compared to other regions, Europe has lower resistance rates due to stringent antibiotic regulations, advanced healthcare infrastructure, and well - established surveillance

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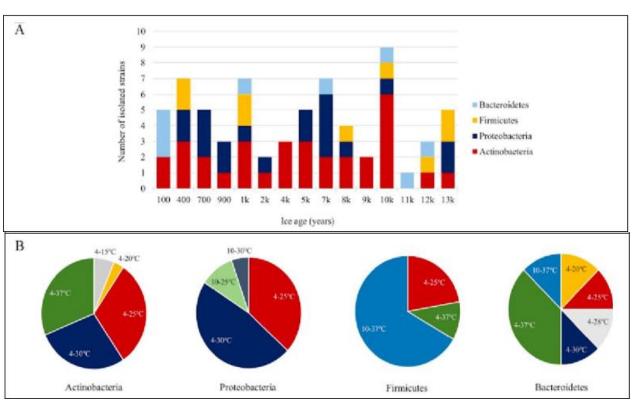
programs like the European Centre for Disease Prevention and Control (ECDC). Countries in Northern and Western Europe, in particular, demonstrate effective antimicrobial stewardship, limiting unnecessary antibiotic prescriptions.

- 3) Hospital Acquired Infections and MDR Pathogens: Despite lower resistance rates overall, Europe still faces challenges with hospital - acquired infections, particularly from multidrug - resistant (MDR) bacteria such as carbapenem - resistant Enterobacteriaceae (CRE) and methicillin - resistant Staphylococcus aureus (MRSA). These infections remain a significant concern in intensive care units and long - term healthcare settings.
- 4) Surveillance and Global Leadership: European countries have established comprehensive monitoring programs like the European Antimicrobial Resistance Surveillance

Network (EARS - Net), which provides data - driven strategies to curb resistance. The EU's strict regulations on antibiotic use in agriculture also contribute to lower resistance rates compared to other parts of the world.

5) Impact on Global Strategies: Europe's success in controlling antibiotic resistance serves as a model for global efforts. Initiatives such as the World Health Organization's (WHO) Global Action Plan on Antimicrobial Resistance draw insights from Europe's policies, emphasizing antibiotic stewardship, infection control, and public awareness campaigns.

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North America

Antibiotic resistance in North America has emerged as a significant public health challenge, mirroring global trends while presenting region - specific concerns. The key factors contributing to this issue include healthcare - associated infections, antibiotic overuse in agriculture, and the growing focus on antimicrobial stewardship initiatives.

- Healthcare Associated Infections (HAIs): Similar to Europe, North America experiences high antibiotic resistance rates in healthcare settings, particularly among immunocompromised patients and those with complex medical conditions. Multidrug - resistant organisms (MDROs) such as *Methicillin - resistant Staphylococcus aureus* (MRSA), *Carbapenem - resistant Enterobacteriaceae* (CRE), and *Vancomycin - resistant Enterococci* (VRE) continue to pose serious threats in hospitals and long - term care facilities.
- Antibiotic Overuse in Agriculture: The widespread use of antibiotics in livestock production contributes significantly to the emergence of resistant bacterial strains. Resistant mycobacteria, including those

responsible for tuberculosis (TB), and other zoonotic pathogens have been linked to agricultural antibiotic overuse. The transmission of resistant bacteria from animals to humans through food, water, and direct contact exacerbates the problem.

3) Focus on Stewardship Initiatives and Civil Awareness Campaigns: Recognizing the urgency of antibiotic resistance, North America has implemented stringent antimicrobial stewardship programs. Public health campaigns aim to educate healthcare providers and the general public on appropriate antibiotic use. Regulatory measures, such as restrictions on antibiotic use in food production and enhanced surveillance of resistance patterns, play a crucial role in mitigating the crisis.

North America's approach to combating antibiotic resistance aligns with global efforts, emphasizing surveillance, research, and policy interventions. However, challenges remain, particularly in addressing the overuse of antibiotics in both medical and agricultural sectors. Moving forward, a

multidisciplinary approach involving healthcare professionals, policymakers, and the public will be essential to curbing the spread of resistant infections.

#### **South America**

Antibiotic resistance is a growing global health crisis, with significant variations in resistance patterns across regions. South America, particularly countries like Brazil, plays a crucial role in this trend due to factors such as overuse of antibiotics, self - medication, and inadequate regulatory frameworks.

## Global Trends in Antibiotic Resistance:

- Rising Multidrug Resistance (MDR): Across the world, bacterial strains resistant to multiple antibiotics such as carbapenem - resistant *Enterobacteriaceae* (CRE) and methicillin - resistant *Staphylococcus aureus* (MRSA) —are increasing. This pattern is mirrored in South America, where drug - resistant *Klebsiella pneumoniae* and *Escherichia coli* are prevalent.
- 2) Agricultural Contribution: The widespread use of antibiotics in livestock and agriculture has accelerated resistance globally. In South America, especially in Brazil and Argentina, antibiotics are frequently used to promote growth in animal farming, contributing to resistance in both animals and humans.
- 3) Limited Surveillance and Regulation: While developed nations have implemented stricter antibiotic stewardship programs, many South American countries face challenges in enforcing regulations. Brazil, for example, has been identified as a hotspot for antibiotic resistance due to the ease of acquiring antibiotics without prescriptions and weak surveillance systems.
- 4) Healthcare Associated Infections: Globally, hospital acquired infections (HAIs) involving antibiotic resistant bacteria are a major concern. South America has reported rising cases of resistant Acinetobacter baumannii and Pseudomonas aeruginosa in healthcare settings, indicating a shared global challenge.
- 5) Environmental and Socioeconomic Factors: Urbanization, poor sanitation, and lack of clean water sources contribute to the spread of resistant bacteria. Many South American countries face these challenges, leading to higher transmission rates of resistant pathogens.

## 3. Conclusion

Antibiotic resistance poses a severe global health threat, driven by the overuse and misuse of antibiotics, poor infection control, and the slow pace of new drug development. The rising prevalence of multidrug - resistant bacteria, particularly among Enterobacteriaceae and Gram - negative pathogens like *Pseudomonas aeruginosa*, has led to increasingly limited treatment options, especially for hospital - acquired infections. The problem is further exacerbated by geographic variations in resistance patterns, highlighting the need for region - specific strategies.

Addressing this crisis requires a multifaceted approach, including the implementation of robust antibiotic stewardship programs, improved infection control measures, enhanced surveillance, and sustained investment in novel antibiotic development. Urgent action is needed to promote responsible antibiotic use in both healthcare and agricultural settings, alongside efforts to develop alternative treatment strategies. Future research must focus on innovative therapeutic solutions, regulatory frameworks, and global cooperation to mitigate the spread of resistant bacteria. Strengthening these initiatives is crucial to preserving the effectiveness of antibiotics and safeguarding public health worldwide.

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