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Resistant Bacteria vs. Public Health – A Review

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Abstract

Currently, antimicrobial-resistant bacteria and the global repercussions of this resistance are emerging as one of the most significant threats to public health. The global scope of the problem is discussed, with recent data showing that antimicrobial resistance (AMR) causes over a million fatalities annually, and projections suggest that this number will rise sharply by 2050. This review aims to provide a comprehensive analysis of this issue, focusing on the mechanisms of antibiotic resistance, its impact on public health and the economy, proposed strategies for addressing the problem, and potential alternative therapeutic approaches. This review is based on a thorough examination of current publications from the World Health Organization (WHO), European Centre for Disease Prevention and Control (ECDC), and relevant scientific literature obtained from databases such as PubMed. The primary objective of this publication is to highlight the escalating nature of this problem and to promote education and awareness in this critical area of healthcare.

Keywords: resistant bacteria, MDR, public health, phages, antimicrobial resistant, antibiotic resistance, mechanisms of resistance

Introduction

The discovery of penicillin by Alexander Fleming in the 20th century marked the beginning of antibiotic therapy, revolutionizing medicine and creating new pathways for treating numerous bacterial infections. Unfortunately, over the years, the misuse and overuse of antibiotics have led to the development of bacterial resistance, which is becoming an increasingly serious problem and poses a threat to global public health. Today, the world faces an antibiotic therapy crisis. The WHO warns that antibiotic resistance causes millions of deaths annually while also negatively impacting economic aspects. This review aims to present the current state of knowledge and the scale of the problem.

Materials and Methods

This study is based on an analysis of WHO and ECDC reports as well as scientific publications obtained from the PubMed database. The referenced articles primarily address mechanisms induced by microorganisms leading to resistance development, epidemiology, the scale of the problem, and the overall impact on public health.

Mechanisms of Antibiotic Resistance

The mechanisms of resistance developed by bacterial cells are diverse and complex and are based primarily on mutations in the genome of the microorganism. Some bacterial cells develop mutations in genes that affect the activity of drugs and allow them to survive. Resistance to certain antibiotics results from the following mechanisms: enzymatic inactivation of the antibiotic, modification of the antibiotic's target site, active efflux of the antibiotic from the cell, decreased permeability of the cell membrane, global changes in important metabolic pathways through modulation of regulatory networks, and resistance from related organism Gene acquisition. It is noteworthy that the existence of resistant bacteria was recognized shortly after the discovery of antibiotics: in 1940, the first strains of penicillin-resistant staphylococci were reported. Similarly, methicillin-resistant staphylococci were reported in 1960, only one year after their introduction (1,2).

a. Enzymatic Inactivation of Antibiotics

Bacteria have developed the ability to produce enzymes that degrade or change the structure of antibiotics, rendering them ineffective. This is a well-known mechanism of acquired antibiotic resistance found in both Gram-negative and Gram-positive bacteria(3). A classic example of resistance due to structural modification of drugs is the presence of aminoglycoside modifying enzymes (AMEs). These enzymes covalently modify the hydroxyl and amino groups of aminoglycoside molecules. A number of AMEs have been reported to date and are the primary mechanism of aminoglycoside resistance worldwide (3). On the other hand, the best characterized example of antibiotic inactivation by destruction is the production of β -lactamase, an enzyme that hydrolyzes the amide bond in the β -lactam ring of penicillin and cephalosporin. More than 1,000 β -lactamases have been described to date, and many more will be described in the future as part of the normal evolutionary process of bacteria (3).

These enzymes are widespread in the genus *Streptomyces* and, together with similar enzymes found in pathogenic and nonpathogenic bacteria, constitute the “ β -lactamase superfamily” of proteins (4). β -lactamases are generally classified into four classes (A, B, C, and D) based on amino acid sequence and the use of catalytic serine or zinc ions (5).

b. Alteration of antibiotic target sites

Mutations in the bacterial genome can occur within genes encoding antibiotic target proteins. These mutations result in conformational changes in the protein that prevent the antibiotic from binding effectively. One example is the altered structure of penicillin-binding proteins (PBPs), enzymes known as transpeptidases, which play an important role in cross-linking peptidoglycan precursors during bacterial cell wall biosynthesis. Since these enzymes are the primary targets of β -lactam antibiotics, structural or functional mutations can make bacteria resistant to these antibiotics (6). Such mutations are an important mechanism of β -lactam drug resistance in *Staphylococcus aureus*.

c. Active efflux of antibiotics from the cell (efflux)

Some bacteria have specialized pumping systems that allow them to efflux antibiotics from the cell and reduce their concentration to harmless levels. This mechanism often works in conjunction with other mechanisms such as antibiotic modification and target modification. These pumps can be substrate specific or can expel a wide range of structurally diverse substances, as seen in multidrug-resistant (MDR) systems (4,7).

d. Reduced cell membrane permeability

This mechanism involves structural changes in the outer membrane, such as reduced porin number, that limit the entry of antibiotics into the cell and prevent them from reaching therapeutic concentrations. For example, *Pseudomonas aeruginosa* has several specific porins, including OprD, that facilitate uptake of antibiotics; OprD has a binding site for carbapenem antibiotics, the absence of which increases resistance to this class of antibiotics(8).

e. Acquisition of Resistance Genes

Bacteria can acquire resistance genes from other microorganisms through horizontal gene transfer, which contributes significantly to the rapid spread of resistance within a bacterial population. Classically, bacteria acquire external genetic material through three main strategies: transformation (incorporation of naked DNA), transduction (phage-mediated), and conjugation (3).

The Scale of the Problem

According to an analysis published in *The Lancet*, in 2021, approximately 1.14 million deaths will be caused by bacteria resistant to antibacterial drugs (AMR), including antibiotics. Projections indicate that this number could increase to 1.91 million annually by 2050.

The study also considered cases where resistance was an indirect cause of death, estimating that this number would increase from 4.71 million in 2021 to 8.2 million in 2050 (9). In an earlier analysis conducted in 2019, bacterial resistance was directly responsible for 1.27 million deaths worldwide and contributed to 4.95 million reported (10). Increasing antibiotic resistance has been observed worldwide. However, the authors of this study predict that the most severe effects of AMR will be felt in regions such as South Asia, Southeast Asia, East Asia, Oceania, and Sub-Saharan Africa (9). According to WHO, in Europe, AMR is directly responsible for 133,000 deaths annually and indirectly contributes to 541,000 deaths per year. A particularly serious threat is the growing resistance to carbapenem antibiotics and colistin; EARS-Net reports that the most common resistant strains in the European Union are *E. coli* and *K. pneumoniae* (10,11). Poland has one of the highest rates of antibiotic use in the EU: according to ESAC-Net data, the average antibiotic use in EU/EEA countries in 2022 was 21.49 DDD (Defined Daily Dose) per 1,000 inhabitants, while the recorded 23.6 DDD per 1,000 inhabitants per day (12).

Health and Economic Consequences

Antibiotic resistance carries significant negative consequences, both in terms of health and economics. Resistance to treatment leads to prolonged hospitalization. It has been shown that patients who received at least one inappropriate antibiotic change had longer total antibiotic therapy cycles and longer hospital stays compared to those who received appropriate antibiotics throughout their treatment (13). Another study found that the length of hospital stay was 1.2 times longer for patients with infections caused by antibiotic-resistant pathogens compared to those without such infections (14). Longer hospital stays increase the risk of complications and infections, decreasing patients' quality of life and leading to higher treatment and healthcare costs. Studies have shown that adverse events are associated with antibiotic therapy in 20% of patients receiving systemic treatment (15,16). The increase in patients with difficult-to-treat infections also adds an extra burden on healthcare systems. The World Bank estimates that the additional healthcare costs due to antibiotic resistance amount to approximately 1.5 billion euros annually. Simulations have shown that by 2050, the global annual GDP will decrease by 1.1% in the case of low antibiotic resistance impact, and by 3.8% in the case of high impact. By 2030, the annual deficit could reach 3.4 trillion dollars (10,17,18). Moreover, morbidity and mortality are rising. In Europe, over 670,000 antibiotic-resistant infections occur each year. In the United Kingdom, more than 44,000 people die annually from sepsis, which is primarily caused by antimicrobial resistance, a number greater than the deaths from lung cancer, which is around 35,000. It is estimated that deaths caused by bacterial resistance to antimicrobial agents surpass the number of deaths from malaria or HIV/AIDS (10,18,19).

Strategies to Combat Antibiotic Resistance

Key strategies to combat antibiotic resistance include rational use of antibiotics, control of nosocomial infections, control of pathogen transmission between patients, public education of patients and health care workers, and development of alternative treatments to antibiotics.

An important change is the appropriate use of antibiotics according to established guidelines; a 2024 study in Korea showed that when patients were referred to an internal medicine specialist and that specialist made appropriate changes in antibiotic therapy, the rate of inappropriate antibiotic use decreased. Of these appropriate changes, 23.7% were to narrow-spectrum antibiotics and 34% were based on microbiological results (13).

Another important aspect is the implementation of proper hygiene procedures. Studies have shown that healthcare workers often fail to perform routine hand washing correctly. Only 20% of physicians adhere to hand hygiene guidelines. Inadequate hand hygiene by healthcare workers can lead to the spread of healthcare-associated infections (HAIs) and antibiotic-resistant pathogens. Furthermore, researchers estimate that up to 30% of HAIs can be prevented by proper hand hygiene (20,21,22). Another important strategy is to educate the public, including health care providers, to promote the rational use of antibiotics and raise awareness of the growing problem of antibiotic resistance. Studies show that the public does not fully understand and misunderstands what antibiotic resistance is. People often do not believe that their actions contribute to the development of antibiotic resistance. Furthermore, some physicians do not have sufficient knowledge about prescribing antibiotics. Surveys have shown that some physicians continue to prescribe certain antibiotics even though they are aware that they have limited efficacy or are unnecessary for certain conditions. Factors include patient demand, the belief that antibiotics can prevent secondary bacterial infections, uncertainty about the etiology of infections, and limited access to sources of information about antibiotic prescribing (23,24). An important issue is the need for the development of new antibiotics as well as innovative therapies that can help reduce antibiotic use. One potential alternative to antibiotics is bacteriophages, which exhibit high specificity for certain bacteria. The use of phages as a therapeutic approach to combat bacterial infections is promising. One approach is to combine phage with other agents, such as depolymerizing enzymes, to increase their bacteriolytic activity against bacteria. Clinical studies have demonstrated that phage therapy is a safe treatment. Studies have shown mixed results regarding its effectiveness. However, the large number of successful clinical treatments of bacterial infections using phage suggests that negative results in clinical trials may be due to correlation with other factors (25,26,27).

Discussion

Antibiotic resistance undoubtedly poses a major challenge to contemporary public health and requires decisive action. The growing resistance of bacteria negatively impacts not only the health and lives of patients but also the entire healthcare system. (28,29). Among the causes contributing to the escalation of this problem are inappropriate use of antibiotics, prescribing medications without proper indications, and abuse of these drugs. Studies show that around 50% of hospitalized patients received at least one antibiotic without proper indications during their stay. In nursing homes, as much as 75% of prescribed antibiotic courses contain incorrect dosages and treatment durations (2). In many countries, the sale of antibiotics is not sufficiently regulated, exacerbating the issue of unjustified consumption. Bacteria, primarily through genetic modification, continue to acquire new resistance abilities to antibiotic therapy, leading to the development of multi-drug resistance (MDR).

Multi-drug-resistant bacteria emerged only after prolonged and widespread use of antibiotics in treating infections caused by these very bacteria (2). MDR limits the use of many antibiotics, significantly reducing therapeutic options. As a result, treatment often relies on less effective or increasingly stronger and more toxic medications. This, in turn, leads to a higher risk of complications, prolonged hospital stays, and increased mortality rates. Another challenge is the spread of resistant strains. Resistant pathogens have the ability to easily transmit between infected patients, potentially leading to outbreaks within hospital wards or even throughout entire healthcare facilities.

With the development of transport systems and tourism, these bacteria can also spread between countries and continents, increasing the global threat posed by antibiotic resistance. The entirety of the mechanisms described, in addition to the clinical problems, also carries negative economic consequences. Prolonged hospitalization and the use of costly therapies lead to increased healthcare costs and significant strain on medical institutions. The spread of resistant pathogens may also result in infections among healthcare workers, further perpetuating the vicious cycle of healthcare system failure. Additionally, productivity losses occur due to extended treatment periods, leading to lost workdays, which causes economic losses. Undoubtedly, the deteriorating situation demands multifaceted corrective actions. A key element seems to be increasing overall awareness regarding antibiotic therapy through education of both patients and healthcare personnel on the responsible use of antibiotics. An important issue is also controlling the spread of pathogens and infections within hospitals. Healthcare workers should adhere more strictly to hygiene protocols. The strategy for combating antibiotic resistance should also include well-functioning national and global surveillance systems that provide continuous monitoring and a quick response in case of emerging threats. One example could be the Global Antimicrobial Resistance Surveillance System (GLASS). Another critical path is investing in scientific research.

It is necessary to develop new drugs and alternative treatment methods to antibiotic therapy. Complementary actions should include international collaboration and the harmonization of health policies tailored to the capabilities of individual countries. (30, 31,32).

Conclusion

Antibiotic resistance is one of the biggest challenges and public health threats today. Undoubtedly, this situation requires urgent intervention at the local, national, and global levels. Literature analysis shows that the problem is very complex and its main cause is the inappropriate use of antibiotics, which has led to the emergence and spread of resistant pathogens. Antibiotic resistance has serious clinical and economic consequences. It leads to the development of complications, prolonged hospitalization, and ultimately increased mortality. As a result, health care costs increase and the entire health care system becomes overloaded. A multifaceted approach is certainly needed to address this problem. The key is to raise awareness among patients and physicians by providing comprehensive education that promotes the rational use of antibiotics. Effective hygiene procedures must be implemented and followed to reduce the transmission of resistant bacteria. The world is also looking to develop new treatments. It is essential to invest in research on new antibiotics and alternative treatments.

Such efforts should be based on global collaboration among scientists, physicians, policy makers, and society. Only by working together can we address the problem of antibiotic resistance, ensure the safety of future generations, and prevent the rise of a “post-antibiotic era” in which even minor injuries and common infections can become a major cause of death (18).

Author’s contribution

All authors contributed to the article.

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