Biomedical Letters ISSN 2410-955X DOI: https://doi.org/10.47262/BL/9.1.20230417

Review article
2023 | Volume 9 | Issue 1 | Pages 56-63

ARTICLEINFO

Received
March 21, 2023
Revised
April 31, 2023
Accepted
May 29, 2023

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Keywords
Antibiotic
Antimicrobial drugs
Resistant infections
Probiotics
Global health

How to Cite
Aabedeen ZU, Shakeel A, Ehsan T, Ziafat S, Ali W, Khan ZA, Abrar M, Azam A, Rao S, Sameen D, Fatima S. Impact of antimicrobial resistance on health and economy: A Comprehensive Review. Biomedical Letters 2023; 9(1):56-63.

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Impact of antimicrobial resistance on health and economy: A comprehensive review

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Abstract

Antibiotics have historically revolutionized the medical science; however the rise of multidrug-resistant pathogenic bacteria puts their worth at risk. The problem of antibiotic resistance has been attributed to both the excessive use of already available drugs and the absence of newer treatments as a result of stringent regulatory requirements and weakened corporate incentives. Resistant infections often need more comprehensive and costly treatments, resulting in longer hospital admissions, higher healthcare costs, and a larger demand for specialized healthcare resources. The expenses are exacerbated by the need for new antimicrobial drug research and development, which is becoming more complex and expensive as a result of resistance mechanisms. Comprehensive efforts are needed to limit the rate of resistance development and include research into new bacteria, resistance mechanisms, and antimicrobial medications. Multidisciplinary approaches are required in the sectors of agriculture, the environment, and healthcare. Probiotics, antibodies, and vaccines are a few examples of progressive complementary therapies that have shown promising outcomes in research and may one day serve as preventive or supplementary treatments. The purpose of this review article is to give an in-depth review of the influence of antibiotic resistance on both the health of individuals and economic stability.

Introduction

In the last several decades, there has been an increase in antimicrobial resistance, which is the capacity of microbes to withstand the effects of antimicrobial medications [1, 2]. In both human health and agriculture, the misuse and abuse of antibiotics have facilitated the emergence and spread of Antimicrobial Resistance (AMR). Current and future medical advancements are in danger from a probable post-antibiotic world [3, 4]. AMR severely reduces the efficacy of antibiotic treatment choices, which raises the rates of morbidity and death. In comparison to susceptible infections, studies have indicated that drug-resistant infections are linked to longer hospital admissions, greater treatment costs, and higher fatality rates [5]. Many routinely used antibiotics are no longer effective due to the emergence of multidrug-resistant bacteria. This has necessitated the use of more expensive and sometimes harmful alternative therapies, causing difficulties for both healthcare practitioners and patients [6]. AMR stresses healthcare systems by raising hospitalization rates, extending treatment durations, and driving up healthcare expenditures. Furthermore, the scarcity of efficient antibiotics impedes the success of medical procedures like surgeries, cancer chemotherapy, and organ transplantation [7]. There are significant ramifications from the present rise of antibiotic-resistant bacteria around the globe and the concurrent decline in the production of new antibiotics [8, 9]. Resistant bacteria significantly decrease the likelihood of properly treating infectious illnesses and increase the dangers of infections and deadly results for patients with blood infections [10].

The most vulnerable are those with weakened immune systems, such as cancer patients, undernourished children, and those affected by Human Immunodeficiency Virus (HIV), for whom adequate medicine is often needed to prevent and treat infections that may be fatal. [11]. Antibiotics are essential for patient care and to prevent difficulties during modern medical operations like organ transplants and prosthetic implants, which are also threatened by antibiotic resistance [12]. One-fifth of all fatalities worldwide are caused by infectious illnesses [13]; respiratory tract infections are the worst, accounting for close to four million deaths yearly. With better access to medical care and medications, these deaths are thought to be somewhat avoidable. The issue of whether this is as always, the case, particularly in regions of the globe where third- and second-line medicines are not accessible, is being raised by the worldwide appearance and spreading of bacteria that are resistant to antibiotics [14]. Given that politicians and medical professionals are typically aware of the growing medical and financial impacts of antibiotic resistance, it is difficult to comprehend the inertia around the issue [15]. There are significant issues with the international response's ambiguity and the inability to put knowledge into practice. To lessen the current and long-term effects of antibiotic resistance, global society's complacency urgently must be replaced with collective action.

The enhanced monitoring systems are critical for following AMR patterns, detecting developing resistance strains, and putting infection control measures in place [16, 17]. Collaboration among healthcare institutions, researchers, and public health organizations is essential for developing effective surveillance networks. Implementing antimicrobial stewardship programs, supporting proper prescription practices, and educating healthcare professionals and the general public about antibiotic stewardship are all critical measures in treating AMR [18]. To solve the issues posed by AMR, it is critical to encourage investment in research and development of novel antibiotics, diagnostics, and alternative treatment techniques [19].

Causes of resistance

Antibiotic usage naturally leads to resistance, whereas irrational antibiotic use hastens the process, resulting in the expulsion of susceptible strains [20]. The rate at which resistant microorganisms arise and are selected increases to use these medications more often. Approximately 80% of antibiotic usage in humans occurs in the community, and at least 50% of this is based on false diagnoses, mostly viral illnesses [21]. Several complex systems contribute to this overuse. The short-term benefits of antibiotic usage for patients, healthcare professionals and drug distributors appear to outweigh worries about future repercussions. Cultural preconceptions, patient requirements, diagnostic uncertainty, financial forces, the level of education among medical staff and pharmacists, and marketing to prescribers, consumers, and suppliers from the pharma companies are among the factors that influence the consumption of antibiotics. Despite the fact that the two European nations' illness burdens are quite comparable, France and the Netherlands use antibiotics four times more often than each other [22]. Studies from various

underdeveloped nations have shown that each consultation often results in the prescription of multiple antibiotics [23].

Antibiotic usage and resistance have a complicated connection. Underuse, caused by insufficient doses, poor medication adherence, and inadequate access to antibiotics, may be just as significant in fostering resistance as misuse [24]. The rates of selection of antibiotic-resistant bacteria rise when broad-spectrum antibiotics are used as a replacement for accurate diagnosis and to improve the chance of treatment success. Additionally, subpar and fake medications contribute to less-than-ideal antibiotic concentrations by failing to manage microbial diversity which is thought to be a risk factor for the emergence of resistance. Over 50 percent of the total antibiotics are thought to be bought privately, without a prescription, from a pharmacy and in the unofficial market from street sellers. Half of the expenditures are for one-day remedies maybe less, an example demonstrating the extent of the issue [25]. Once resistant strains have been chosen, conditions like overcrowding and poor cleanliness help them proliferate. One such is daycare facilities, which provide several chances for the spread of infectious illnesses and the development of resistant *Streptococcus pneumonia*. These settings are excellent for the storage and transmission of these germs because of the presence of young, vulnerable children who have repeated illnesses and the administration of several, often broad-spectrum antibiotics. Some bacterial strains have been more effective than others at spreading widely in the hospital environment [26].

Transmission factors of antibiotic resistance

At this time, the solution to this widespread problem lies in knowing the numerous factors that contribute to antibiotic resistance [27]. The development of antibiotic resistance in bacteria is a naturally occurring phenomenon. The selection of antibiotic resistance has been influenced using various antibiotics in healthcare systems, the environment, agriculture and livestock. Sanitation practices, infection control guidelines, water hygiene practices, pharmaceutical quality, diagnostic and treatment procedures, and travel or movement restrictions are other significant variables that have the potential to increase antibiotic resistance. The most important phenomenon that may transfer a gene of antimicrobial resistance to the host creatures is plasmid transmission [28]. In addition to the mutation of numerous genes found on the chromatid of the microbe, plasmid sharing between organisms is essential for the transmission of antibiotic resistance [29] (**Fig. 1**). Antibiotics may have an impact on this process by transferring resistance components, and they may also impose selection pressure on the emergence of resistance. The understanding of the dynamics of resistance transmission has increased. At the regional level, the feco-oral route is the most significant route of transmission, particularly for resistant strains of tetanus. Community-acquired (CA)-MRSA, which typically spreads as a result of prolonged hospital stays or unsanitary hospital settings, is yet another useful case for understanding the mechanics of resistance transfer between humans [30]. Resistant N gonorrhea may also be transmitted via sexual interaction.

A variety of views on the effects of antimicrobial resistance

The hospital, a 3rd payer, the patient, and society may all be included when evaluating the effects of antibiotic resistance [31]. Studies that focus on one viewpoint may understate the whole impact of antimicrobial resistance; consequently, it is critical to understand the study's perspective in order to properly evaluate its findings.

Hospital vantage point

The influence of resistance, as seen from the hospital's viewpoint, has been explored most often. Since information on in-hospital mortality, morbidity, and the costs associated with antibiotic resistance is often simple to access, hospitals are more likely to implement changes in response to the information assessed on-site [32]. It has been reported that the effects of antibiotic resistance by measuring hospital length of stay and in-hospital death rates. However, there have been fewer studies on the economic consequences [33]. It is crucial to appreciate that the hospital's viewpoint on the impact of antibiotic resistance offers a constrained understanding of the impact of healthcare insurance because a large portion of clinical practice is now provided outside of hospitals [34]. A link between antimicrobial resistance and a 1.3-2-fold rise in mortality, costs, and fatalities among individuals with high resistance compared to more susceptible illnesses is also reported [12]. However, there is limited statistical data available about expenses at these locations because

the suppliers of this information, third-party payers, are protective of the data they gather, and it is difficult to match claims data with microbiological findings without compromising patient anonymity.

Patient viewpoint

Measures of mortality and hospitalization length are used to assess the short-term direct effect of resistance on the affected patient. However, long-lasting, and indirect impacts of resistant illnesses may have serious consequences [35]. For instance, even if a patient does not have an MRSA infection, they are often isolated and given vancomycin as an empirical treatment if they have a background of MRSA infection and arrive with a new fever [36]. The effects of a persistent sickness on one's health and outlook, the time sacrificed from family and from the workplace due to extended hospital admissions, one's capacity for recovery, and even the psychological burden of having a persistent infection all require greater clarification at the patient-level [37] (**Fig. 1**). Antimicrobial resistance affects patients who have not caught an infection from a resistant bacterium. Due to increasing rates of resistance among common infections, broad-spectrum medications are becoming more important for the treatment of numerous bacterial diseases. These substances are often more costly, more harmful to the protective microflora, sometimes more poisonous, and occasionally less effective [38]. To treat community-acquired pneumonia in hospitalized patients, third-generation cephalosporins and perhaps fluoroquinolones have been suggested, demonstrating the decrease in the utilization of narrow-spectrum drugs, such as penicillin, in the remedy of a variety of ailments when societal resistance rates reach a specific threshold [39].

Societal viewpoint

There is currently little knowledge of how antibiotic resistance affects worldwide. According to the Office of Tech Assessment's estimate, the nationwide expenditure of resistance to antibiotics in the Us was $4 billion annually in 1995. However, this evaluation solely looked at the impacts of resistance on patients, who were directly affected and ignored other consequences, which would have multiplied the estimate many times over. To help decision-makers, further research on the effects of resistance outside of the patient and clinic levels is required.

Assessing the effect of resistance due to technical issues

Adjusting the duration of stay (LOS)

Appropriate adjustment for changes in hospital LOS before the initiation of illness in persons with resistant infections and the sample, group is a critical concern in the design of studies that investigate the consequences of antibiotic resistance. Hospital length of stay (LOS) before the incident is directly correlated with cost, subsequent LOS, and death. LOS before infection may be used to match case and control patients or this can be achieved by integrating this variable in a multivariate model. Additionally, pre-infection disease severity and comorbidities need to be controlled [40].

Choosing a control group

Different techniques may be employed in the design of research that investigates the impacts of antibiotic resistance. The results between patients who had contracted a resistant strain of a microorganism and those who had contracted a vulnerable strain of the very same organism [40] are also reported. By comparing the outcomes of patients with MRSA-caused central line infections to those of patients with methicillin-susceptible S. aureus infections, this strategy may evaluate the independent effect of acquiring a resistance determinant [41]. In other research, the results of infected patients with a resistance bacterium were contrasted with those of uninfected control participants chosen following predetermined criteria. This analysis compares the burden of carrying a resistant infection to the burden of having none. The estimate of negative occurrences related to resistance is significantly increased by the latter kind of comparison. For instance, Engemann *et al*., [42] revealed that individuals with MRSA wound infections have a median hospital charge that is significantly higher ($92,363) than patients with methicillin-resistant *S. aureus* wound infections ($52,791), and that people with the disease with either type of illness have a considerably higher median charge ($29,455) than patients without infection.

Timing of the infection's start

Most of the research believes that the initial positive culture result is a good indicator of when the illness

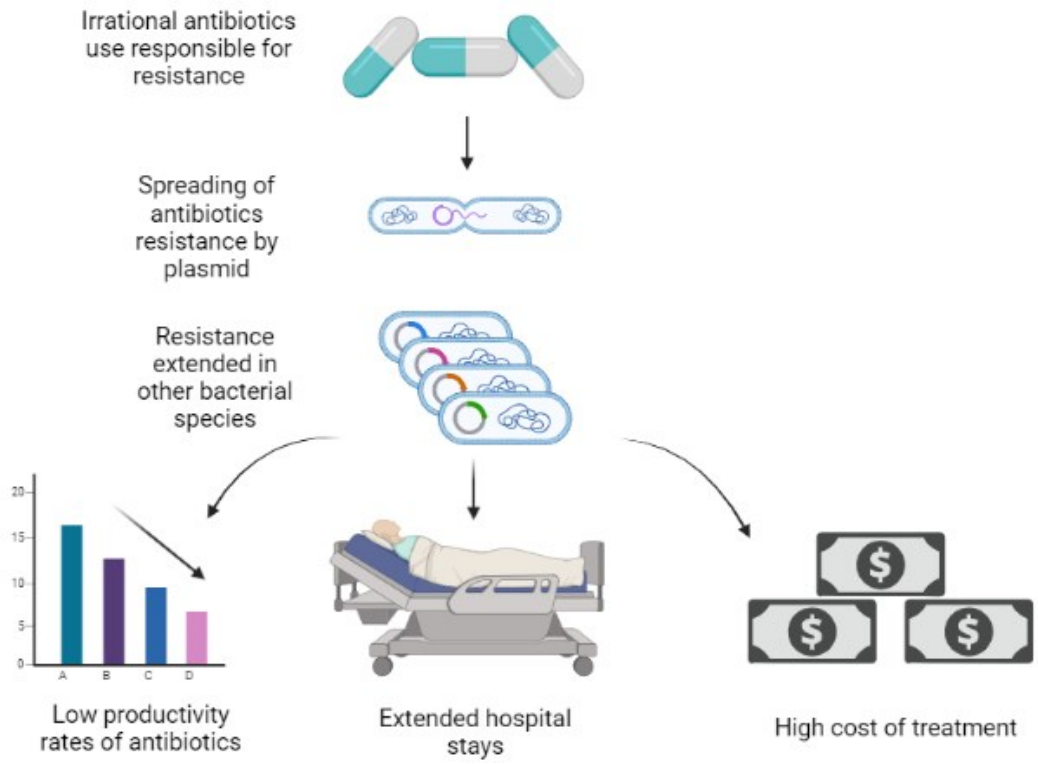

Fig. 1: Spread of antibiotics resistance through plasmid in bacteria and its impact on health and economy [51].

started [43]. Despite the fact that positive culture results are usually obtained several hours after the illness develops or after therapy has failed, as in the case of persistent urinary infections, this may understate the actual effects of resistance. Delays are additionally more likely to have an impact on outcomes when the patient is infected with a highly resistant strain, the patient is in critical condition, or their immune system is impaired [42].

The severity of the underlying illness at the time of diagnosis

The importance of the time frame of sickness intensity evaluation is an often-overlooked component in the accurate evaluation of the root cause of disease severity [43]. If the severity of the illness is evaluated while the patient is still actively sick, it could act as a key link between exposures (such as the illness) and the outcome of interest. It is critical to assess the degree of illness 148 hours before the first signs of infection since adjustment for an important mediator often results in an underestimating of the influence of the exposure of concern on the outcomes [44]. Interpreting the findings of studies that score the severity of the illness at the time the infection occurs should be done with caution since they may considerably underestimate the amount to which resistance influences outcomes [41].

Estimating the financial impact of antibiotic resistance

Measurement of hospital expenditures, hospital fees, and resource use are three methods that may be used to assess the financial cost of resistance in the hospital. The price of medications, diagnostics, and other patient safety expenses are all included in hospital charges [45]. A hospital needs to ensure that its expenditures are met, thus it charges fees to medical facilities, which appear on a patient's bill [46]. Medicare, Medicaid, and bigger insurance companies will not cover the entire amount of the payment since they receive discounts, as a result, the price on the bill for every patient is higher than the real hospital expenses to make up for these losses [47]. Because they most accurately represent the true financial burden of the hospital, hospital expenses may be a valuable outcome indicator for a specific institution, but they can be challenging to get.

Hospital charges, on the other hand, are often straightforward to get from administration databases

and constant from patient to patient across most situations, while reflecting real costs less accurately. Although adjustments may be made by the ratio of cost to charge, they often overestimate the real cost [48]. Utilization of resources more precisely evaluates the treatments or services that a patient uses. However, in order to compare, the use of resources must be transformed into monetary values. These medical care economic metrics are not usually established by a market-based pricing structure. The cost of therapy for a certain patient is established unfairly and falsely, and it may fluctuate across locations and throughout various time periods [49]. Depending on their chosen mode of payment, hospitals may use a variety of strategies to control expenses. For instance, if reimbursement is based on per diem, if compensation is based on diagnosis-related group or capitation, the hospital would prioritize decreasing expensive days of stay, such as ICU or multiple surgery days, rather than total LOS, whereas if payment is based on overall expenditures [50]. Bacteriophages, or viruses that infect bacteria, have been studied as possible antibiotic alternatives. Phage therapy employs the use of specialized phages to target and destroy bacteria, allowing for a more focused and personalized approach to treatment. Studies on the treatment of antibiotic-resistant illnesses have shown encouraging outcomes [52].

Conclusion

Antimicrobial resistance is a major danger to both global health and the global economy. It reduces the efficacy of current treatment choices, raises healthcare expenses, and reduces productivity. Bioinformatics has considerable promise for understanding and managing the health and economic consequences of antibiotic resistance. It is an important tool for policymakers, academics, and healthcare providers because of its capacity to analyze large-scale genetic data, follow resistance trends, guide precision medicine techniques, and quantify the economic impact of resistance. To limit the burden of AMR, effective methods such as antimicrobial stewardship and research and development are required. Collaboration among healthcare professionals, politicians, researchers, and the general public is required to sustain antimicrobial medication efficacy and protect public health.

Conflict of interest

The authors declare no conflict of interest.

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