

Challenges and strategies in the fight against antimicrobial resistance

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Abstract

This study aims to evaluate the scientific literature on the challenges and strategies adopted in the fight against antimicrobial resistance. This study is a literature review, carried out in the SciELO, BVS, and PubMed databases, to analyze the challenges faced and the strategies employed in the fight against antimicrobial resistance. The challenges identified in the fight against antimicrobial resistance include the inappropriate use of antibiotics, the lack of regulation, the limited access to adequate treatments in certain areas, and the rapid adaptation of pathogens. Regarding the strategies, adopting measures for the rational use of antimicrobials, public awareness policies, and medical training, investments in research for the development of new antimicrobials, improvements in epidemiological surveillance, and the implementation of strict regulations on the use of antibiotics stand out. These results aim to provide a basis for more effective public policies in the fight against antimicrobial resistance. With the growing impact of antimicrobial resistance on both public health and the global economy, it is necessary and/or essential to implement effective strategies to contain its spread. Furthermore, the implementation of public policies, such as the WHO global plan and the Brazilian national plan, plays a fundamental role in mitigating the problem. Cooperation between the health sectors, pharmaceutical industries, and society is essential, since it can prevent the worsening of this crisis, ensuring the effectiveness of future available treatments.

Keywords: public health surveillance, antibiotics, bacterial drug resistance, health strategies.

Desafios e estratégias na luta contra a resistência antimicrobiana

Resumo

O objetivo deste estudo é avaliar a literatura científica sobre os desafios e estratégias adotadas no combate à resistência antimicrobiana. Este estudo é uma revisão bibliográfica, realizada nas bases de dados SciELO, BVS e PubMed, com o objetivo de analisar os desafios enfrentados e as estratégias empregadas no combate à resistência antimicrobiana. Os desafios identificados no combate à resistência antimicrobiana incluem o uso inadequado de antibióticos, a ausência de regulamentação, o acesso limitado a tratamentos adequados em áreas de cuidado e a rápida adaptação de patógenos. Em relação às estratégias, destacam-se a adoção de medidas para o uso racional de antimicrobianos, políticas de conscientização pública e treinamento médico, investimentos em pesquisas para o desenvolvimento de novos antimicrobianos, melhorias na vigilância epidemiológica e a implementação de regulamentações rigorosas sobre o uso de antibióticos. Esses resultados visam fornecer embasamento para políticas públicas mais efetivas no combate à resistência antimicrobiana. Com o crescente impacto da resistência antimicrobiana tanto na saúde pública quanto na economia global, é necessário e/ou essencial implementar estratégias eficazes para conter sua disseminação. Além disso, a implementação de políticas públicas, como o plano global da OMS e o plano nacional brasileiro, desempenha papel fundamental na mitigação do problema. A cooperação entre os setores de saúde, indústrias farmacêuticas e sociedade é essencial, pois pode evitar o

agravamento desta crise, garantindo a eficácia dos futuros tratamentos disponíveis.

Palavras-chave: vigilância em saúde pública, antibióticos, farmacoresistência bacteriana, estratégias de saúde.

1. Introduction

Currently, antimicrobial resistance (AMR) represents one of the greatest challenges for global public health, threatening the effectiveness of essential treatments and increasing the risk of complications in common infections. According to the World Health Organization (WHO), the definition of antimicrobial resistance (AMR) is the ability of microorganisms (bacteria, fungi, viruses, and parasites) to change when exposed to antimicrobials and to resist these medications, making them ineffective. Likewise, the term RMA is the broadest term for resistance to different types of microorganisms and covers resistance to antibacterial, antiviral, antiparasitic, and antifungal drugs (WHO, 2023).

The existence of this resistance is based on the natural interaction between microorganisms in the environment as well as its increase resulting from a series of factors, such as the high consumption of antimicrobials and their inappropriate use, the excessive use of antimicrobials in food, the population's lack of knowledge about the inappropriate use of some medicines, and environmental pollution caused by the dumping of medicine residues on the soil or water (Silva et al., 2020).

Over the years, with the indiscriminate use of antimicrobials, pathogenic microorganisms have developed sophisticated mechanisms to evade the action of these medications, turning infections that were once simple to treat into serious health threats. And science and medicine have sought innovative solutions to face this growing threat. From discovering new antimicrobials to developing alternative therapies, the fight against antimicrobial resistance requires a multifaceted approach. Raising awareness about the rational use of antibiotics, strengthening infection control policies, and investing in research into new treatments are just some of the strategies that have been implemented to contain this problem (Andrade et al., 2023).

The objectives of this study are to investigate the challenges and main strategies for combating this global threat. By understanding the roots and consequences of antimicrobial resistance, as well as potential solutions, we hope to contribute to awareness and action for a future in which antimicrobial treatments can continue to be an effective tool in medicine.

2. Materials and Methods

This study consists of a literature review on antimicrobial resistance, using indexed sources to identify data on the microbiological profile, prevalence, resistance patterns, associated factors, and challenges faced in public health.

2.1 Data sources and search strategy

The literature search was conducted in the following databases:

Virtual Health Library (BVS), Scientific Electronic Library Online (SciELO), PubMed, and Google Scholar

For the search strategy, Health Sciences Descriptors (DeCS) and Boolean operators AND and OR were used to refine the results and include relevant articles on the topic. The search terms included:

Antimicrobial Resistance OR Multidrug-Resistant Bacteria

Public Health Surveillance AND Epidemiology of Bacterial Resistance

Healthcare-Associated Infections OR Community Infections

Antibiotic Use AND Strategies to Reduce Resistance

2.2 Study selection criteria

The studies were selected non-systematically, considering the relevance of the content for understanding antimicrobial resistance and its implications for public health.

Inclusion Criteria:

Articles available in the selected databases, published in Portuguese, English, or Spanish.

Studies addressing antimicrobial resistance in clinical and community pathogens.

Publications discussing strategies to contain drug resistance.

Exclusion Criteria:

Articles focusing on antifungal or antiviral resistance.

Duplicate studies across the consulted databases.

Papers without full-text access or lacking relevant information on antimicrobial resistance.

2.3 Data collection and analysis

The search was conducted randomly, without a predefined systematic protocol. The selected articles were fully read, and their data were extracted qualitatively to discuss key findings related to the microbiological profile, resistance prevalence, and control strategies.

This approach allowed for the compilation of relevant information on the impact of antimicrobial resistance on public health and highlighted challenges and strategies for mitigating the problem.

3. Literature review

3.1 Microbiological profile

The knowledge of the microbiological profile of the infection impacts the reduction of patient morbidity and mortality rates (Silva et al., 2020). However, the profile of multidrug-resistant microorganisms may vary in different locations. Resistant microorganisms can be found in several places, but the main ones are rivers and hospitals. For example, *Escherichia coli*, found in rivers, is often associated with bacterial multidrug resistance.

The species and strains can also vary in different environments within the same hospital. Although the most virulent ones are found in hospitals, the main agents of microbial resistance are prescriptions originating from primary care due to multiple factors, such as risk perceptions, patient expectations, the ideologies of the professionals (Corrêa et al., 2022), as well as the limitation of the structure and services offered in primary care.

For Corrêa et al. (2022), rivers are the main recipients of antimicrobial residues received by urban, industrial, and hospital sewage, causing a major impact on the selection of resistant bacteria present in water and sediment. Antibiotic-resistant organisms in rivers vary in different urban areas and increase when they are close to areas that use antibiotics, such as cultivation areas, hospitals, and industrial sewage. The presence of metals also contributes to the increase in antimicrobial resistance, as do the different seasons of the year, especially the rainy season.

In a study carried out at the Burns Hospital Geral “José Pangella” in Vila Penteado, it was observed that in the first 48 hours, the wounds were already colonized by gram-positive bacteria and responded to topical antimicrobials. After a week, the wounds began to be colonized by gram-negative bacteria, both those of hospital origin and gastrointestinal and respiratory origin, with increased morbidity and mortality (Silva et al., 2020).

Among the pathogens found, the most prominent were those with the potential for serious infection, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*, with *Pseudomonas* being the most prevalent in wounds. These microorganisms require broad-spectrum antibiotics. However, their large-scale use favors fungal co-infections and resistance. Group A Beta Hemolytic *Streptococcus*, *Acinetobacter baumannii*, and *Enterococcus* spp. were also found. These pathogens are especially important given their virulence and resistance to available antibiotics. This study also shows the predominance of gram-negatives over gram-positives (Araújo et al., 2020).

A study conducted in which 21 hospitals from various regions of Brazil were evaluated showed a higher rate of resistance of *Pseudomonas aeruginosa* to antimicrobials than those described in other countries. Cross-resistance to important drugs such as carbapenems, piperacillin-tazobactam and aminoglycosides, and quinolones, and their combined regimens was reported (Figueiredo et al., 2007).

3.2 Prevalence and patterns of resistance

Antimicrobial resistance is defined as the ability of microorganisms to resist the effects of antibiotics. This characteristic can be inherent to the bacteria or acquired during the infectious process. According to the United Nations (UN), bacterial resistance represents one of the greatest threats to global health. This problem compromises essential priorities, such as human development, and significantly impacts areas such as the economy, food, tourism, and migration flows. In response, cooperation, consultation, and monitoring mechanisms

have been implemented, which have different levels of adherence by countries (Giono-Cerezo et al., 2022).

It is estimated that around four million people contract healthcare-associated infections in the European Union (EU). Of these, approximately 37,000 die as a result of hospital-acquired infections caused by resistant microorganisms. Notably, the majority of these deaths (67.6%) are attributed to multidrug-resistant bacteria (Silva et al., 2020).

Potentially drug-resistant (PDR) pathogens include methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas* sp., *Acinetobacter* sp., *Stenotrophomonas maltophilia*, and extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria. These microorganisms exhibit significant resistance, making them generally insensitive to antibiotics recommended for the treatment of community-acquired infections (Cardoso et al., 2015).

There are several patterns of antimicrobial resistance, which have been acquired through indiscriminate use over the years. For example, urinary tract infections (UTIs) are one of the main reasons for consultation in medical practice, second only to respiratory infection. Urinary tract infections (UTI) are one of the main causes of consultation in medical practice, second only to respiratory infections. The authors Braoios et al. (2009) carried out a study that showed the prevalence and antimicrobial resistance profile of the microbial species most commonly isolated from patients with community-acquired UTI, in the city of Presidente Prudente, SP, in the period of two years, between January 2006 and December 2007 and as a result the resistance profile of the *E. coli* samples revealed that, in the community studied, these microorganisms present high rates of resistance (> 20%) to ampicillin (52.1%), cephalothin (41%), sulfamethoxazole + trimethoprim (38%) and tetracycline (29.1%).

In 1999, a guide for the treatment of uncomplicated urinary tract infections was published, recommending that sulfamethoxazole + trimethoprim be the empirical treatment of choice, provided that the regional prevalence of resistance to this antimicrobial does not exceed 20% (17). Therefore, this antimicrobial would no longer be recommended for empirical treatment in the region studied, and other drugs would need to be adopted. If we use the same criteria for all antimicrobials, ampicillin, cephalothin, and tetracycline should also not be indicated.

This makes the study of pharmacoresistance in these pathogens urgent, since it is related to several factors, including the indiscriminate use of antimicrobials, failures in infection control protocols, and the spread of resistance genes. This scenario reinforces the need for integrated strategies to mitigate the problem, including epidemiological surveillance, the adoption of rational prescription policies, and the development of new antimicrobial therapies. Finally, understanding the prevalence and profile of bacterial resistance in different populations is essential for the formulation of public health policies that aim to contain the spread of these strains, preserving the effectiveness of available antibiotics and ensuring better clinical outcomes.

3.3 Factors associated with antimicrobial resistance

The increase in antimicrobial resistance is a challenge driven by several factors, from the indiscriminate use of antibiotics as the main cause, to self-medication combined with inadequate prescription, which favors the selection of resistant microorganisms, making infections more difficult to treat. Furthermore, patients' low adherence to complete treatment allows surviving bacteria to develop stronger defense mechanisms. In the hospital environment, the lack of control over the spread of these pathogens, combined with inadequate hand and surface hygiene, further contributes to the problem. In the agricultural sector, the excessive use of antibiotics in animals intended for human consumption also accelerates this process, creating a worrying cycle of resistance.

In a study by authors Trautner et al. (2022) on the risk factors associated with antimicrobial resistance and adverse short-term health outcomes among adult and adolescent outpatients with uncomplicated urinary tract infection, this study found that approximately 1 in 5 episodes of uUTI were caused by isolates that were not susceptible to the initial antimicrobial prescribed. In 29.0% of these cases, a new antimicrobial was dispensed within the 28-day follow-up period. These cases demonstrated where treatments may fail despite guidelines being generally followed, suggesting that adjustment of some guidelines to accommodate the growing problem of antimicrobial resistance may be necessary.

Considering that the phenomenon of bacterial resistance is not an individual problem, but a collective and global one. The control of multiresistant microorganisms is a current bioethical issue and involves many discussions due to the increasing evolution of microbial resistance, followed by the fact that the pharmaceutical industry is unable to keep up with the evolution of this resistance. In general, antimicrobial resistance is a global problem, and the creation of antimicrobial stewardship programs can be an excellent solution (Viterbo de Faria et al., 2016).

3.4 Challenges and strategies

Considered a silent pandemic, antibiotic resistance currently being experienced is an issue that needs to be addressed by global public policies. The consequences of resistance compromise not only the therapeutic resolution of pathology but also affect the success of other more complex procedures.

With the increase in the number of bacteria resistant to available antibiotics, it was necessary for global health organizations, such as the World Health Organization (WHO), the World Organization for Animal Health (OIE), and the Food and Agriculture Organization of the United Nations (FAO), to create an action plan with strategies in which the objective would be to reduce the development of new 'superbacterias' in the long term, where all countries called up would have to use as a basis the protocols created to adapt their national plans aimed at the experience of each country, preventing the return of the pre-antibiotic era (Camou, 2017).

The formulation of the action plan to address antimicrobial resistance (RAM) began in 1998 when it was recognized by the WHO as a public health problem, but this implementation plan was only published in 2014. The approved plan presents objectives, goals, and definitions of roles and responsibilities of the actors involved, as it is a multisectoral problem that not only affects the human health sector but also affects the global economy and agriculture (Silva, 2020).

Therefore, one of the first challenges encountered in containing antimicrobial resistance is understanding that the response to confronting it depends on several stages of the production chain, use, and commercialization of antimicrobials, where a series of economic sectors are involved (Silva, 2020).

When we address the challenges encountered in the RAM response in the health field, the increase in incidence is linked to the high consumption and inadequate prescription of these antibiotics, where the factors that influence these obstacles are the difficulty in having resources available to implement actions to address RAM and the expectation of doctors to satisfy patients with the drug prescription (Araújo, 2022).

Therefore, with the challenges presented, the main objectives addressed by the action plan proposed by the World Health Organization are based on five pillars to contain the evolution of RAM, which are: adequate prescription, community education, strengthening of scientific knowledge through surveillance and research, and compliance with legislation on the appropriate use of antibiotics (WHO, 2015). And within these objectives, the countries involved presented their national action plans. The Brazilian National Plan includes raising awareness about antimicrobial resistance among both professionals and patients, strengthening scientific knowledge through surveillance and research, reducing the incidence of infections with sanitation and hygiene measures, optimizing the medicinal use of antimicrobials, and increasing investment in studies for new antibiotics, diagnostic methods, and vaccines (Brasil, 2018).

4. Conclusions

With the growing impact of microbial resistance on both public health and the global economy, it is necessary and/or essential to implement effective strategies to contain its spread. The high morbidity and mortality rates related to resistant microorganisms highlight the need for epidemiological surveillance, rational prescription of antimicrobials, and the development of new therapies. Furthermore, the implementation of public policies, such as the WHO global plan and the Brazilian national plan, plays a fundamental role in mitigating the problem. Cooperation between the health sectors, pharmaceutical industries, and society is essential, since it can prevent the worsening of this crisis, ensuring the effectiveness of future available treatments.

5. Authors' Contributions

Lígia Maria Oliveira de Souza: Conceptualization, Supervision, Writing – Review & Editing. *Alessandra Savi Bellizzi*: Investigation, Data Curation. *Paloma Marcela Vigilato*: Methodology, Formal Analysis. *Leidiane Barbosa Santos*: Investigation. *Camylla Pimentel Pereira*: Formal Analysis, Writing – Original Draft. *Rosângela de Almeida Roxo*: Resources, Validation. *Gustavo de Oliveira*: Software, Visualization. *Bárbara Priscila Alves de Souza*: Project Administration. *Andrea Paola Britos Gómez*: Supervision, Funding Acquisition.

6. Conflicts of Interest

No conflicts of interest.

7. Ethics Approval

Not applicable.

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