Antimicrobial Resistance and One Health: A Comprehensive Approach to Zoonotic Transmission and Food Security

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Abstract

Our food security is under threat from a growing global concern like antimicrobial resistance (AMR) in which microbes evolve mechanisms against antimicrobials. The World Health Organization (WHO) and other health authorities have also categorized it as growing threat. The consortium of conventional and advanced agriculture methods is contributing to control the prevalence of AMR, but these are not sufficient to address this challenge. This chapter is providing a comprehensive analysis of AMR by the One Health approach. The analysis of several case studies has revealed that the interaction between human, animal, and environmental health has increased the overall prevalence of resistant zoonotic diseases. This chapter focuses on cross-section collaboration between researchers, practitioners, and policymakers in public health, veterinary medicine, and agricultural sustainability information which will help to develop more effective strategies for this emergent AMR issue. These tactics will in line with the global efforts of protecting food security and public health from AMR. A detailed concept of how the One Health framework helps in understanding and addressing AMR's impact on zoonotic transmission and food security has been elaborated in this chapter.

Keywords: One health, Antimicrobial resistance (AMR), Food security, Public health, Zoonotic transmission

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Introduction

1. Antimicrobial Resistance

Antimicrobials are used to cure the diseases which are caused by the infectious organisms. For the past few decades, antimicrobials have been used extensively in food-producing animals, particularly in lower-middle income countries as prophylactics and growth promoters. This widespread use has led to the development of resistance against the pathogens that were previously sensitive to them and this has resulted in the global issue of antimicrobial resistance (Salam et al., 2023).

Antimicrobial resistance (AMR) can be defined as the reduced ability of microbes including bacteria, viruses, fungi, and parasites to respond to the drugs that are used for inhibiting their growth or for killing them. This results in increased mortality and morbidity due to the reduced efficacy of pharmaceutical substances like antibacterial, antivirals, antifungals, and anti-parasitic drugs. Over the past few years, the problem of AMR has been exacerbated (Ahmed et al., 2024).

1.1. Key Drivers of AMR

The key drivers of resistance are overuse of antimicrobials, improper sanitation, and discharge of drugs or their residues through industrial effluents and fecal matter into the environment. These factors accelerate the spread of AMR (Samreen et al., 2021).

1.2. Mechanisms of Transmission of Resistance

Two mechanisms govern the transmission of resistance;

- Horizontal Gene Transmission (HGT): It is the primary mechanism of resistance through which resistance genes disseminate in the environment. It can occur through transformation, transduction, conjugation, and through the mobile genetic elements (MGEs). The environment microbes act as the reservoir of resistant genes and these are then transferred through HGT to other pathogens (Irfan et al., 2022).

- Vertical Gene Transmission (VGT): It transfers genes from parents to the offspring (Irfan et al., 2022). During binary fission, the resistance genes are transmitted from the dividing cell to its daughter cells. In this way, the genes are maintained from generation to generation (Tao et al., 2022).

1.2.1. Types of Resistance and Mechanism of Development of Resistance

The HGT and VGT directly or indirectly result in the following types of resistance;

- Intrinsic resistance: It is the inherent capacity of microorganisms to be resistant to certain classes of antimicrobials (Salam et al., 2023).
- Acquired resistance: This is due to the acquisition of resistance genes through the mechanisms of HGT (Reygaert, 2018).

The commonly used mechanisms of resistance development are as follows;

- Limiting drug uptake: This type of mechanism is common in gram-negative bacteria, which have reduced permeability to many antimicrobials, particularly those targeting the cell wall, due to the presence of an outer membrane made up of lipopolysaccharides (Belay et al., 2024).
- Drug inactivation: Some bacteria make use of enzymes to degrade the drugs, making the bacteria resistant to them. For example, the β-lactam antibiotics are degraded by β-lactamases (Muteeb et al., 2023).
- Drug efflux: This mechanism gives rise to resistance to multiple drugs. Bacteria make use of protein pumps to actively pump the antimicrobials out of the cell, preventing them from accumulating in the bacterial cytoplasm. For example, the MexAB-OprM efflux pump can throw many classes of antimicrobials out of *Pseudomonas aeruginosa* (Muteeb et al., 2023).
- Drug target modification: This mechanism is commonly used by most bacteria to render the drug ineffective. In this mechanism, enzymes are used to acetylate, phosphorylate, or adenylate the drug as a result the drug is no longer able to kill or inhibit the growth of bacteria (Bo et al., 2024). For example, gram-negative bacteria use aminoglycoside-modifying enzymes (AMEs) to catalyze the chemical changes in the structure of aminoglycosides (Gauba & Rahman, 2023).
- Drug target alternation: In this mechanism of resistance the bacteria change the target of the antimicrobial as a result of which the particular antimicrobial can no longer bind or bind to a lesser with the target site. Genetic mutations reduce the expression of proteins that make up the target side of the drug eventually leading to reduced effectiveness (Bo et al., 2024).

Intrinsic resistance may make use of limiting uptake, drug inactivation, and drug efflux; acquired resistance mechanisms used may be drug target modification, drug inactivation, and drug efflux. Whereas, acquired resistance mechanisms may be due to drug target modification, drug inactivation, and drug efflux (Reygaert, 2018) as shown in Figure.1.

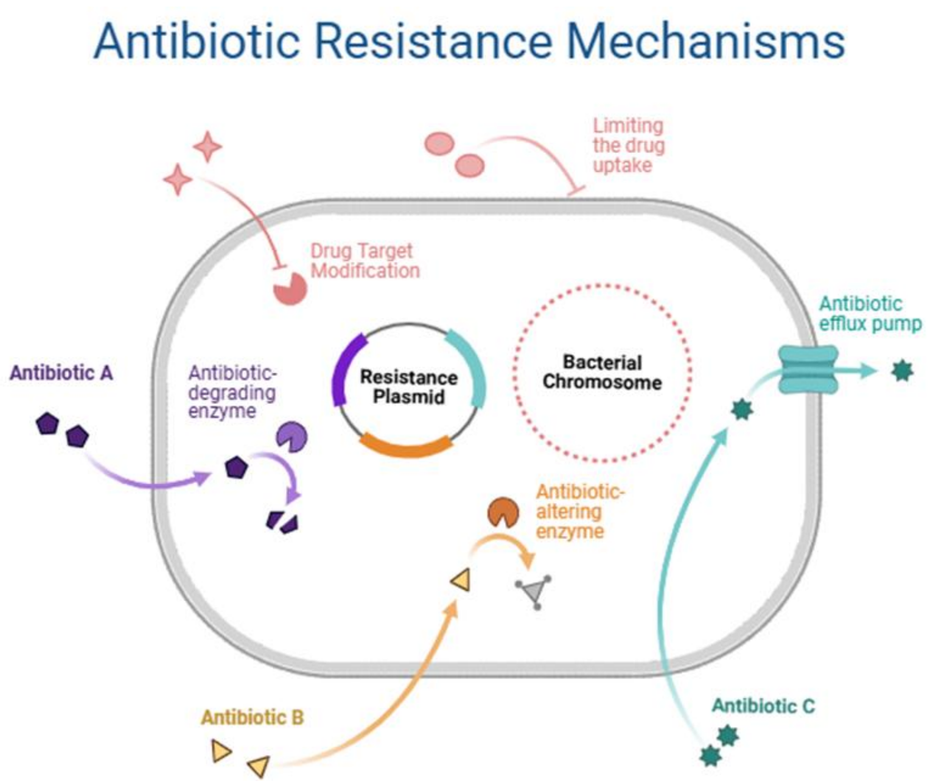

Fig. 1: Predominant intrinsic and acquired mechanisms of resistance in pathogens

1.3. Impact of AMR on Public Health

It has been estimated that AMR would kill 10 Million people per year by 2050, predicting its impact to be tremendous. A research study has demonstrated that AMR is responsible for more than seven lacs deaths per year. It has also been revealed by many studies that Enterobacterales, many of which inhabit the human gastrointestinal tract, are now resistant to carbapenem and colistin which are last-resort drugs for treating multidrug-resistant (MDR) infections. Despite the development of new antimicrobials microbes continue to evolve mechanisms of resistance against them within a few years (Irfan et al., 2022). The Economic Impact of AMR must also be taken into account because as the resistance exacerbates the total cost of treatment also increases. In the United States Centers for Disease Control and Prevention (CDC) has calculated that the overall cost of AMR per year is 55 dollars and in Europe financial burden of AMR was estimated to be about 1.5 billion Euros (Prestinaci et al., 2015). These facts and figures have made it compulsory for surveillance systems to adopt a "One Health" approach, which requires collaborative efforts at the human, animal, and environmental interface to combat AMR.

2. Zoonotic Diseases

The diseases that are transmitted from animals to humans or vice versa have been defined as zoonotic diseases by the World Health Organization (WHO). The zoonotic pathogens can be viruses, prions, fungi, and bacteria. Currently, more than two thousand zoonotic diseases have been identified so far, the well-documented zoonotic diseases are Q fever, influenza, brucellosis, anthrax, COVID-19, and rabies (Dafale et al., 2020).

The transmission of these diseases takes place through;

- Ingestion
- Inhalation
- Other pathways that can facilitate the entry of these pathogens into the mucous membranes.

2.1. Zoonotic Pathogens as a Carrier of AMR

The factors that have intensified the threat posed by zoonotic diseases are international travel, modern animal husbandry practices, deforestation, AMR, climate change, and overpopulation. A significant challenge is posed by zoonotic AMR pathogens alone. These pathogens can move from Food-Producing Animals (FPAs) to humans through the consumption of food products contaminated by them, as well as through increased contact between the farmers and these animals (Sharan et al., 2023).

A study conducted in 2019 demonstrated that the use of third-generation cephalosporins in poultry led to the development of resistance in *E.coli,* which eventually caused serious fatalities in humans. Several other studies have reported the presence of plasmid-mediated resistance genes in livestock such as the colistin resistance gene and New Delhi Metallo β-lactamase-1 ($bla_{\text{NMD-1}}$). Furthermore, metagenomics studies have revealed that the use of antimicrobials in animals at sub-therapeutic levels eventually changes the resistance profiles of commensal microbes found in humans.

Therefore, the resistance genes that are transmitted from animals to humans pose a significant threat to public health and this again emphasizes the need for one health measures to reduce the mortality and morbidity caused by such zoonotic AMR pathogens.

3. One Health

The term "One Health" was coined in the 19th Century, after the link between human and animal health was established by Rudolf Virchow. This term means that human, animal, and environmental health are all interconnected (Velazquez-Meza et al., 2022). It has now been recognized that one health is core to the prevention and control of infectious diseases present at the interface of human, animal, and environmental health (Rabinowitz et al., 2013).

3.1. One Health Approach

The link between AMR and poor environmental health infrastructure has been highlighted by some studies. In two countries of southern Africa namely Uganda and Malawi research was conducted that illustrated that the prevalence of ESBL- producing *E.coli* in humans was positively correlated with wet-season and close contact with animals. Another study conducted in Kenya demonstrated that there is significant flux of AMR genes between animals and humans. Furthermore, in Europe as well several researchers have provided evidence of intermixing of resistance genes between soil, humans, and animals (Musicha et al., 2024). AMR being a multifaceted issue in the world has brought together several international agencies including WHO, Food and Agriculture Organization (FAO), and World Organization for Animal Health (WOAH) to develop a Global Action Plan against it.

3.2. The Spread of AMR and WASH Systems

An important part of the One Health approach is the WASH (water, sanitation, and hygiene) system. In regions where the WASH system is employed and strong there is very little evidence for ESBL-*E.coli* and *K. pneumoniae* transmission between humans, animals, and the environment. The presence of these bacteria in healthcare settings informs us that the infection control and prevention (IPC) strategy or WASH program in these settings is not strong or is not properly employed, placing the public at risk of adverse outcomes (Musicha et al., 2024).

It must be noted that the "One Health" approach is critical to address the AMR problem as it unifies all the sectors and stresses the importance of research in the priority areas of the ecosystem and the wildlife. It also demonstrates the importance of collaboration among the veterinarian, public health professional, and all the stakeholders to use an integrative approach to combat AMR (White & Hughes, 2019).

4. AMR and Food Security

Antimicrobial resistance (AMR) may reverse antibiotics critical benefits, not just in people, where decades of progress in healthcare outcomes are jeopardized, but also in the agricultural sector. As the world moves towards the Sustainable Development Goals (SDGs), food safety is a vital part of improving and strengthening global health (Founou et al., 2021). The application of antibiotics in agriculture is subject to considerable measures to influence food system behaviors, such as supporting a more responsible application of antibiotics on farms through market-level measures (Regan et al., 2023).

AMR continues to be of great interest to various food stakeholders. Food can become contaminated at any point, from the field to the store, by bacteria that are resistant to antibiotics or by genes that cause pathogenic bacteria to become resistant to antibiotics (Samtiya et al., 2022). Bactericides, fungicides, and other pesticides are vital tools for managing plant diseases. However, applying them can leave traces on crops and in the atmosphere, with potentially negative implications. The use of streptomycin, oxytetracycline, copper-based compounds, and some fungicides is also associated with increasing plant pathogen resistance to these drugs (Miller et al., 2022). A wide variety of dietary items, both animal and vegetable, contain most antibiotic residues. The primary causes of antibiotics in food include misuse (overdosing, disregarding the withdrawal time), drinking water tainted with antibiotics, and improperly disposing of animal waste (Ghimpețeanu et al., 2022).

5. Global Initiatives to AMR

According to current estimates, antimicrobial resistance (AMR) is a developing public health concern that will cost the world economy USD 100 trillion by 2050 and result in over 10 million deaths annually (Chindelevitch et al., 2022). In less developed nations, the use of unnecessary antibiotics in animal feed to promote growth is still mostly unregulated. Developing countries continue to employ antimicrobial drugs to stimulate animal development to maintain animal health, increase productivity, and raise farmer earnings. However, these contradict Swedish agricultural data that indicated no drop in output after the ban exercise (Manyi-Loh et al., 2018).

According to European monitoring programs, Sweden has one of the lowest rates of antibiotic use for animals in Europe and a lower incidence of AMR in animals than most of the other EU Member States (Wierup et al., 2021). Taking into consideration the WHO Global Action Plan on AMR, nations are developing and implementing national action plans on AMR, which should first of all raise awareness and understanding of AMR. Food and Agriculture Organization (FAO) helps governments, farmers, dealers, and other stakeholders to move towards responsible antimicrobial use in agriculture to reduce antimicrobial resistance (WHO, 2023). Despite widespread endorsement of global efforts to counter antimicrobial resistance (AMR), there has been scant research into overcoming barriers to carrying out AMR national action plans in low and middle-income nations (Khan et al., 2020). The FAO, World Organization of Animal Health (WOAH), and WHO were collaborating during the avian influenza epidemic in Asia and Africa to empower the One Health approach and intersectoral collaboration. The Asia Highly Pathogenic Emerging Diseases (HPED) program was from 2009 to 2014. The program, supported by the European Commission was carried out by FAO, WOAH, and WHO in close collaboration with the ASEAN and SAARC secretariats. The HPED initiative, in turn, resulted in the establishment of a regional tripartite coordination framework in the Asia-Pacific area to facilitate collaboration between animal and human health sectors (Gongal et al., 2020).

The guidelines or standards that have been established to direct the use of antibiotics in clinical and agricultural contexts vary from one nation to the next and between industrialized and developing nations. This emphasis is on the global heterogeneity in antibiotic use patterns (Van Boeckel et al., 2015). However, a big population, demographic disparities in healthcare systems in developing countries, and socioeconomic level (transmittable illness prevalence, income level, educational position) all have a detrimental impact on antibiotic policies (Ayukekbong et al., 2017).

6. Global Research Priorities to AMR

AMR is a serious public health concern that is still growing. The creation of new antibiotics, diagnostics, and preventative measures as well as the development of methods to reduce the spread of drug-resistant bacteria and resistance depend on basic microbiological research to fill gaps in understanding (Mattar et al., 2020). Both combating infectious diseases and their prevention, monitoring, and accurate diagnosis depend on prevention, monitoring, and accurate diagnosis. However, the cornerstone of treatment is moving forward with advances in innovative treatment such as traditional antimicrobial drugs, combinations of these drugs, and other alternative therapies like bacteriophages or personalized medical methods. Improvements in treatment adherence may also be made using data technologies to address the poor use of recommended antibiotic regimens, a key cause of AMR (Llewelyn et al., 2017).

Determination of research priority involved a multi-phase process that included a scoping analysis of knowledge gaps and expert feedback through open calls and surveys to determine research priorities. A refined Child Health and Nutrition Studies Initiative strategy that strictly allowed for the selection of priority based on global representation and applicability. It also recognizes the disparities in diagnostic, antibiotic, and infection prevention measures accessibility, availability, and use in low-resource settings (Bertagnolio et al., 2024). Data on resistance for high-income countries (HICs) for which resistance data from surveillance systems such as the European Food Safety Authority (EFSA), the National Antimicrobial Resistance Monitoring System (NARMS), the Japanese Veterinary Antimicrobial Resistance Monitoring System (NARMS) was available through open access websites and reports (Venkateswaran et al., 2024). Gaining antimicrobial security will require us to balance AMR studies between novel agents and methods to sustain and optimise the effectiveness of current agents. More equitable funding for antimicrobial usage optimisation, including research on ways to protect and enhance the effectiveness of both novel and existing antimicrobials (Charani et al., 2021).

Most antibiotics have so far been found by investigating naturally occurring substances, such as by looking for antibacterial molecules in soil-dwelling microorganisms (Atanasov et al., 2021). According to a 2017 estimate, developing a new antibiotic would cost 1.5 billion US dollars, but the income generated would only be 46 million, which would account for the market dropouts. It has been proposed that incentive structures be changed to promote the development of antibiotics; the UK is already experimenting with a subscription-based pricing approach (Mahase, 2020). The development of new antibiotics must be started right now to lessen the burden of AMR (Wright, 2017).

Conclusion

A revolutionary approach that goes beyond the conventional boundaries between environmental health, veterinary medicine, and human medicine is required to combat antimicrobial resistance (AMR). This chapter has demonstrated how the One Health framework provides a comprehensive concept for understanding and addressing AMR's impact on zoonotic transmission and food security. The evidence presented indicates the urgent need for coordinated actions, integrated surveillance systems, and constant global collaboration. A roadmap has been created by recognizing effective international initiatives and critical research priorities for future action. Governments, academic institutions, and stakeholders from a variety of industries must remain committed to the implementation of proposed strategies. We can only successfully battle AMR while preserving food security and maintaining public health for future generations by working together collaboratively.

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