Understanding and Controlling Antimicrobial Resistance in Foodborne Pathogens

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Abstract

Antimicrobial resistance (AMR) in food borne pathogens is a severe health problem due to the continuous increase in resistant bacteria and genes into the food chain through environmental contamination, animal feces, and human handling of foods. Bacterial pathogens are well known agents of food borne diseases including *Clostridium botulinum*, *Bacillus cereus*, *Listeria monocytogenes*, and *Staphylococcus aureus*. Essential methods of food processing decrease the bacterial infection, but stressed cells remain or discard resistance genes in the environment, amplifying AMR. It develops genetically through mutations and through mobile genetic elements such as plasmids through mechanisms of efflux pump, ribosomal protection and enzymatic inactivation. Also, bacteria and fungi formation of biofilm increases the resistance to antibiotics and antifungal drugs. A global focus towards tackling the AMR crisis is necessary to adopt alternative treatments including metal nanoparticles, antimicrobial peptides, and phage therapy. Therefore, combining the modern approaches of alternative therapies and strong surveillance system in One Health context can strengthen the efforts to combat AMR. There is a need for a concerted effort from scholars from around the world to gain knowledge, disseminate new ideas, and enhance the ability to protect future generations from the adverse effects of foodborne AMR.

Keywords: Antimicrobial resistance, Alternative therapy, Foodborne pathogens, Horizontal gene transfer, One Health, Phage therapy

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Introduction

Food is the basic need for survival, but it also can act as vehicle for transmission of pathogens like bacteria, virus, or parasite that may have contaminated the food during processing. Due to the high prevalence and heterogeneous nature affecting the population, these illnesses have now emerged as a major public health concern all over the world. According to WHO, about 600 million instances of foodborne illnesses occur every year and food-borne pathogens are responsible for about 70% of such incidences through contamination of foods, water and soil with their metabolite and toxins (FAO, 2021: Ge et al., 2022)

Antimicrobial resistance (AMR) in food-borne pathogens constitutes a severe threat to public health since resistant bacteria and genes spread through the food chain through different routes. It can be acquired through soil and water, contact with animals especially fecaes, and human activities. Contaminating animal products during slaughtering and plants by irrigation. Besides these, food handling and processing further increase the spread of AMR (Verraes et al., 2013).

The food processing and preservation procedures have two functions towards controlling bacteria in foods. These methods have positive results in decreasing bacteria concentration, but a few of them may remain in a stressed or sub-lethally damaged state. Bacterial cells can also discharge their genetic materials, including resistance genes, into the surroundings and potentially spread AMR (Deák & Farkas, 2013).

The pathogens causing the spread of AMR are found in animal-derived foods including poultry, beef, pork, and seafood, and plant derived foods including leafy greens and grains. Factors like dust, water, and soil increase the risk through contamination by feces, manure fertilizers and contaminated water sources. The unhygienic nature of food handlers together with improper way of food processing also play a part in the exacerbation of the problem. Also, fermented foods and those with probiotics, together with plants generated through genetic modification that contain the resistance marker genes complicate the spread of AMR through food chains (Samtiya et al., 2022).

1. Foodborne Pathogen

Bacteria constitute the highest number of causative agents of foodborne diseases and vary in shape, kind and behavior. Among the pathogenic bacteria, *Clostridium botulinum*, *C. perfringens*, *Bacillus subtilis*, and *B. cereus* are heat-tolerant because they form spores. Some bacterial species of pathogenic significance, such as *Staphylococcus aureus* and *Clostridium botulinum* are known to form heat resistant spores. Majority of the pathogens are mesophilic and their activities are most favorable in the temperature range of 20-45°C. However, some foodborne pathogens which are known as psychrotrophic can grow at refrigeration temperature below 10°C; such pathogens include *Listeria monocytogenes* and *Yersinia enterocolitica* (Bacon & Sofos, 2003). The pathogens with the highest frequency included *Escherichia coli*, *Salmonella spp, Staphylococcus aureus*, and *Listeria species* (Alsayeqh et al., 2021). *Campylobacter spp., Staphylococcus spp., Enterococci, Listeria monocytogenes,* and *Enterobacterales* such as *Salmonella spp.* and *E. coli* are frequently identified on animal farms. These can be emitted into the atmosphere and spread on the surface water, with potential health consequences for human beings and acting as pathways for the dissemination of antibiotic resistant genes (Argudín et al., 2017).

2. Transmission to Humans

Campylobacter spp. is generally acquired through food products, especially meat products with poultry being the main source. Poultry meat is estimated to be responsible for approximately 50–80% of human campylobacteriosis; the most common species is *Campylobacter jejuni* (Acke et al., 2011). Antibiotic-resistant staphylococci, coagulase positive and negative: *S. aureus*, *S. epidermidis*, and *S. xylosus*, are often recovered in poultry, beef, and ready to eat cured meats (Fijałkowski et al., 2016). Milk has remained a major route through which foodborne pathogens that cause diseases in humans are transported. The bacterial flora is composed by lactic acid bacteria (*Lactococcus, Lactobacillus, Leuconostoc, Streptococcus* and *Enterococcus spp.*); *Enterobacteriaceae; Staphylococcus spp.* and *Micrococcaceae* (Zastempowska et al., 2016). Importantly, it must be understood that water-borne pathogens can be transferred in various ways, including direct contact with the environmental water, or through fish consumption (Zhong et al., 2022).

3. Resistant Genes and Antibiotic Resistance

The *Campylobacter* strains demonstrated significantly high resistance to fluoroquinolones, including ciprofloxacin and nalidixic acid and tetracyclines. The key resistance patterns are the gain of a mutation at the Thr-86 position in the *gyrA* gene for quinolone resistance, and the *tet(O)* gene for tetracycline resistance. Resistance to macrolides such as erythromycin is unusual and is associated with changes in the 23S rRNA gene as well as the presence of the *erm(B)* gene. The staphylococci originating from meat products are persistently associated with resistance genes such as *blaZ*, *mecA*, *erm* (*A, B, C*), and *tet* (*K, L, M, O*) (Witte, 1999).

4. Mechanisms of Antimicrobial Resistance in Foodborne Pathogens

4.1. Genetic Mechanisms

The antimicrobial resistance in foodborne pathogens primarily arises from horizontal gene transfer mediated by mobile genetic elements, including plasmids, transposons, and integrons, while chromosomal mutations play a secondary role. The food environment facilitates gene transfer and resistance development, particularly under stresses imposed by food preservation systems. Over-reliance on biocides in food production and processing exacerbates the issue by selecting biocide-resistant strains. Sub-lethal exposure to biocides further drives the emergence of bacteria with enhanced multi-drug efflux pump activity, leading to cross-resistance to antibiotics (Walsh & Fanning, 2008). The antimicrobial resistance in foodborne pathogens arises through genetic mutations or horizontal gene transfer via mobile elements like plasmids and transposons. The resistance mechanisms include efflux pumps, ribosomal protection, and enzymatic inactivation of antibiotics. The key resistance genes, such as *mecA*, *tetK*, and *aacA-aphD*, confer resistance to beta-lactams, tetracyclines, and aminoglycosides, making such microbes' significant multidrug-resistant pathogens (Haq et al., 2024).

4.2. Role of Biofilms

Biofilm is a polymeric substance in which bacterial cells are lodged surrounded by a protective extracellular slime espousing genetic exchange, and resistance to antibiotics along with preventing the desiccation. The biofilms consist of structural elements including extracellular DNA, proteins periodate-soluble and insoluble polysaccharides biofilm matrix components that have diverse roles. This matrix prevents the entry of antimicrobial agents and plays a major role in the development of antimicrobial resistance (Balducci et al. 2023).

4.3. Ecological and Evolutionary Drivers

Ecologically, sources like soil, water, and micro-biomes in humans, animals, and food, serve as reservoirs of resistance genes. The selective pressures from antimicrobial use in agriculture, aquaculture and clinical practices act as the driving forces for the acquisition and dissemination of evolutionary factors. The horizontal gene transfer increases the rate at which resistance occurs, while ecological factors and evolutionary changes keep and intensify AMR in various settings (González Zorn & Escudero, 2012). Strategies like inhibiting efflux pumps and eliminating resistance-bearing plasmids could help restore antibiotic efficacy and mitigate the spread of resistance (Walsh & Fanning, 2008).

5. Role of Agriculture in AMR Development

Antibiotics are widely used in agriculture, including livestock, poultry, fisheries, and crop disease management, with a primary role in promoting growth and preventing infections in animals. However, their usage in veterinary medicine contributes to the development and spread of antimicrobial resistance (AMR). The use of highly important and critically important antibiotics without careful management and the lack of new antibiotics in recent years turn a significant global threat to disease control, animal health, food security, and the environment (Singh, et al., 2024).

Agriculture plays a significant role in the development of antimicrobial resistance (AMR) through various transmission pathways in food production environments, including plant-based food, terrestrial animals, and aquaculture. The key sources of AMR transmission include fertilizers, irrigation, and water, with feed and humans identified as major contributors to animal production. High-priority antimicrobial-resistant bacteria (ARB) and genes, such as carbapenem-resistant *Enterobacterales* and fluoroquinolone-resistant *Campylobacter spp.*, were found in manure, soil, and water (EFSA Panel on Biological Hazards (BIOHAZ) et al., 2021).

6. Environmental Contributions to AMR Proliferation

6.1. Soil Contamination

Soil environment is relevant to the development and dissemination of AMR with agriculture being a source of substances containing antimicrobials. The spread of antibiotics through animal waste, used as fertilizers brings in residual antibiotics into the soil ecosystem changes microbial populations in soil and increases, antibiotic-resistant strains. This leads to selection pressure that enhances resistant microorganisms and genome transference of ARGs specific to plant and human symbiotic microbes (Ifedinezi et al., 2024). The various processes leading to the development of resistance in soil bacteria are as varied as the nature of the soil niche. There is clear evidence that horizontal gene transfer is the mechanism responsible for transferring resistance genes in soil bacteria. The process of transformation that is one of the types of horizontal gene transfer involves the acquisition of free DNA in the surroundings and adherence to soil particles including clay minerals (Shi, et al., 2023). The patterns for the development of AMR are closely related to the inherent patterns of soil bacteria resistance mechanisms. Some of the important mechanisms include where bacteria breaking down the antibiotics into inactive compounds, altering the chemical structure of the antibiotics, and efflux pump through which the bacterial cells force the antibiotics aside (Peterson & Kaur, 2018). The development and spread of antimicrobial resistance (AMR) are also shaped by the physicochemical properties of soil, such as pH levels, organic matter content, and the presence of metals and minerals. The soil pH can influence microbial activity and the availability of antibiotics, while organic matter provides nutrients that sustain microbial communities, potentially enhancing gene exchange. Metals and minerals, particularly heavy metals, can co-select for resistance genes by applying selective pressure similar to antibiotics, further facilitating the persistence and transfer of AMR within soil ecosystems (Zhou et al., 2021).

6.2. Water Contaminations

A significant portion of antibiotics consumed by humans is excreted in biologically active forms, entering wastewater treatment plants (WWTPs) where they undergo biodegradation, bind to sludge, or exit unchanged in effluent. Factors such as WWTP type, retention time, and influent composition influence antibiotic persistence and removal. Antibiotics in sludge and effluent contribute to environmental contamination, posing risks through land application and discharge into rivers. Grey water, black water, and reclaimed water, used increasingly for irrigation and other applications, introduce antibiotics and resistance-driving chemicals into previously uncontaminated environments, amplifying antibiotic-resistant bacteria. The interaction of microbial communities, antibiotics, and organic matter in these systems significantly affects antibiotic fate and resistance proliferation (Singer et al., 2016).

6.3. Role of Aquatic Environment in AMR Proliferation

Aquatic environments, such as lakes, rivers, oceans, and other water bodies, play a crucial role in maintaining ecological balance, supporting biodiversity, and providing resources for both humans and animals. However, these ecosystems are increasingly polluted due to human activities, particularly the widespread use and improper disposal of antibiotics (Nguyen & Huynh, 2023). In water bodies antibiotics and their residues put selective pressures favoring the survival of resistant bacteria. The water ecosystem also acts as a reservoir for AMR genes just like the soil ecosystem and promotes the transmission of such genes. The genetics of microorganisms are quite clear in getting change in presence of antibiotics through mechanisms of mutation, conjugation transformations, and transduction lead to disseminate resistance (Zubareva et al., 2022).

7. Strategies for Controlling AMR

To control AMR, some of the strategies include rational antibiotic usage, strict limitation on unregulated access to antibiotics, improving hand hygiene to reduce the spread of resistant pathogens, and strengthened measures to prevent infections. To combat AMR it is necessary to understand the molecular mechanism of resistance, accelerating the research of discovering drugs and vaccines, involving multifaceted and integrated regulatory approaches at the global, national, and local level (Uchil et al., 2014). The WHO suggests the following strategies to overcome antimicrobial resistance globally (WHO, 2001).

- Strengthening collaboration among governments, NGOs, professional organizations, and international agencies.
- Developing network to check antimicrobial use and resistance.
- Implementing international measures to address counterfeit antimicrobial drugs.
- Providing incentives for research and development of new drugs and vaccines.
- Developing new programs and reinforcing existing ones to manage and contain AMR.

The five strategic objectives of WHO's Global Action Plan, outlined in Table 1, highlight key strategies to address and regulate concerns related to AMR.

7.1. Surveillance and Monitoring

Antimicrobial resistance surveillance systems are organized and systematic processes designed to measure the prevalence or incidence of AMR through ongoing or periodic monitoring, conducted using defined methodologies and specific indicators (Dunne, et al., 2000). Effective surveillance of antimicrobial resistance is essential to monitor therapy guidelines, guide public health interventions, and support antimicrobial stewardship and drug development. However, current systems, particularly in Europe, face fragmentation, structural issues, and insufficient integration of epidemiological and clinical data. The key challenges include limited genetic typing, inadequate early warning systems, poor coordination between human and veterinary surveillance, and restricted access to food surveillance data due to commercial sensitivities. These gaps delay translational approaches, hinder research on target microorganisms, and stall drug discovery (Tacconelli et al., 2018).

Although the AMR ratio is increasing day by day in low income countries due to limited resources surveillance systems are facing challenges. The surveillance systems of WHO are aiming to find out these gaps and the World Health Organization's (WHO) Global AMR Surveillance system identifies these gaps and reduces these gaps by tracking infections, resistance profiles and usage of antibiotics in different sectors of One Health. These systems are critical for supporting the development of standard treatment guidelines, assessing interventions to hinder AMR, generating early detection of emerging resistant strains and rapid identification and control of outbreaks. The development of AMR surveillance in resource-limited settings is important to minimize the impact of AMR at the global level (Seale et al., 2017).

Table 1: Possible actions to reduce the threat of AMR (Samtiya et al., 2022).

Possible Actions	Effects
Increase awareness	Awareness programs are supported by mass, and social media repeated messaging regarding issues related to AMR, which may decrease antibiotic usage and AMR rates.
Support knowledge through observation	Organizations (govt./non-govt.) along with industry and academia can improve the practical knowledge to combat AMR concerns
Cleanliness, hygiene, and preventive measures	Proper hygiene and cleanliness by following necessary guidelines can help to decrease AMR issues.
Regulate the use of antimicrobials	Guidelines should be compulsory, especially for antibiotics used to treat infectious diseases in animals and humans.
Improve economic situation	There is a need for investment in the advancement of novel antimicrobial treatments, analytical tools, and vaccines. Shortage in such investment reveals the trends of continued AMR.

7.2. Judicious Antimicrobial Use

The judicious antimicrobial usage in animal farming acts positively in lowering the development of antimicrobial resistance (AMR) because it poses dangers to humans and animals. The present research in livestock farms investigates affordable approaches to decrease AMR including additive elements like essential oils, clay minerals, organic acids and probiotics as well as targeted vaccination programs and modified care methods. The proper animal health and productivity remain unaffected by the implementation of these methods together with biosecurity protocols (Santinello et al., 2022). The development of new veterinary antibacterial products proves essential for judicious antimicrobial use because of their safe and effective nature. The clinical success of these products depends on antibacterial effect assessment from culture and susceptibility testing in addition to pharmacokinetic and pharmacodynamics data which are used for determining proper dosage administration for maximum therapeutic effect and minimized resistance development (Miller et al., 2021).

7.3. Alternative Therapies

The increase in antimicrobial resistance (AMR) and biofilm-related infectious agents in food materials is elevating the threat of antibiotic resistance, therefore it is necessary to explore and find out unique and alternative treatment options. Modern strategies to combat AMR and biofilm-related infections involve metal nanoparticles along with quaternary ammonium compounds, chitosan derivatives and antimicrobial peptides, phage therapy and stimuli-responsive materials in order to lower the ratio of such ailments in food and food products (Xu et al., 2021). The phage therapy is acting a potential solution to combat antimicrobial resistance. Using bacteriophages, its proteins alone or in combination with antimicrobial agents (Pal, et al., 2024). Boasting the immune system using antimicrobial peptides (AMPs) is a possible solution to reduce the use of antibiotics, delivering better therapeutic results (Mba & Nweze, 2022). The characteristics of nanoparticles allow them to disrupt bacterial cells, generating reactive oxygen species and altering protein function (Basavegowda & Baek, 2021).

7.4. Innovations in Food Safety

Innovative food packaging solutions, using bacteriophages serve both as an AMR management tool and an improved system for maintaining food safety. Bacteriophages have the selective ability to affect harmful foodborne bacteria while preserving beneficial bacterial populations thus making them viable natural antimicrobial substitutes against synthetic agents. Bacteriophage fortification in food packaging films enables both microorganism elimination and contributes to AMR management (Wagh et al., 2023).

7.5. The One Health Approach

To overcome foodborne pathogens, it is essential to address the One Health approach. The One Health approach entails speed-up worldwide advancement and development of innovative solutions to secure the future along with improved collaboration for better collective action together with investments in sustainable solutions and enhanced global governance mechanisms and accountability.

The AMR can be mitigated by using antibiotics for treating only bacterial infections rather than using in food production to increase growth. The medical and agricultural management of antimicrobials needs strict regulation as well as environmental surveillance for bacterial resistance to actually reach success (Velazquez-Meza et al., 2022).

8. Challenges and Future Directions of AMR

Expanding research about antimicrobial resistance in foodborne pathogens require extensive problem-solving and numerous promising future developments. Medical practices and animal farming segments heavily depend on antimicrobial usage as a main solution but the funding for antibiotic development remains insufficient while limited profit prospects hinder new drug creation (Ahmed et al., 2024). The absence of rapid diagnostic and delayed implementation of surveillance systems make it more challenging to mitigate AMR. Similarly, the combination of poor international coordination together with non-existent regulatory policies for antibiotic use creates a worse problem between human health care and animal agriculture and environmental protection (Aijaz et al., 2023).

Conclusion

Increasing antimicrobial resistance in foodborne pathogens is a challenging threat to food safety and public health throughout the world. Successful AMR control depends on the investigation of genetic mutations and horizontal gene transfer. Similarly, actions against antimicrobial misuse in agriculture and healthcare settings are necessary to combat AMR. Along with AMR combating strategies, it is necessary to promote the use of alternative therapies like phage therapy as well as antimicrobial peptides and nanoparticles. The "One Health" approach combined with advance surveillance systems and sustainable practices should welcome these solutions to strengthen AMR mitigation efforts. The AMR crisis requires worldwide research alliance and alternative strategies implementation to secure food safety protection for our future generations.

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