# Zoonotic Transmission of Antimicrobial Resistance in Pakistan: Alternative Measures to Address the Silent Pandemic

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## Abstract

Antimicrobial resistance is causing serious public health concerns in the 21st century, particularly of zoonotic origin. Pakistan is facing increasing challenges of a rise in resistance due to misuse and irrational use of antibiotics in veterinary and community settings, which render it ineffective. Some of the common zoonotic pathogens which showed high resistance towards antibiotics are *Salmonella*, *Brucella*, *Mycobacterium*, *Campylobacter* and *Staphylococcus* including methicillin-resistant *Staphylococcus aureus* which are mainly transmitted from animals to humans particularly via direct contact with infected animal or during handling of animal and consumption of infected animal products such as undercooked meat and unpasteurized dairy products. Some of the measures, including phage therapy, use of probiotics and prebiotics, and use of plant extracts, can be used as alternative measures to control antimicrobial resistance. Moreover, One Health offers a variety of strategies to stop the zoonotic spread of antimicrobial resistance and maintain the effective use of antimicrobials for both human and animal treatments.

Keywords: Antimicrobial resistance, Zoonotic transmission, Zoonotic pathogens, Silent pandemic, One Health, Foodborne diseases

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## Introduction

Antimicrobials, including antibiotics, antifungals, and antivirals, are the drugs that are used to inhibit or kill microorganisms, which further prevent or treat infectious diseases of humans, animals and plants (Purssell, 2020). Antimicrobial resistance occurs when microorganisms, including bacteria, viruses, fungi, or parasites, no longer respond to the antimicrobial medications used against them. As a result, antimicrobial agents become ineffective, leading to severe diseases, which become difficult to treat, ultimately leading to death. There can be multiple reasons for antimicrobial resistance, including misuse or overuse of antimicrobials (Tang et al., 2023). It is estimated that approximately 10 million deaths will occur yearly by 2050 worldwide (Naghavi et al., 2024). Thus, one of the necessary and important challenges for researchers is to fight antimicrobial resistance for the sake of a disease-free environment of animal and human communities because the issue of zoonotic transmission is increasing day by day (Jansen et al., 2019). However, resistance is an emerging issue worldwide, but mainly in developing countries. The resistance issue in Pakistan is a significant public health concern among community settings and can be easily transmitted among animal and human communities, as it can be from human to animal or animal to human, commonly known as zoonotic transmission (Olaru et al., 2023). This review provides a brief overview of antimicrobial resistance (AMR), mainly highlighting the connection between humans and animals. Many strategies and approaches are being used to understand the issues caused by antimicrobial resistance (AMR), including the development of new antimicrobials agents, along with the techniques and systems to monitor AMR in both human and animals as well as educating the responsible persons about the use of antibiotics in clinical and animal settings, and understanding the effects of AMR on the environment and public health.

### Zoonotic Transmission and Mechanism of Antimicrobial Resistance

Zoonotic transmission of antimicrobial resistance (AMR) is commonly the transmission of resistant bacteria from animals to humans and vice versa. The transmission can be by multiple ways, including direct contact with animals, contaminated food, or due to contact with contaminated water or soil (Dafale et al., 2020). The main mechanism in spreading of AMR among them is the horizontal gene transfer (HGT), a mechanism in which resistance genes may transferred between bacteria via plasmid, bacteriophage or other mobile genetic elements

including transposons, also known as jumping genes, further allowing bacteria including non-pathogenic ones to acquire resistance genes from pathogenic bacteria and spread across species particularly among food-producing animals (Argudín et al., 2017). The treatment procedures by using the antimicrobial, particularly antibiotics, support the interchange of resistant elements within or across bacterial growth, resulting in the formation and survival of resistant clones. However, in the case of antibiotics such as carbapenems and some generations of cephalosporins, plasmids play a significant role (Raza et al., 2023). The factors commonly involved in the development of resistance to antimicrobial agents are shown in Figure 1.

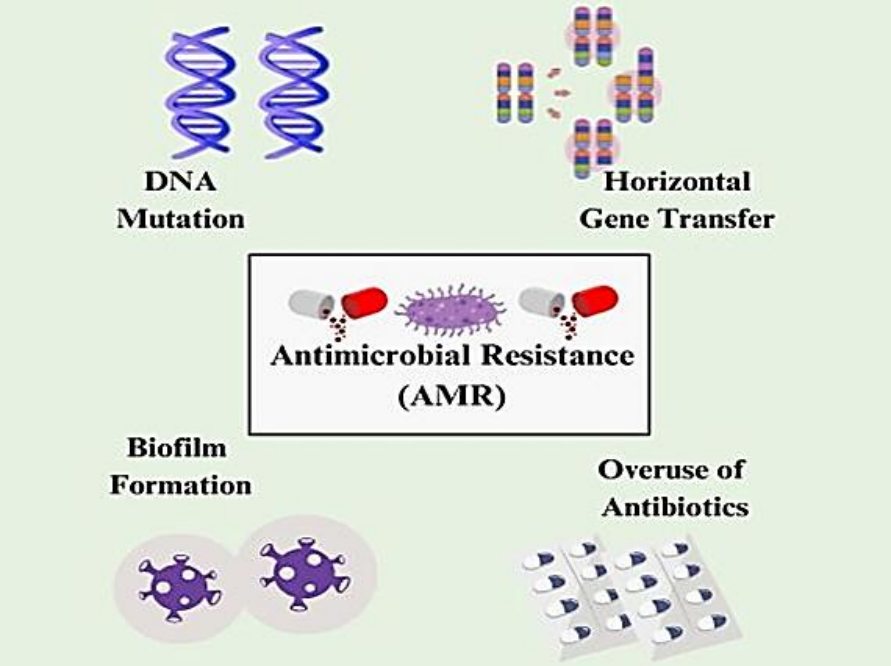


Fig. 1: Factors involved in the development of antimicrobial resistance.

## Main Causes of Zoonotic Antimicrobial Resistance

The main causes of zoonotic antibiotic resistance are the misuse and overuse of antibiotics among animals and humans. In addition, self-medication and frequent access to antimicrobials in community and veterinary settings are also major causes of resistance to medications. Additionally, more than 60% population in Pakistan relies on self-medication (Dhedhi et al., 2021). The companies in Pakistan recently have 647 operational licenses from the Drug Regulatory Authority of Pakistan for the production of drugs, while none of the licensed production units have received approval from the United States Food and Drug Administration (FDA). Pharmacists in Pakistan usually provide antibiotics and medications without a doctor's prescription. Therefore, anyone has easy access to buy over-the-counter antibiotics, including "watch" and "reserve" antibiotics, which strictly need prescriptions (Rasheed et al., 2019).

## Antimicrobials Used in Livestock Production

The use of antimicrobials in and during livestock production is called antimicrobial utilization. This utilization contributes to the spread of antimicrobial resistance. About 70% of the antimicrobials are used worldwide to facilitate the increase of growth and feed production, along with preventing sickness in livestock (Tiseo et al., 2020).

Table 1: Occurrence of zoonotic bacteria and resistant antibiotics from different animal sources.

| Sr. No. | Pathogen | Sample type | Occurrence (%) | Highly resistant antibiotics | References |
|---|---|---|---|---|---|
| 1 | *Salmonella* | Meat | 57% | Erythromycin (100%), cefepime (98.24%), colistin (94.73%) | (Fatima et al., 2023) |
| 2 | *Salmonella* | Poultry Products | 25.67% | Oxacillin (100%), clindamycin (100%), erythromycin (100%) | (Siddique et al., 2021) |
| 3 | *Campylobacter* | Meat | 20.83% | Enrofloxacin (79.2%), ciprofloxacin (100%), amoxicillin (71.2%) | (Nisar et al., 2017) |
| 4 | *Campylobacter* | Poultry Products | 57 % | Nalidixic acid (100%), ampicillin (79 %), ciprofloxacin (76 %) | (Akbar et al., 2024) |
| 5 | *Staphylococcus* | Slaughterhouse and Meat | 50% | Methicillin (100%), ciprofloxacin (100%), tetracycline (100%) | (Sadiq et al., 2020) |
| 6 | *Staphylococcus* | Milk | 37.14% | Cefoxitin (100%), gentamicin (50%), tylosin (50%) | (Javed et al., 2021) |

The majority of mortalities due to antimicrobial resistance in Pakistan occurred particularly due to several bacteria, including *Salmonella enterica*, *Staphylococcus aureus*, *Streptococcus pneumoniae,* and carbapenem-resistant *Enterobacter* or non-*Enterobacter,* which are also mentioned in the list of priority pathogens by the World Health Organization (Organization, 2024b). While other bacteria, including *Brucella*, *Campylobacter,* and other bacteria, are also zoonotic pathogens that may also acquire antibiotic resistance and may become a cause of serious

illness in animals and humans. The prevalence of some of the significant zoonotic bacteria isolated from different animal sources from various cities of Pakistan is described in Table 1.

### *Salmonella* and Antibiotic Resistance

*Salmonella* is a zoonotic disease also known as salmonellosis, which can be transmitted between animals and humans mainly via contaminated food and during contact with infected animals. *Salmonella* usually survives in the intestines of various warm and cold-blooded animals, including humans (Nadeem et al., 2025). Being an enteric bacterium, *Salmonella* may be excreted via feces. In addition, contaminated food from animal origin, including vegetables contaminated with bacteria, is the source of infection, particularly for humans. Salmonellosis, particularly the non-typhoidal one, is a self-limiting disease that requires neither hospitalization nor medication, as it can only be treated by the uptake of water and electrolytes. But *Salmonella* can also be spread from the intestine to the other parts of the body, resulting in severe illness, which is particularly common among infants, elderly persons, and patients with underlying immunocompromised diseases (Michael & Schwarz, 2016). Humans typically get Salmonellosis by consuming contaminated food such as undercooked meat, eggs, and dairy or dairy products. It can also be transmitted by direct contact or indirect contact with infected animals, such as contact with feces of infected animals or by petting them, as cats, dogs, and poultry animals are commonly carriers of *Salmonella* (Asif et al.).

Another way to get salmonellosis is during improper handling of food, such as with unwashed hands or on contaminated surfaces (Nazir et al., 2025). Antimicrobial resistance (AMR) occurs when *Salmonella* develops the ability to survive in the presence of antibiotics and makes the antibiotics ineffective, which were once effective. AMR makes Salmonellosis difficult to treat, thus leading to a greater chance of severe and prolonged disease, and ultimately death. (Nguyen et al., 2021). The common antibiotics, including β-lactams, aminoglycosides, tetracyclines, quinolones, cephalosporins, and trimethoprim-sulfamethoxazole, are mainly used to treat infections due to *Salmonella*. Some strains of *Salmonella* have developed resistance to many antibiotics, including aminoglycosides, β-lactams, chloramphenicol, quinolones, tetracyclines, and trimethoprim, leading to the development of multidrug-resistant strains with the passage of time (Punchihewage-Don et al., 2024).

### *Mycobacterium* and Antibiotic Resistance

Zoonotic tuberculosis is mainly caused by the bacterium known as *Mycobacterium bovis* which causes zoonotic tuberculosis in humans as it can be spread from animal to human particularly via direct or indirect contact with infected animals such as foodborne transmission which mainly involve the consumption of unpasteurized milk or undercooked meat from infected animals (Abbas et al., 2025). The airborne transmission may also occur by close contact with infected animals or their carcasses via inhalation of infectious aerosols. Another way of transmission can occur, known as skin exposure, as bacteria from infected animals can enter and spread through open cuts or wounds on the skin (Kock et al., 2021). Cattle are the most common animal reservoir for *M. bovis,* but it can also be found in other animals, including wild animals. In humans, this zoonotic tuberculosis can affect various organs, including the lungs and lymph nodes (Devi et al., 2021).

However, zoonotic tuberculosis is a growing public health concern, particularly in developing countries, including Pakistan, where surveillance and control authorities are almost inadequate (de Macedo Couto et al., 2022). According to a recent study evaluated that *M. bovis* strains maintained (100%) gene mutations extending resistance to isoniazid, streptomycin, ethambutol, and fluoroquinolones, while resistance gene mutation towards rifampin was found in 80% of *M. bovis* strains (Soliman et al., 2024). In addition, the infection poses a serious and growing public health concern, particularly in low-income areas, including Pakistan, due to the high prevalence of livestock, consumption of unpasteurized dairy products, along with high drug resistance patterns in cattle populations (Fareed et al., 2024).

The prevention can be done by following some of the protocols including proper pasteurization of dairy and dairy products, to make control programs for cattle tuberculosis, by following safe and hygienic food handling protocols and early detection and treatment of both animal and human tuberculosis to avoid any future issues as this infection was neglected a lot in various countries including Pakistan (Kasir et al., 2023).

### *Brucella* and Antibiotic Resistance

Brucellosis is a bacterial zoonotic disease that can be spread from animal to human in several ways, such as direct contact with infected animals or via ingestion of animal products, and mainly causes fever known as undulant fever or Malta fever. The direct contact of *Brucella* can happen when bacteria enter the body through cuts, wounds, or mucous membranes while handling the infected animals or their parts, including their tissues or body fluids (Iqbal et al., 2025). The transmission can also be caused by inhalation of this airborne bacterium, and also by contact with the blood, placenta, or semen of infected animals. This zoonotic bacterium can be transmitted to humans by the consumption of unpasteurized dairy or dairy products and uncooked or undercooked meat from infected animals (Jawad, 2024).

The animals commonly infected with Brucellosis are domestic animals, wildlife, and even marine mammals. While cattle and dogs are considered the most common hosts. Therefore, people such as slaughterhouse workers, veterinarians, laboratory personnel, and those who work with livestock are at higher risk (Sharma et al., 2023). Brucellosis is endemic in Pakistan and poses a public health concern due to emerging challenges of antibiotic resistance. The emergence of antibiotic resistance makes brucellosis more difficult to treat. Pakistan faces a significant burden of brucellosis, particularly in livestock-dependent regions, where high prevalence rates are found in both humans and animals, with an estimated 13.13% sero-prevalence in many areas (Qureshi et al., 2023). The factors contributing to antibiotic resistance in the case of Brucellosis are due to overuse and misuse of antibiotics. In addition, poor sanitation and poor hygiene may also lead to the spread of antibiotic-resistant bacteria. The issue can somehow be prevented only by awareness and safe and hygienic handling of animals and animal products (Ma et al., 2023).

### *Campylobacter* and Antibiotic Resistance

In Pakistan, *Campylobacter*, particularly *Campylobacter jejuni*, is mainly transmitted zoonotically, and it can be through contaminated food, water, and by direct contact with infected animals, but the common issue of antibiotic resistance makes it a public health concern (Zhang

et al., 2023). Domestic animals, including poultry and cattle, serve as animal reservoirs for *Campylobacter* species. The common routes of transmission include foodborne transmission, such as consumption of undercooked meat, milk, and poultry products, and waterborne transmission, such as contaminated water can be a source of zoonotic disease. In addition, direct contact with infected animals can also be a source of infection (Mulu et al., 2024). However, *Campylobacter* species are increasingly acquiring resistance against many antibiotics. In the past years, the rise of antibiotic resistance, particularly in the case of *Campylobacter,* has become a major concern in developed and developing countries, particularly in Pakistan (Dessouky et al., 2022).

### *Staphylococcus* and Its Antibiotic Resistance

In Pakistan, the transmission of antibiotic-resistant zoonotic *Staphylococcus aureus,* particularly methicillin-resistant *Staphylococcus aureus* (MRSA), is a major concern. Livestock, particularly dairy cows and poultry, are the main and common reservoirs for MRSA (Sajid et al., 2025). Consumption of milk from infected animals is also a common cause of zoonotic transmission of *Staphylococcus*. Thus, the overuse or misuse of antibiotics in both human and animal communities is a wrong practice and the main factor in developing antibiotic resistance. In addition, multidrug-resistant *S. aureus* is emerging in Pakistan, particularly in hospital settings (Roy et al., 2024).

### Alternative Measures to Combat Antimicrobial Resistance

Keeping in view the issue of antimicrobial resistance, as AMR has become a major health concern of the 21st century, several alternative methods are used as antimicrobial agents such as Phage therapy, probiotics, antimicrobial peptides, fecal microbiota transplantation, metal ions and other compounds including nanoparticles and plant-based compounds such as plant extracts or their essential oils (Singha et al., 2024). One of the alternative strategies to use instead of antibiotics to prevent antibiotic resistance among animals and humans is Phage therapy. The bacteriophages, which are actually the viruses that mainly infect and kill bacteria and help in treating infections with fewer side effects instead of antibiotics, as bacteriophages have natural antibacterial properties in them (Opperman et al., 2022).

Another measure which can be adopted is to promote a healthy gut microbiome with probiotics and prebiotics, which further help to compete with harmful bacteria and ultimately can reduce the risk of infections (Appanna & Appanna, 2018). Another measure is to adopt improved hygiene practices, including regular handwashing before and after handling of animals and animal products as it can reduce the risk of infections and ultimately lead to less use of antibiotic treatments (Organization, 2024a). The most emerging practice nowadays is the use of plant extracts as alternatives to antibiotics for treating zoonotic diseases, as various plant extract and their essential oils have natural antimicrobial and anti-inflammatory properties. Plants contain a variety of bioactive compounds, including alkaloids, tannins, polyphenols, and flavonoids, which can exhibit antimicrobial efficacy. Plant-derived compounds may offer a safer alternative to conventional antimicrobials, which can further prevent antimicrobial resistance, which is now a global issue of the 21$^{st}$ century (Rasheed et al., 2023).

### One Health Approach to Tackle Antimicrobial Resistance

Antimicrobial resistance is a global health concern that affects all lives, including humans, animals, and even the environment. In addition, the One Health approach is a strategy that aims to fight antimicrobial resistance by addressing the health of humans, animals, and the environment, as shown in Figure 2. This approach is important as resistant microorganisms can spread easily through several ways, including healthcare facilities, food, and the environment, and make antimicrobials ineffective and more difficult to treat infections, which further increases the risk of disease spread (Mackenzie & Jeggo, 2019).

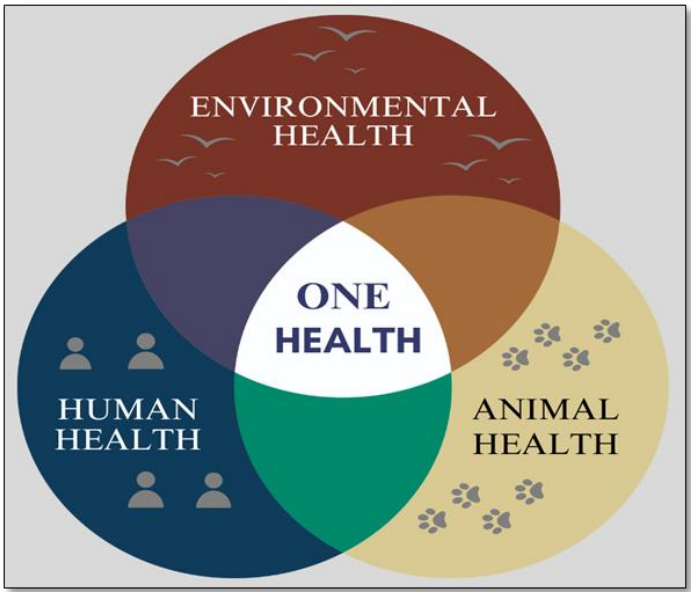


Fig. 2: One Health approach to combat the threat of antimicrobial resistance

Among veterinary settings, antibiotics are routinely administered in animals to prevent infections and to tackle the issue of insufficient hygienic conditions. In different regions of the world, some significantly important antibiotics including fluoroquinolones and cephalosporins are administered in low dose to animals in different veterinary settings mainly in poultry, leading to the spread of antimicrobial resistant microorganisms, presenting the risk to enter in the human food chain either via meat, manure or water (Gohar et al., 2024). The non-selective use of antibiotics, particularly fluoroquinolones, as veterinary medicine leads to the development of quinolone resistance in *Salmonella* spp., which further infects the gastrointestinal tract of humans. It is evident that the misuse of antimicrobials in one field can cause the development of resistance in another field (Khokhar et al., 2023). Thus, the increased prevalence of antimicrobial-resistant pathogens poses a high risk to human health. However, the One Health approach has proven as a better solution to fight the threats of the antimicrobial resistance pandemic at every level to ensure a better outcome (Kumar et al., 2019).

The World Health Organization (WHO) has established several important pillars to help fight antimicrobial resistance, with the first pillar focused on improving public awareness

regarding antimicrobial resistance as the resistant issue develops due to the misuse and over-the-counter availability of antibiotics, particularly in rural areas where patients cannot afford the diagnostic or microbiological tests. In addition, many agriculturists use antimicrobial drugs, including the last resort antibiotic, namely colistin, as a growth promoter in animals. The second pillar is to strengthen the global surveillance and research for this issue by monitoring resistance rates in humans, animals, or environmental samples, and to ensure the safe use of antimicrobials. The third pillar explains the use of preventive measures as individuals at overcrowded places and with poor nutrition are most prone to antimicrobial resistance. Thus, the implementation of proper sanitation and healthy living should be adopted (Khokhar et al., 2023). The fourth pillar is to limit the use of antibiotics as growth promoters and prophylactics. The last pillar focused on creating a supportive environment to tackle the transmission of antimicrobial resistance. However, there is an urgent need for research and development to develop more alternative medications and vaccines. In simple way, One Health combats antimicrobial resistance through public awareness, surveillance, regulation, stewardship, infection control, sanitation, and innovation by research and development (Organization et al., 2023).

Conclusion

Overall, zoonotic pathogens are of significant concern as they directly or indirectly affect our lives, and their transmission could pose a risk of serious illness in humans. Antimicrobial resistance is still a significant health issue in developed and developing countries, particularly in Pakistan. The future perspective for antimicrobial resistance zoonotic transmission highlights the need for a "One Health" approach which emphasizes the connection of human, animal and environmental health to tackle the emerging issue of antimicrobial resistant infections as the resistance issue can be improved by strengthening surveillance and control programs to monitor antimicrobials use in veterinary and community settings.

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