

AMR IN VETERINARY MEDICINE: A GROWING THREAT TO ANIMALS AND PUBLIC HEALTH

Huzaila Mudassar^{1*}, Muhammad Talha Aziz², Mohammed Abdulmoheed¹, Umar Khaliq¹ and Ahmad Raza³

1. Riphah College of Veterinary Sciences, Riphah International University
2. Master's in Public Health, St. Francis College Brooklyn, NY, USA
3. Faculty of Veterinary Science, University of Agriculture Faisalabad, Pakistan

*Corresponding Author: huzailamudassar10@gmail.com

ABSTRACT

Antimicrobial resistance (AMR) is one of the biggest threats to world health – this is when microbes become resistant to the medicines that are used to stop them from working. This study is a One Health approach to the evolution of antimicrobial resistance (AMR) in humans, animals, wildlife, and the environment. The overuse of antibiotics accelerates the processes of spontaneous mutation and horizontal gene transfer (conjugation, transduction, and transformation) by bacteria that help them become resistant. Food-producing animals have used antibiotics to stimulate growth and ward off disease for years, and in the poultry and dairy industries, the bacteria have become resistant to antibiotics and have spread to meat, milk, and even insects. Companion animals are also becoming more multidrug-resistant due to the extensive use of their treatments, and the presence of resistant genes and organisms in the wildlife and environmental reservoirs, including wastewater and agricultural runoff. The implications are serious, with zoonotic diseases, reduced treatment options, and significant economic losses to the agriculture and healthcare industries. There is global action needed to address AMR, such as the Global Action Plan by WHO, which focuses on surveillance, awareness, infection prevention, and sensible use of antimicrobials. The study concludes that there is no single sector that can tackle this complex problem alone and, therefore, that cooperation between veterinarians, doctors, farmers, and environmental scientists is required to combat AMR on an ongoing basis.

Keywords: Antimicrobial Resistance (AMR), One Health, Veterinary Medicine, Zoonotic Diseases, Antimicrobial Stewardship, Public Health

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Introduction

Antimicrobial Resistance (AMR) is the ability of microorganisms, such as viruses, parasites, fungi and bacteria, to resist an antimicrobial that was previously effective in killing them [1]. AMR is one of the most imminent health issues of the century owing to the spread of antimicrobial resistance and limited discovery of new antimicrobial medicines to combat the issue [2]. Overexposure to antibiotics in multiple industries, including medicine, agriculture and livestock, is a major factor in this problem both for treating disease and for raising poultry and livestock [3]. Veterinary medicine has a central role in the AMR crisis because animals can be carriers of resistant organisms as well as the genes associated with resistance, which can be passed through food chains, health care facilities, and natural habitats [4]. AMR is sometimes called the "Silent Pandemic" because it requires immediate attention and a One Health approach involving veterinarians, physicians, farmers, and researchers, as well as being responsible for antimicrobial use and effective surveillance [5].

Causes of AMR:

AMR is driven by several contributing factors such as practices related to humans (overuse and misuse of antimicrobials, inadequate prevention of infections, and limited awareness); practices related to animals (extensive antibiotic use in livestock and aquaculture, spread via food chains and direct contact); factors related to the environment (release of antibiotics and resistant bacteria into water bodies, soil, and waste systems); and factors related to wildlife (spread through contact with wildlife and the encroachment of their habitats)[6]. There are two ways that bacteria might become resistant to antibiotics: by HGT or spontaneous gene mutation [7]. A transfer of information between distantly related species (parent and children) is called HGT. The foreign DNA, which is acquired through the HGT pathway, is one of the reasons responsible for the development of antibiotic resistance in bacteria [7]. Most antibacterial products in use in the clinic are found in nature, in the environment, primarily in soil [8]. The main source of antibiotic resistance genes (ARGs) found in therapeutically relevant bacteria is the ambient resistate. There are intrinsic genetic factors of resistance to these chemicals in bacteria that live in association with them [9].

There are three ways by which bacteria can acquire foreign DNA: conjugating pilus, via transduction (virus) and via transformation (bare DNA from environment) [7]. Transformation is the most prevalent kind of HGT mechanism [7]. Apart from cell-to-cell contact, another very effective gene transfer mechanism is conjugation, which is frequently associated with the development of resistance in hospitals [10]. Some Gram-negative bacteria have been shown to be stimulated to conjugate by contact with low

levels of two antibiotics (e.g., two doses of gentamycin and chloramphenicol) or aminoglycosides (e.g., streptomycin) [11].

AMR in Food Producing Animals:

The legacy of using antibiotics is not easily separated from those in agriculture and animal husbandry, because the drugs were regulated by agronomists and not veterinarians or veterinary pharmacologists, and so were used mainly as growth promoters or as disease preventives. Such a wide application was considered necessary to quadruple meat production in the last years [12]. It continued until the FDA allowed antibiotics in animal feed without veterinary prescription as part of a decision made to increase protein production at a low cost in low-income countries, which is still the case today. Antibiotics, including aminoglycosides and beta-lactams, are frequently used to treat mastitis in dairy cows, and can be excreted in milk or released into the environment as contaminants. Milk can be contaminated and cause hypersensitivity reactions in humans or foster the development of AMR when consumed [12].

Handling and consumption of contaminated chicken meat have been described as the common modes of transmission of AMR bacteria leading to infections in humans. The increasing emergence of AMR also in these food-producing animals has led to the search for alternative strategies to limit this phenomenon. The most critical measure is to implement an antibiotic stewardship program that is specifically tailored to this situation, and that involves improved biosecurity practices, provision of antimicrobial drinking water, use of bacteriophages and the use of vaccination protocols, and improved hygiene measures in slaughtering [12,13]. The following procedures are also very basic, as it was described that plasmid-mediated ESBL/pAmpC-producing bacteria can be vertically and horizontally transmitted in broilers, in the hatchery and between farms, and that the acquisition of resistance is very rapid even in commensal *E. coli* [13]. Also, insects are now recognised as potential sources of protein as alternative food sources, such as cockroaches, houseflies, ants, and mosquitoes, which have been found to carry AMR, are known to be in human habitats and may serve as a pathway for transmission from the environment to humans [12].

AMR in Companion Animals:

It is common for pets to experience infections at the wound site after surgery, dental infections, and respiratory infections, as well as urinary tract infections, and may require antimicrobial treatment. Owners often have strong emotional bonds with their pets, leading to the provision of more comprehensive healthcare, causing animals to be more likely to use antibiotics for treatment of illness and injuries. This has led to increased multi-drug resistance (MDR) of pathogenic bacteria in pets, because of susceptibility testing of UTI isolates [14]. Resistance to first-line antibiotics

and last-resort antibiotics like ampicillin, imipenem, colistin, methicillin, some cephalosporins, tetracyclines, fluoroquinolones, and glycopeptides, such as vancomycin, has been reported. Pets have very common infections which include UTI's, post-surgical wound infections, dental infections and respiratory infections, and frequently these need to be treated with an antimicrobial [15]. Owners are more emotionally attached to their pets than other species, and consequently, animals are likely to get more comprehensive care for illness and injury than other species, leading to more use of antibiotics. This has led to increased multi-drug resistance of bacterial pathogens in dogs and cats, as demonstrated by resistance testing of UTI isolates [16]. Resistance has been reported for first-line and last-resort drugs, such as ampicillin, imipenem, colistin, methicillin, various cephalosporins, tetracyclines, fluoroquinolones, and glycopeptides like vancomycin [16].

In one study, *Staphylococcus* spp. isolated from dogs with ear infections were multidrug-resistant and were also resistant to penicillins, which were the least effective antibiotic group [14]. The UTI isolates of *E. coli* were the most oxytetracycline-resistant and ampicillin-resistant; the study found a decline in the effectiveness of enrofloxacin, cephalexin, and oxytetracycline, and an increase in *P. aeruginosa* resistance and *E. faecalis* resistance [18].

AMR in Wildlife:

Wildlife species that live or feed in or near dwellings and rearing areas can be in contact with humans and domestic livestock. For example, individuals or their pets could handle rodent faeces and ingest them if it's in or on food. In addition, rodents might be exposed directly to animal waste and excrement when they live near animal rearing areas and human dwellings. Also, hunters, trappers, and veterinarians are in direct contact with wild animals. Several zoonotic diseases have been shown to be transmitted this way, such as brucellosis and tularemia. No need to suspect its meaning in AMR deals [19].

It would be helpful to do some research on the risk of transmission of antimicrobials associated with hunting and trapping. The networks of game meat surveillance that are in place in many nations could be expanded upon by such investigations [19]. Wild animals can also eat meat that has been contaminated with animal viruses by domestic animals. Animal products are known to often contain AMR, and wildlife can be found eating the giblets or dead animals (stillborn calves or lambs) if they are not removed after home slaughter. Considering such contamination routes may be important to prevent the transmission of AMR to animals [19].

AMR in Environment:

Some typical examples of AMR hotspots are wastewater treatment plants, pharmaceutical waste, and Agri-water. A clear causal link between the presence of antimicrobial residues and resistance genes in these systems and human illnesses has been hard to establish [20]. Until more extensive epidemiological and genetic tracking is made, therefore, any conclusions about environmental factors should not be viewed as definitive sources. Resistant pathogens have been found at this interface; however, in isolate-based studies, *E. coli* and *Staphylococcus aureus* resistant to multiple antibiotics have been isolated from dairy and poultry environments, and multidrug-resistant *Klebsiella pneumoniae* has been isolated from clinical and environmental sources. These findings underscore the importance of a robust multi-sector surveillance to link environmental signals to outcomes of human and animal health [20].

Impact of AMR:

AMR makes it possible for resistant zoonotic infections to spread from animals to humans, endangering human health and food supply [21]. Reservoirs of resistance have been created by the overuse of antibiotics in animals to treat sickness and encourage development. This makes it easier for MDR bacteria like *Salmonella* and *Campylobacter* to spread through animal handlers or the food chain [22]. Bacterial strains that are resistant are readily transmitted from one species to another. Similarly, indirect environmental exposures which perpetuate additional disease transmission result in AMR in wildlife. Resistant microorganisms are spread by manure-based fertilizers to the environment and can infect produce and rivers, which are then eaten by humans. Moreover, they are also similar in harboring AMR genes with human commensal microbiota and typical ambient microflora. When a disease is resistant, there is a limited treatment option, leading to the spread of disease breaks among sheep, cattle, and poultry that results in large financial loss and affect food supplies [21]. Economic and agricultural negative resistance effects have knock-on repercussions that are disruptive for commerce and national security. To fully address AMR's significant current and potential negative effects on animals, which in turn increase the risks of human exposure, a proper One Health approach that includes surveillance and interventions for human, animal, and environmental health is still required [23].

Strategies to combat AMR:

In May 2015, the WHO, with the support of the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE), created the GAP On AMR at the World Health Assembly to address AMR from a "One Health" perspective [19]. At this meeting, the leaders agreed and committed to their countries to develop multisectoral national action plans (NAPs) on AMR [24]. Countries then pledged to enact the NAPs after their development and support in response to AMR. The GAP on AMR focuses on five objectives to tackle AMR, and these include: 1) to improve the awareness and understanding of AMR through effective communication, education and training; 2) to strengthen the knowledge and evidence base through surveillance and research; 3) to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures; 4) to optimize the use of antimicrobial medicines in human and animal health; and 5) to develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions. Hence, the importance of the need to collaborate with stakeholders from various countries engaged in human health, animal health, agriculture, and environment monitoring, AMR, and conducting further research to curb the spread of AMR [25]. These objectives suggest the need for AMR response through a "One Health" approach that considers the human, animal, agriculture, and environment dimensions of AMR [24].

Conclusion:

AMR is a developing threat which impacts far beyond health and animals; it is an inter-connected problem involving food-producing animals, companion animals, wildlife, and the environment. Excessive use of antimicrobials in animals and pets and poor environmental controls has helped the spread of antimicrobial-resistant organisms that can be spread to humans via food, direct contact, or the environment. The impact is great: billions of economic damages, fewer treatment choices, and increased zoonotic risk. The solution is not possible in any single sector; it takes a coordinated One Health approach, bringing together vets, doctors, farmers, and environmental scientists. International initiatives such as the WHO Global Action Plan offer a pathway to action through enhanced surveillance, prudent use of antimicrobials, and raising awareness. In conclusion, AMR requires long-term efforts from all sectors of human, animal and environmental health – only by working together and proactively will we be able to continue using antimicrobials for generations to come.

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