Zoonotic Risks of Antimicrobial Resistance: Alternative Strategies to Combat this Silent Pandemic

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ABSTRACT

Over the past 20 years, antimicrobial resistance (AMR) has grown to be a global concern to public health systems everywhere. From the invention of the initially developed medicines that consistently improved human health throughout the antibiotic time period, antimicrobial overuse and abuse in both veterinary and human medicine has contributed to the global AMR epidemic. This chapter provides a thorough summary of the epidemiology of antimicrobial resistance (AMR), emphasizing the relationship between people and animals that produce food as well as the laws and policies that are now in place throughout the world. The challenges posed by antimicrobial resistance (AMR) will be addressed through a variety of strategies, such as developing novel antimicrobials, bolstering the monitoring system for AMR in both human and animal groups, better understanding the ecology of resistant bacteria and resistant genes, raising stakeholder awareness of the responsible use of antibiotics in animal production and clinical settings, and addressing the effects of AMR on public health and the environment. Given the worldwide scope of antimicrobial resistance (AMR) and the fact that bacterial resistance is impervious to barriers, the essay concludes with particular recommendations aimed at various stakeholders and organized around a comprehensive approach. The well-known zoonotic illnesses include hemorrhagic colitis caused by Escherichia coli, brucellosis caused by Brucella abortus, bovine tuberculosis caused by Mycobacterium tuberculosis, or anthrax caused by Bacillus anthracis. Similar to this, the majority of antibiotics are not entirely broken down before being released into the food chain where they bioaccumulate and impact different ecological niches. The comprehension of AMR mediated by zoonoses is a global issue that affects not only scientific researchers but also farm animal producers, medical personnel, patients, and consumers. In order to maintain the efficient use of antibiotics in human as well as animal medicine many alternative methods used.

Key words: Zoonosis, Antibiotics, Resistance, Risk factors, Control.

CITATION

Hussain M, Imtiaz H, Badshah T, Khan AMA, Azam MA, Fan C, Wei CR and Azhar R, 2023. Zoonotic Risks of Antimicrobial Resistance: Alternative Strategies to Combat this Silent Pandemic. In: Altaf S, Khan A and Abbas RZ (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 4: 172-185. https://doi.org/10.47278/book.zoon/2023.146

CHAPTER HISTORY Received: 12-Feb-2023 Revised: 25-April-2023 Accepted: 08-Aug-2023

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1. INTRODUCTION

Over the past 20 years, antimicrobial resistance (AMR) has grown to be a global concern to public health systems everywhere. From the invention of the initially developed medicines that consistently improved human health throughout the antibiotic time period, antimicrobial overuse and abuse in both veterinary and human medicine has contributed to the global AMR epidemic. This chapter provides a thorough summary of the epidemiology of antimicrobial resistance (AMR), emphasizing the relationship between people and animals that produce food as well as the laws and policies that are now in place throughout the world. The challenges posed by antimicrobial resistance (AMR) will be addressed through a variety of strategies, such as developing novel antimicrobials, bolstering the monitoring system for AMR in both human and animal groups, better understanding the ecology of resistant bacteria and resistant genes, raising stakeholder awareness of the responsible use of antibiotics in animal production and clinical settings, and addressing the effects of AMR on public health and the environment. Given the worldwide scope of antimicrobial resistance (AMR) and the fact that bacterial resistance is impervious to barriers, the essay concludes with particular recommendations aimed at various stakeholders and organized around a comprehensive approach. The well-known zoonotic illnesses include hemorrhagic colitis caused by Escherichia coli, brucellosis caused by Brucella abortus, bovine tuberculosis caused by Mycobacterium tuberculosis, or anthrax caused by Bacillus anthracis. Similar to this, the majority of antibiotics are not entirely broken down before being released into the food chain where they bioaccumulate and impact different ecological niches. The comprehension of AMR mediated by zoonoses is a global issue that affects not only scientific researchers but also farm animal producers, medical personnel, patients, and consumers. In order to maintain the efficient use of antibiotics in human as well as animal medicine many alternative methods used.

It is hard to develop a world that can control human and animal health. Globally, there is serious worry about the rise of new infectious agents and resistance to drugs in existing pathogens. In the early 19th century, the discovery of antibiotics revolutionized the healthcare system by preventing millions of deaths. Humans use different types of antibiotics such as Aminoglycosides, Beta-lactams, Glycopeptides, Macrolides, Oxazolidinones, Quinolones, Tetracyclines, and Sulphonamides in the treatment of most diseases (Etebu and Arikekpar 2016). These antibiotics are used as bactericidal (to kill bacteria) as well as bacteriostatic (to inhibit the growth and replication of bacteria). Bacteriostatic antibiotic classes are macrolides, sulphonamides chloramphenicol, lincosamides (clindamycin), and tetracyclines while beta-lactams, aminoglycosides, glycopeptides (vancomycin), quinolones polymyxins (colistin) are bactericidal drugs (Patil and Patel 2021). Each group of antibiotics has its specific mode of action. For example, aminoglycosides, chloramphenicol, lincosamides, tetracycline, and macrolide have a direct action on RNA to inhibit the synthesis of protein and thus have a bactericidal effect. Cephalosporin, penicillin, and glycopeptide inhibit cell wall synthesis, sulfonamides inhibit folate synthesis, and fluoroquinolone inhibits DNA synthesis. Frequent and continuous usage of antibiotics has led to drug resistance called antimicrobial resistance (AMR) globally but is more prevalent in developing countries (Chokshi et al. 2019).

Pathogens can become resistant to antibiotics over time, making infections more difficult to cure and raising the risk of disease spread, life-threatening sickness, and death. AMR is among the greatest threats to human and livestock populations in terms of productivity and public health noticeably in countries like Pakistan, India, Bangladesh, Nepal and Sri Lanka. AMR is becoming dangerous in developing countries, because of the easy availability and frequent use of antibiotics (Sharma et al. 2018). The majority of antibiotics that enter the bodies of humans and livestock are not completely utilized, causing the release of unmetabolized forms into the surroundings. Antibiotic resistance among the native microbiome and altered sensitivity of the bacterial population are results of the increased level of antibiotics in varied environments. The presence of antibiotics in surroundings causes changes in the genomes of bacteria leading to the emergence of genes that are resistant to antibiotics. During a process called horizontal gene transfer, microorganisms acquire antibiotic-resistance genes (Tang et al. 2023). Integrons (genetic components with a site-dependent recombination mechanism), transposons(DNA sequences represent a kind of mobile genetic component), and plasmids (A little circular DNA structure that exists in bacterium) serve as carriers of genetic material between infectious agents through transformation (Foreign genetic material (DNA) is taken in by bacteria from the environment), transduction (The genetic material of one bacterium is carried to another by a virus.), and conjugation (Direct contact between bacteria results in the transfer of genetic material) (Bello-López et al. 2019).

Livestock is the most common carrier for the propagation of resistant pathogens. A large population of bacteria resides in the gastrointestinal (GI) tract of animals and humans (Argudín et al. 2017). The spread of infectious germs in the GI tract that are resistant to antibiotics passes the resistant gene to additional pathogens, changing the microbial community structure already present there. Injecting overdose antibiotics in livestock herds produces AMR not only in the normal flora of the GI tract but also in the zoonotic pathogens (Guardabassi et al. 2018). The term “Zoonoses” is derived from the Greek word “Zoon”, which means animal, and “noses”, which means illness (Narayan, et al. 2023). According to the World Health Organization (WHO), any disease or infection that is naturally transmissible from vertebrate animals to humans or from humans to animals is classified as zoonosis 61% of human pathogens have a zoonotic nature. AMR in animals and the human population is threatening in this century. Researchers are also working on zoonotic infectious agents but there is still a lack of appropriate administration, legislation, and controlled usage of antibiotics. Humans and animals with resistance to several drugs have few or no antibiotic alternatives. AMR may result in rising expenses and the instability of medical systems. When a new antibiotic gets approved, resistance to it will eventually develop (Inoue, 2019).

An enhancing distance between rising AMR and the creation of new antibiotics is noticed. The increase in AMR and failure to develop new effective drugs reached an alarming level. AMR spreads briskly and effective antibiotic development is too slow as a result new pathogens mainly bacteria that have zoonotic importance are out of control (Chandra et al. 2019). The sensitivity of pathogens decreases in response to previously used antibiotics and newly developed drugs as a result resistant genes are transferred. AMR especially in zoonotic pathogens is like a time bomb that will be threatened in the future more aggressively. One cause of this threat is that, despite the medical demand for new antimicrobials, the healthcare sector hesitates to invest and develop novel medicines because doing so would require spending more than eight hundred million dollars for up to ten years for each approved agent. The risk of freshly discovered molecules may prove unsuccessful in the short term but could serve as an additional prevention factor. The drugs industry has given preference to long-term utilization of medications for combating persistent diseases because it considers that study into inventing fresh antibiotics is less profitable (Gostin, 2021).

2. AMR MECHANISMS

As a result of AMR bacteria evolve and stop responding to antibiotics, making infections more difficult to cure and raising the risk of infection development, life-threatening diseases, and mortality. Bacteria utilize different mechanisms to counter antibiotic effects. Methods of enzymatic degradation (beta-lactamases synthesis by bacteria), efflux pump (through eliminating antibiotics that enter the cell), new metabolic pathways (the development of modified proteins), changes in membrane permeability to antibiotics(resistant to hydrophobic substances e.g bacteria like Escherichia coli have an outer membrane that offers a form of impermeability to substances like macrolide and beta-lactam drugs), and alteration of bacterial proteins acting as antimicrobial target(Antibiotics intrinsic receptor modification, such as ribosomal changes) are utilized by bacteria (Reygaert, 2018). Utilization of antimicrobial agents does not affect some bacterial strains: innate resistance is a feature that is present from birth. Resistance is acquired through changes in genetics such as mutation and horizontal transmission of the genome from different forms of bacteria. Mostly resistance is acquired through mutation and horizontal transfer of genetic material from one strain to another strain. A higher growth curve of bacterial replication also plays a role in the increasing number of resistant bacteria. Viruses (bacteriophages) and plasmids transfer resistant genetic material by transduction and conjugation. Plasmids transmitted both vertically and horizontally in acquiring resistance. Resistance in many categories of antibiotics is developing as a result of new patterns. Redundancy and infidelity at the molecular level are included in these patterns (Ferri, et al. 2017).

3. ZOONOTIC PATHOGENS AS A CARRIER OF AMR

Environmental contamination, drug resistance, and persistent illnesses that cause severe mortality along with elevated morbidity have all put livestock and human communities at risk. The emergence and rapid growth of epizootics, zoonotic, and epidemics have brought attention to the health risks at the global level and the significance of comprehending how infectious agents are transferred between humans and livestock. Most infectious diseases spread from the animals through different biological agents like gram-positive and gram-negative bacteria, viruses, prions, parasites and fungi. More than two hundred zoonotic diseases are present in different geographical regions and some spreading worldwide. Inhalation, ingestion, and other routes that contaminate mucosal membranes are the methods of zoonotic disease transmission. Animal tissue found in undercooked meat, infected vegetables, dairy products, shellfish, and unpasteurized milk are also sources of infection (Mohammed et al. 2016).

Several researchers have documented numerous instances of antimicrobial-resistant bacteria present in livestock. ESBL (extended-spectrum beta-lactamase) producing bacteria, MRSA (Methicillin-resistant *Staphylococcus aureus*), vancomycin-resistant enterococcus, MDR (multi-drug resistant) *Salmonella,* and *E. coli* are some of them. Many AMR zoonotic pathogens are also present in aquatic life transferring infection to the water bodies, human population, and soil microbiota. *Streptococcus iniae*, *Aeromonas hydrophila*, *Vibrio vulnificus*, *Photobacterium damselae*, and *M. typhi* are the pathogens of fishery that are zoonotic and AMR spreading (Nisa et al. 2023). The misuse of antibiotics in animals and seafood is exclusively related to ineffective regulations and monitoring systems. Lack of awareness regarding modifications in AMR pattern in the system which indicates the challenge cannot be successfully tackled from an ecosystem viewpoint by the research that has already been done in the field of AMR. A crucial step in lowering the hazards to people's health is to identify potential human exposure points to zoonotic infections in the animal business using an ecosystems approach (Michael and Schwsarz 2016).

3.1. *SALMONELLA ENTERITIDIS*

Salmonellosis is among the most common diseases caused by food in the world. *S. enterica* is the primary cause of salmonellosis illnesses in both humans and livestock (Pal et al. 2015). *S. enteritidis* mostly spreads infections in human communities through tainted poultry meat and eggs. To be able to comprehend ways of spreading and managing salmonellosis, it is crucial to know the evolutionary history and distribution of S. Enteritidis strains originating from chickens. To identify the origins and modes of *S. enteritidis* disease spread, genomic approaches offer unbiased and trustworthy techniques. Pulsed-field gel electrophoresis and gold standard methods are used for genotyping of this bacterial strain. Antimicrobial resistance is a global issue in the animal sector and as well as in the human population Salmonella strains have increased the resistance against various types of antibiotics. Salmonella resistant to multiple drugs is a serious threat in modern days in the perspective of public health (Vågene et al. 2018).

3.2. *CLOSTRIDIUM PERFRINGENS*

A pathogen called *Clostridium perfringens* can be detected in the digestive tract of mammals, avian species, and their surroundings. In favorable conditions, this gram-positive, rod-shaped, anaerobic, spore-forming bacterium shows clinical signs in animals when its growth curve rises and causes economic damage in the poultry industry of broilers and other birds (Borriello, 2018).

4. ANIMALS AS POTENTIAL CARRIERS OF ANTIBIOTIC RESISTANCE AND ZOONOTIC INFECTIONS

As zoonotic bacteria develop resistance to antibiotics, they pose more risks. Different MRSA strains from animals, including ST 130 throughout Europe, CC93 in Denmark, and ST398 in the Netherlands, have been discovered to spread among people. Growing worries are being expressed concerning animals as a potential reservoir for zoonotic diseases that can circulate among individuals due to the likelihood of zoonosis. There is evidence linking the overuse of antibiotics in animals to rising antimicrobial-resistant bacteria in people. Fluoroquinolones are frequently used to treat infectious diseases in livestock. Overuse of fluoroquinolones resulted in AMR Campylobacter diseases. According to a Food and Drug Administration (FDA) report on human health, eating chicken contributed to the development of fluoroquinolone-resistant Campylobacter in the human population. The microbe colonies of both healthy humans and livestock have been shown to have Enterococcus faecalis expressing the vanA resistance genes (VRGs), however, before 21 century, neither healthy humans nor livestock in the US had this infection. This difference was anticipated due to the widespread usage of avoparcin in farming practices (Dafale et al. 2020).

Due to the abundance of VRGs in animals, there are numerous potential for human infection and antimicrobial-resistant bacteria colonization. Numerous microorganisms are responsible for zoonotic illnesses (Ahmed and Baptiste 2018). Zoonoses can be categorized according to their etiological causes into viral, bacterial, parasitic, fungal, chlamydial, and microbial zoonosis (MacGregor and Waldman 2017). Bacterial zoonosis includes anthrax, salmonellosis, tuberculosis, Lyme disease, brucellosis, and plague (Asante, 2019). Viral zoonosis includes Ebola, AIDS, and rabies. For those who work with animals, understanding the spread of diseases, management methods, and disease prevention is crucial. As a work-related risk, it will aid in zoonotic disease prevention and management. Rabies, avian influenza, Rift Valley fever, Zika fever, dengue fever, hantavirus infection, and AIDS are famous zoonotic diseases that spread through viruses. Irrational use of antibiotics in the fields of agriculture, aquaculture and human health systems results in AMR (Ghasemzadeh and Namazi 2015).

Table 1: Gram-positive and gram-negative bacteria transferring infections and AMR.

Diseases	AMR	Antibiotics	Animals	Reference
Cellulites, septicemia and meningitis	*E. coli, Salmonella sp. Campylobacter sp. Streptococcus suis*	Methicillin, Cephalosporin, Cefotaxime	Birds	(Maciel et al. 2017).
Allergies and blood infection Pyoderma	*Staphylococcus pseudintermedius, Staphylococcus sp.*	Methicillin, Ofloxacin, Methicillin, Clindamycin, Fluoroquinoles	Cats, Dogs and Horses	(Cavana et al. 2023).
Avian Tuberculosis Diarrhea Enterocolitis Enteritis	*Mycobacteria, Neisseria gonorrohoeae* *E. coli, Salmonella, Campylobacter* *Campylobacter, Salmonella* *Campylobacter sp.*	Azithromycin, Gentamycin, Chloramphenicol Sulfamerazine, Dihydrostreptomycin Ciprofloxacin, Tetracycline, Enrofloxin, Nalidixic acid Nalidixic acid, Ciprofloxacin, Tetracycline	Avian (Poultry, Duck and Chicken)	Dai et al. 2020).
Urinary tract infection Mastitis Bovine Tuberculosis Typhoid	*E. coli* *Staphylococcus aureus, Klebsiellapneumoniae, Salmonella* *Brucellaabortus, Mycobacterium bovis* *Salmonella typhimurium, Salmonella enterica*	Ampicillin, Fluoroquinolones, Cefotaxime Methicillin, Amoxicillin, Clavulanic acid Norfloxacin, Amoxicillin Penicillin, Oxytetracycline, Streptomycin, Sulfonamide	Livestock Dairy Cattle	
Diarrhea, gastritis	*Salmonella* and *Vibrio spp.*	Cephalothin Ampicillin Chloramphenicol	Sea fish	(Yena et al 2020).
Elementary tract infection Septicemia Urinary tract infection	*Klebsiella pneumoniae, Salmonella spp.* *Staphylococcus aureus, Campylobacter, Salmonella* *Enterococcus faecium, Campylobacter sp*	Various Beta lactamases Levofloxacin, Penicillin, Tetracycline Nalidixic acid. Quinolones, Fluorquinolones	Pigs	(Bader et al. 2017).

5. VECTOR-BORN ZOONOTIC INFECTIONS

Antibiotic-resistant zoonotic disease is often thought of as originating from a site of direct host–receiver interaction. The relationship between resistant vector-borne disease commonly impacts the pathogen, host, and human, resulting in unanticipated complications. Vector-born zoonotic diseases (VBZDs) are spreading more quickly in terms of infectious diseases that are directly transmitted and resistant to antibiotics. Infectious diseases that affect people make up a disproportionate amount of newly emerging infectious disorders. Predominantly spread by hematophagous, blood-feeding, and arthropods. Over 90 percent of all vector-borne diseases are spread by flies, ticks, mites, and mosquitoes. Several widespread bacterial diseases, such as Lyme disease, Rocky Mountain spotted fever, and ehrlichiosis spread by Ixode and Ehrlichia (Khan, 2015).

6. DYNAMICS AND DETERMINANTS OF VECTOR-BORNE DISORDERS

The spread of infection from the native host to the receiver of a vector-borne disease depends upon a variety of circumstances. One of the main factors causing an upsurge in vector-borne diseases is a decline in host availability. Rats are the main targets which are decreasing and as a result, vector-born diseases increasing. Yersinia pestis attacks the human population when there is a decline in the rat population. Human behaviors and alterations to the environment are also main factors in the spreading of vector-borne diseases. Deforestation, urbanization, pollution, and other factors are also important in the spread of VBZDs (Cator et al. 2020).

7. ANTIBIOTICS RELEASE IN THE ENVIRONMENT

Antibiotics that fail in complete digestion in the body are consistently released in the ecosystem through veterinarians' workplaces, medical debris, drug manufacturers, dairies, poultry and other sources such as both household and urban filth. Remnants of drug residues are regularly found in a variety of aquatic entities, including streams, water in the ground, and ponds that are the result of aquatic operations and the result of water runoff directly from wastewater treatment plants (WWTPs). Since WWTPs absorb un-metabolized antibiotics from many sources through sewage and urban waste, they are widely recognized sites for the growth of antibiotic-resistant bacteria (ARBs) and play a role in the spread of antibiotic-resistant bacteria (ARB) and antibiotic-resistant gene (ARG). A small amount of antibiotic residues are also found in soil. The main source of antibiotics in soil is farm animals, waste from sanitation facilities, and dung. Bacteria in aquatic entities and soil frequently face exposure to antibiotics. These bacteria develop resistance to antibiotics using any mechanism for the development of resistance. Even a minimum concentration level of antibiotics in both aquatic and soil environments will be a risk to human and animal health (Arshad and Zafar 2020).

Table 2: Zoonotic infections by bacteria.

Etiology	Disease	Organs involved/ signs, symptoms	Animal host	Reference
Bacillus anthracis	Anthrax	respiratory organs, Skin, or GI tract	Bison, elks, white-tailed deer, goats, sheep, pigs, dogs, mink, cattle, equine	(Ngetich, 2019).
Actinomyces bovis	Actinomycosis	soft tissues, skin, and abscess, Swelling of lymph nodes	cattle, equine	(Murakam et al. 2018)
Brucella abortus, Brucella melitensis, Brucella suis, Brucella canis	Brucellosis	Weight loss, back discomfort, joint pain, poor appetite, and a fever	Cattle, dogs, goats, sheep, and pigs	(Alamian and Dadar,2020).
Burkholderia mallei	Glanders	Fever, sweating, muscle aches, chest pain, muscle tightness, headache	Horses, donkeys, and mules	(Khakhum et al. 2019).
Borrelia burgdorferi	Lyme disease	Fever, headache, skin rash, erythema migrans	Cats, dogs, and horses	(Steere et al. 2016).
Bordetella bronchiseptica	Bordetellosis	breathing issue	Canine and feline	(Brockmeier et al. 2019).
Yersinia pestis	Bubonic plague	bleeding from a natural opening, chills, diarrhea, fever, stomach ache, and vomiting	prairie dogs, mice, voles, chipmunks, dogs, rabbits, ground squirrels, Rock squirrels, wood rats	(Barbieri et al. 2020).
Salmonella enterica, S. bongor	Salmonellosis	Enteritis	Domestic animals, birds, and dogs	(Wibisono et al. 2020).
Mycobacterium bovis, M. caprae, M. microti	Tuberculosis	Respiratory organs bone marrow	Cattle, sheep, swine, deer, wild boars, camels, and bison	(Michelet et al. 2020).
Leptospira interrogans	Leptospirosis	Fever, abdominal pain, jaundice, and red eye	Wild and domestic animals including pet dogs	(Philip et al. 2020).

An increase in antibiotic-resistant bacteria and the transfer of antibiotic-resistant genes leads to infectious diseases. Antibiotics spread from their source to the environment involving bioaccumulation, biotransformation, and slowly accumulated antibiotics in water and soil. Antimicrobial drugs build up in larger quantities and then propagate further as an outcome of their stability in the environment. Some antibiotics are degraded easily like penicillin and most antibiotics take a long time for their degradation like macrolides, tetracyclines, and fluoroquinolones. The higher half-life of these long-lasting antibiotics increases their persistence in the environment (Grenni et al.2018).

8. ECONOMICALLY THREAT OF AMR

AMR may result in rising expenses and the instability of healthcare systems. People with AMR nosocomial infections (primarily circulation illness) or those who become ill after consuming food tainted with resistant germs recover more slowly, and septicemic infections and mortality are more common. Due to the prolonged hospitalizations and the consumption of costly drugs, the expense of healthcare has risen in this scenario. Also, new medications carry increased toxicological concerns as well as more frequent adverse drug reactions (ADRs). Healthcare expenses are thought to be about €1.5 billion each year in Europe, including €600 million in production. In the USA $55 billion lost results as AMR-related infections

Table 3: Antibiotics, Half-life, and their concentration in different environments.

3roup of Antibiotic	\ntimicrobial drugs	Conc (mg/kg/L)	Half-life (days)	Reference
\minoglycoside	/ancomycin Gentamicin	L0 (sandy loam)	L6 4	Chung et al. 2017).
3eta-Lactam	\mpicillin \moxicillin	).2 (soil) L0 (aquatic environment)	).43 3.89h	Lonsdale et al. 2019).
Cephalosporin	Cefradine Cefuroxime Ceftriaxone	L0 (surface water)	6.3 3.1 L8.7	Shahbaz, 2017).
Fluoroquinolones	Ofloxacin Levofloxacin Norfloxacin Ciprofloxacin	).045 (soil)).225 (wastewater) 30 (soil)).542 (soil)	990–1386 4.2 52 L153–3466	Mohammed et al. 2019).
Macrolides	\zithromycin Clarithromycin	L(soil) L(soil)	L2.82 36.48	Dinos, 2017).
Sulfonamides	Sulfamethoxazole Trimethoprim	L0(water waste)).17(water waste)	49 11.5	Tačić et al. 2017).
Tetracycline	Doxycycline Tetracycline	L0(water)).1 (soil)	49 578	Kasumba et al. 2020).

*As per EUCAST database

higher cost than HIV infections (Ahmad and Khan 2019). Experts caution that because reporting system constraints affect the death and morbidity data connected to drug-resistant bacteria, the cost impact on the healthcare industry is expected to be greater. In developing countries, the situation is alarming and the economic cost of the health care system is higher as compared to European countries. Under this circumstance, a successful AMR plan must concentrate on global collaboration, enhanced national efforts, discovery of innovative medications, successful governmental and public awareness campaigns, and government intervention, as well as improved communication between higher education institutions and drug companies, clients, veterinary professionals, and healthcare providers (Watkins and Bonomo 2020).

9. USE OF ANTIBIOTICS IN THE AGRICULTURE SECTOR AND AMR

The antimicrobial-resistant bacteria and their antibiotic-resistant genes have been extensively shown to be present in the ground, animals, and plants that produce food, and throughout the entire food chain. Following the use of enrofloxacin and moxifloxacin on farms that raised poultry in the Netherlands, the prevalence of fluoroquinolone-resistant strains of Campylobacter rose from 0 to 14% in broiler chicks and from 0 to 11% in farm staff members (Mdegela et al. 2021). Many antibiotic-resistant bacteria like Salmonella, Campylobacter, and *E. coli* are zoonotic and present in domesticated animals. Staphylococcus aureus methicillin-resistant (MRSA), Campylobacter spp multiresistant, and *E. coli* ß-lactam-resistant are pathogens present in farm animals. These microbes from livestock that produce food can infect people through a variety of channels, including aquatic or polluted environments, straight animal interaction, and food-borne pathways such as eating polluted or cross-infected foods of animals. There is also strong evidence that beneficial bacteria, including those found in the digestive tracts of humans and livestock, like *E. coli* and *Enterococcus spp*., may serve as a possible storehouse for resistance genes that can be passed between bacterial species, including those that can infect both human population and livestock with infections (Mshana et al. 2021).

10. ANTIMICROBIAL-RESISTANT AND PUBLIC HEALTH CONCERNS

Recently, a large number of international medical organizations recognized AMR as a major issue in global healthcare and a risk to the current healthcare system that could make it challenging to control many infectious diseases and drastically degrade current treatments. AMR, a global epidemic that is on the rise, is typically linked to the "selective pressure" brought on by the incorrect, excessive, or improper use of antibiotics in animals as well as humans (Bortolaia et al. 2016). A poorer standard of living, invasive infections by bacteria, an upsurge in recurrence rates of infections, and long-term and subsequent opportunistic infections of gram-positive and gram-negative bacteria are all linked to infections by antibiotic-resistant strains. These issues are unmistakably becoming worse, just like infections caused by salmonella-resistant human pathogens, *Campylobacter spp*. and enterococci with vancomycin-resistant connected to an increased risk of issues, a rise in disease incidence, a rise in treatment errors, and a rise in fatalities (Sanderson et al. 2019). According to the European Centre for Disease Control (ECDC), antibiotic resistance by bacteria accounts for twenty-five thousand fatalities annually ((EFSA and ECDC 2019). AMR caused 0.1 million deaths in the United States of America and eighty thousand fatalities in the Chinese mainland. According to figures, five thousand individuals in the United Kingdom per year pass away from infections such as E. coli and K. pneumonia, with bacterial resistance to medicines accounting for 50% of these deaths. Microbes that produce carbapenemase which include Enterobacteriaceae producing New-Delhi metallo-protease-1, antibiotic-resistant Acinetobacter, have emerged and are spreading quickly. The resistance to multiple drug diseases caused by oxacillinase 48, carbapenemase, and Klebsiella pneumonia poses a major risk to the general population since they expose people to inadequate antibiotic alternatives (Bakthavatchalam et al. 2016).

11. CONTROL STRATEGIES FOR AMR (ANTIMICROBIAL RESISTANCE)

Stewardship of antibiotics plays a crucial role in AMR management measures. It is utilized in one program that is relevant to human, veterinary, and WHO health. Antimicrobial stewardship is a rational set of actions that promotes the appropriate use of antibiotics. AMR curve decrease is also aided by effective infection prevention and control. Antibiotics used effectively and research into new antibiotic alternatives are both important in controlling this dangerous threat to both the human and animal communities. AMR-related bacterial infections and zoonotic diseases can also controlled by vaccination, health promotion, and research into the AMR process. AMR monitoring and surveillance programs play a vital role in checking the spread of infections and AMR (Ayukekbong et al. 2017).

12. PLANTS EXTRACT

Plant extracts and their products used in the treatment of bacterial infections since ancient times. Menthol as a primary component of peppermint oil effective in bacterial infections hence products containing menthol able to eradicate gram-positive and gram-negative resistant bacteria. Some plant extracts used in combination with antibiotics have a great effect on microbial activity and growth. Guaco, guava, clove, garlic, lemongrass, ginger, carqueja, and mint are used in different studies. The synergistic effect of these extracts on *S. aureus* was evaluated. Antibiotics like tetracycline have good synergistic effects (Jouda, et al. 2016).

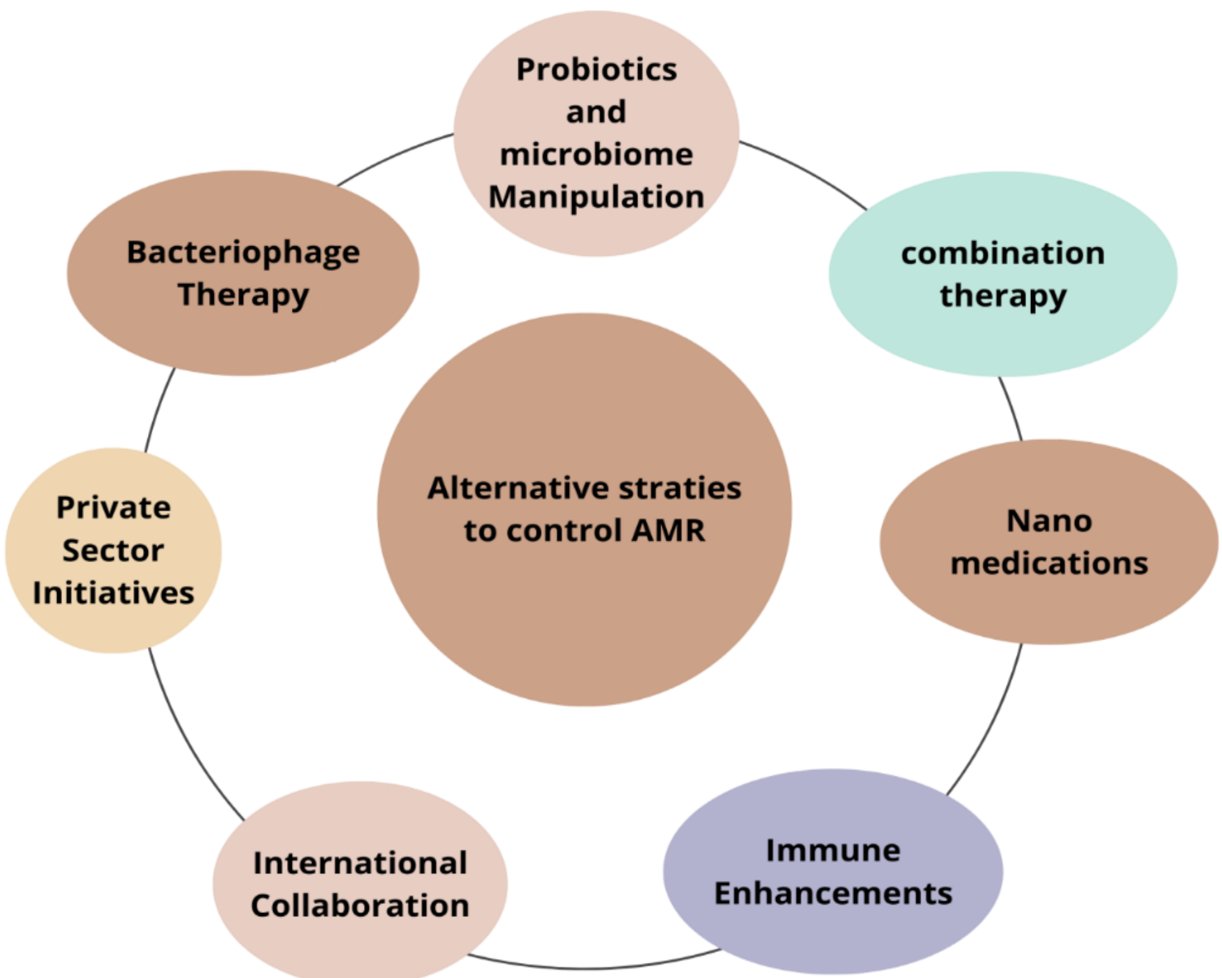

Fig. 1: Alternative control strategies for controlling antimicrobial resistance.

13. ESSENTIAL OILS

Due to the significant amount of biologically active compounds, including volatile and aromatic components, essential oils have been extensively used over the years in medical treatments. Essential oils from *Lippia alba*, *Salvia officinalis*, *Salvia triloba*, *Salva triloba,* and other medicinal plants have a great effect on bacterial growth. Oils from eucalyptus, peppermint, palmarosa, and orange are also very effective (Chouhan et al. 2017).

14. PREBIOTICS AND PROBIOTICS

A class of nutrients known as prebiotics is broken down by the gut flora. Throughout recent years, there has been a growing interest in how they relate to human health in general. They can nourish the gut bacteria, and as a result of their decomposition, fatty acids with short chains circulate into the bloodstream and influence not only the gut but also other organs. Carbohydrates are the most known prebiotics. Probiotics are live microorganisms when given to a host in sufficient quantities, improve their health (Joseph et al. 2023).

15. NANOMEDICINE

The use of nanotechnology in medicine is Nanomedicine. It is possible to target a specific organ, tissue, cell, and bacteria with manufactured particles. Targeting provides the advantage of concentrating high levels of antibiotics at the location where bacterial eradication is required, which should reduce the total therapeutic antibiotic dose. These advantages of nanocarrier formulations might tackle current resistance issues and expand the range of antibiotics used in clinical settings (Wang et al. 2020).

16. BACTERIOPHAGE THERAPY

The phages include viruses that attack their bacterial hosts. There are several common characteristics to take into account while selecting phages for therapeutic application. The phages must first effectively eliminate the target bacterial pathogen with negligible bacterial survival. The phages should also be simple to create in high-titer preparations, multiply, and purify. Third, the phages must be stable throughout a range of concentrations so that prolonged storage at frigid temperatures does not result in a significant loss of infectivity. The third need is that the phage preparations be sterile and free of endotoxins or other hazardous impurities. No harmful genes are known or suspected to be present in the phage genomes. Fifth, the phages shouldn't have the capacity to function like generalized transducing phages (Luong et al. 2020).

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