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REVIEW

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One health initiative to mitigate the challenge of antimicrobial resistance in the perspectives of developing countries

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Abstract

Background Antimicrobial resistance is among the critical global public health crises nowadays.

Main body of the abstract Despite its global nature, antimicrobial resistance disproportionately affects developing countries due to scant diagnostic services, insufficient prescription procedures, inadequate dissemination of information to patients, unauthorized sale of antimicrobials, use of substandard or falsified drugs, poor drug regulatory mechanisms, non-human use of antimicrobials, lack of awareness, expertise, and funds, and also lack of political will to implement the necessary measurements. Furthermore, the disposal of human and animal wastes close to human residences, and lack of access to clean water contribute to the dissemination of antimicrobial resistant bacteria and antimicrobial-resistant genes. Antimicrobial resistance is predicted to reduce gross domestic product by 1.1–3.8% by 2050. These include a $60-$100 trillion loss resulting in increased morbidity and mortality in developing countries. The world's highest mortality rate from antimicrobial resistance infection is observed in Africa. To alleviate such life-threatening challenge, One Health strategies like effective communication, education, training, surveillance, detection and joint effort across disciplines and sectors are urgently needed. Global and national preparedness to identify and prioritize antimicrobial resistance-relevant pollutants, surveillance and monitoring of antimicrobials is important.

Short conclusion Therefore, the present review aims to address the collaborative efforts for joint action by several sectors and multidisciplinary areas under the umbrella of One Health to combat antimicrobial resistance challenges in developing countries.

Keywords Antimicrobial, Antimicrobial resistance, One Health, Developing country

Background

The ability of microorganisms to withstand the effects of antimicrobial drugs is known as antimicrobial resistance (AMR). It develops when an antimicrobial loses its ability to effectively stop bacterial growth. According to World Health Organization (WHO) recommendations, AMR should be used specifically to describe resistant microorganisms, since humans and animals themselves have not become antimicrobial resistant (Aslam et al. 2021). The WHO reports that AMR is dangerously high worldwide and morbidity and mortality are increasing (Larsson and Flach 2022). It is expected to reduce global gross domestic product (GDP) by 1.1–3.8% by 2050. These include a $60–$100 trillion loss in economic productivity, increased treatment costs (leading in increased morbidity and mortality in many developing countries' underfunded frail health care systems), and inability to achieve universal health coverage and the Sustainable Development Goals (SDGs). This requires further investigation, especially in developing countries, as they will

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be disproportionately affected (World Bank 2017; Kruk et al. 2018; WHO 2021d, e, f, a, b, c). According to the study, the amount of antibiotics consumed worldwide between the years 2000 and 2015 was risen by 65%, increasing from 21.1 to 34.8 billion DDDs (defined daily doses), while the antibiotic consumption rate increased by 39% over the year, from 11.3 to 15.7 DDDs per 1000 inhabitants per day study duration. The increase in global consumption was mainly due to increased consumption in developing countries. In 2015, four of the six countries with the highest consumption rates were developing countries. In developing countries, antibiotic use increased by 114%, from 11.4 to 24, five billion DDDs, and the antibiotic use fee multiplied via way of means of 77%, from 7.6 to 13.5 DDDs per 1000 people per day. The antibiotic use rate of broad-spectrum penicillins, the most commonly used class of antibiotics (39% of all DDDs in 2015), increased globally by 36% between 2000 and 2015. The largest increase was in developing countries (56%). In developing countries, antibiotic consumption rates for the three most commonly used classes, cephalosporins, quinolones, and macrolides, increased by 399, 125, and 119%, respectively (Klein et al. 2018).

The fight against AMR must take into account people, animals, plants and the environment at the same time; because it has multiple drivers. The quadripartite organizations (FAO, OIE, WHO and UNEP) have established a joint action plan of One Health and just announced that they are setting the strategic framework for working together on AMR (WHO 2022b). To attain the best possible levels of human, animal, and environmental health, One Health is characterized as an integrated effort of several disciplines collaborating on a local level, at the national level, and internationally (Gongal et al. 2020).

Through surveillance, prevention and mitigation, the One Health movement seeks to protect human, animal and environmental health. Achieving optimal health and sustainability for people, animals and the environment at the same time is the main goal of One Health. Practical guidelines include using a systems approach to define the complex system under consideration and dividing the method into three levels of collaboration (political, institutional and operational). Emerging infectious diseases, risks of companion animals, water and food security, socio-economic and cultural environment, AMR, pollution, climate change, biodiversity, habitat loss and human encroachment on wildlife are eight global challenges for the twenty-first century that should be addressed with the One Health approach (Prata et al. 2022). Among these 8 challenges, we focus on the AMR-One Health approach in our present review.

Therefore, the aim of this review is to address the collaborative efforts for joint action from multiple sectors and multidisciplinary areas under the umbrella of One Health to tackle AMR challenges from the perspectives of developing countries.

Antimicrobial use in humans, animals, and plants

Infected humans, animals and plants are treated with antimicrobial agents. Without effective antimicrobial agents, various human medical procedures such as surgery, care of infants, cancer chemotherapy, care of the critically ill, invasive diagnostic and transplant drugs and treatment procedures are severely hampered with a corresponding increase in morbidity and mortality from secondary microbial infections. Ceftriaxone, cefotaxime and other cephalosporin are used to treat various human infections like urinary tract, abdominal, lung and bloodstream infections (Temkin et al. 2018).

Antimicrobial agents have various uses in animals including domestic animals, fish in aquaculture systems, bees, and livestock for various purposes such as therapeutic, prophylactic, developmental, and livestock production. It is estimated that the amount of antimicrobials used in animals worldwide is greater than in humans (Bacanlı and Başaran 2019; Jans et al. 2018).

The global use of antimicrobials is projected to increase by 67% by 2030 due to changing production patterns in middle-income countries. Reducing the use of antimicrobials as growth promoters in animal husbandry is one of the most difficult challenges. Although they are commonly used for mass prophylaxis in some countries, the European Union (EU) has banned the use of antimicrobials as growth promoters in animals since 2006 (Humphreys and Fleck 2016). Despite this, many countries still use them (Góchez et al. 2019).

Ceftiofur is the most widely used veterinary cephalosporin (Velazquez-Meza et al. 2022). In 2017, about 18 tons of 3rd and 4th generation cephalosporins were used in Europe, mainly in animals intended for human drugs (EMA 2019). In the US, the total use of cephalosporin for animals in 2018 was approximately 31.44 tons (FDA 2018). Additionally, antimicrobial doses used in aquaculture may be higher than those prescribed for livestock. Hence, residues of antimicrobial agents remain in fish products and can remain in the water for a long time through excretion. These residues spread rapidly in water bodies and exert selective pressure (Watts et al. 2017). There is evidence of bacterial transmission from animals to humans as similar strains of resistant bacteria were found in both humans and food animals (Pirolo et al. 2019). Drug resistance in *E. coli*, *Salmonella* and *Klebsiella* to colistin, was reported in both food animals and humans (Bich et al. 2019); human extra-intestinal extended spectrum cephalosporin-resistant *E. coli* was raised from food animals (Lazarus et al. 2015). The incidence of resistant infections in humans decreased by 24% when antimicrobial usage in animals was reduced (Tang et al. 2017).

In order to treat infections in both plants and animals, both terrestrial and aquatic, antimicrobials are essential (WHO 2021b). Tetracyclines, streptomycin and certain other antimicrobial agents are used to treat and prevent bacterial infections of fruits such as apples and pears (e.g., fire blight caused by *Erwinia amylovora*) (Sundin & Wang 2018). Moreover, other antimicrobials are occasionally or experimentally used to treat plant diseases (OIE 2019).

Bactericides, fungicides and pesticides are key antimicrobial agents in controlling plant diseases. However, their use can leave residues on plants and in the environment that can have negative effects. Increased resistance in plant pathogens to streptomycin, oxytetracycline, copper-based compounds and some fungicides has been associated with their use. Similarly, the recent increase in the prevalence of *Aspergillus fumigatus,* the species that causes aspergillosis in humans, has been of concern (Miller et al. 2022). Antimicrobial-resistant fungi are known to be produced by the use of antibiotics in agriculture and are spread to people through the environment (FAO 2018). The foods with antimicrobial residues that can dessiminate AMR might be animal-origin foods (Nisha 2008), vegetables (Phillips et al. 2004).

Mechanisms of antimicrobial resistance

Antimicrobial resistance occurs when the target microbe evolves a physiological mechanism to overcome the effects of the drug. This can be due to a change in the structure or composition of the bacterial envelope, the production of enzymes that break down the target substance, etc. (Reygaert 2018).

Inherited resistance and acquired resistance are the two principally known effects in both Gram-negative and Gram-positive bacteria. Inherent or innate or intrinsic resistance is the most basic form of resistance. It could be related to the lack of an antimicrobial receptor, low affinity, impermeable cell walls, or enzyme synthesis. It arises through spontaneous mutation without drug exposure (Urban-Chmiel et al. 2022). The natural resistance to several antimicrobials, including -lactams, aminoglycosides, rifampicin, triclosan, and fluoroquinolones, is also thought to be caused by a number of genes, including AmpC, blaSHV, TrxA (thioredoxin), TrxB (thioredoxin reductase), etc. (Aslam et al. 2021).

Acquired resistance occurs when inherently susceptible microorganisms acquire the ability to remain unaffected by the drug. Vertical gene transfer (transfer of genetic material from parent to offspring) and horizontal gene transfer, HGT, (transfer of genetic material from cell to cell) are two ways in which antimicrobial resistance genes (ARGs) can be acquired. They can both occur simultaneously. By acquiring new resistant genes and processes, HGT causes a population of microorganisms to have improved resistance profiles. HGT can arise via transformation, transduction, or conjugation. HGT enables transmission between species and plays an important role in the spread of AMR. Any physical or chemical agent can cause mutations in the organism. However, due to differences in structure, there are differences in the type of mechanisms of resistance used by Gram-negative bacteria compared to Gram-positive bacteria. Gram-negative bacteria utilize all four major mechanisms, while gram-positive bacteria are less likely to restrict mechanisms of drug uptake and drug efflux (due to lack of lipopolysaccharide, LPS and outer membrane) (Reygaert 2018; Samtiya et al. 2022).

There are four main molecular mechanisms by which bacteria can resist the effects of antimicrobials like modification of the target site, modification or destruction of the antimicrobial, antimicrobial efflux via efflux transporters, and reduced antimicrobial influx through the thickened membrane (Fig. 1) (Kapoor et al. 2017; Laws et al. 2019; Zhu et al. 2022).

The rise of multidrug-resistant strains of *E. coli, P. aeruginosa*, and other bacteria is caused by well-known ARGs such blaTEM, blaCTXM, blaKPC, blaNDM, blaVIM, and mcr-1 (Ejaz et al. 2021). A striking example of One Health dissemination of ARGs, detected in raw meat, and specimens collected from migratory birds and human isolates (Ilbeigi et al. 2021).

Decreased uptake

Gram-negative bacteria have a much thinner cell wall, protected by a lipopolysaccharide molecule in the capsule, an outer membrane and what is known as the periplasmic space. In short, it is a much more heavily armored vehicle that reduces the antimicrobial influx (Reygaert 2018).

Efflux pumps

The membrane proteins maintain low intracellular concentrations of antimicrobial agents while exporting them from the cell. They pump drugs out of the cell at the same rate at which they enter. For instance, the OprK protein of *Pseudomonas aeruginosa's* outer membrane can carry different antimicrobials to the surface of the bacterium. Then drug resistance develops because the concentration of the antimicrobial in the bacteria is not sufficient to produce an antibacterial effect. However, antimicrobial agents can be specific to efflux pumps (Correia et al. 2017; Kapoor et al. 2017).

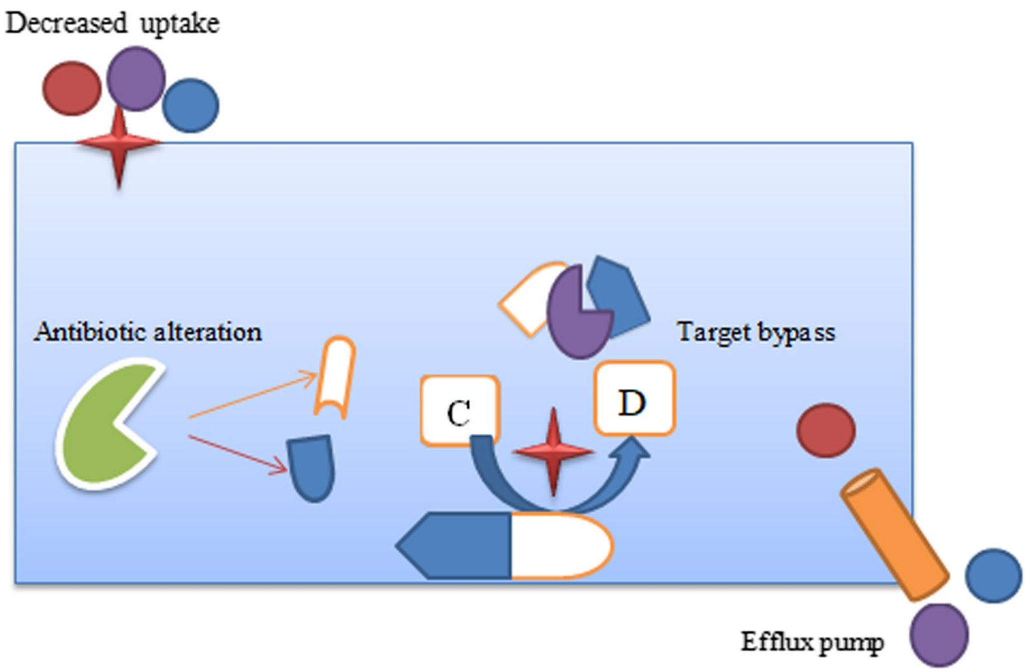

Fig. 1 Molecular mechanism of antimicrobial resistance. The diagram shows that enzymatic inactivation of antimicrobials (antibiotic alteration), alteration of a drug target (target bypass), decreased outer membrane permeability (decreased uptake), and active drug efflux (efflux pump) are the four basic mechanisms of AMR

Target site modifications

Chromosomal spontaneous mutation of a bacterial gene inhibits drug binding. Small changes in the target molecule can have a significant impact on antimicrobial binding since antimicrobial interaction with target molecules is typically highly selective (Kapoor et al. 2017).

Antimicrobial alteration

Three primary enzymes such as β-lactamases, aminoglycoside-modifying enzymes (AMEs) and chloramphenicol acetyltransferases inactivate antimicrobials. Penicillins, cephalosporins, monobactams and carbapenems are hydrolyzed by β-lactamases. AMEs provide extended spectrum resistance, preventing binding to the 30S ribosomal subunit and reducing the affinity of a charged molecule (Kapoor et al. 2017).

Drivers of antimicrobial resistance

The main drivers of AMR include the misuse, overuse or unnecessarily high consumption of broad-spectrum antimicrobials, lack of access to clean water, sanitation and hygiene for humans and animals, the prescribing of fixed-dose antimicrobial combinations, even without knowing a proven advantage over single drug compounds, social factors such as self-medication, use of antimicrobials without a prescription, inadequate infection and disease prevention and control in healthcare facilities and on farms, poor access to quality, affordable medicines, vaccines and diagnostics; lack of awareness, lack of AMR policies and monitoring systems, inadequate microbiology laboratory infrastructure, etc. as well as cultural activities such as mass bathing in pilgrimage season and pollution from the pharmaceutical industry (Koduah et al. 2021; Sharma et al. 2021; WHO 2021a).

Developing countries with poor access to antimicrobials and dense transmission networks have recorded AMR prevalence rates greater than 50% (Sulis et al. 2022). Disposal of human and animal waste near human houses and farms is common and, indeed, inevitable in resource-limited settings with inadequate or unsafe sanitation (Alam et al. 2019). The AMR platform formation is not instant in developing countries. It takes several years of cross-sector engagement, consensus building, a resilient governance structure, and concerted discussion of issues and ideas. For example, in Ghana, the need for a national AMR policy was discussed in 2011, the policy was finalized in 2017 and launched by the President in April 2018 (Koduah et al. 2021).

Inappropriate use of antimicrobials (without prescription)

Due to inadequate information provided at the time of prescription, ignorance of the issue of inappropriate antimicrobial use, or financial constraints (which may prevent certain patients from purchasing costly or unaffordable antimicrobials), some patients may not pay close attention to their antimicrobial prescriptions (Fernandes et al. 2014; Fox-Lewis et al. 2018).

Sub-standard or falsified or unlicensed medicines

The new WHO definitions indicate that falsified or counterfeit medical products are those that intentionally or fraudulently misrepresent their identity, composition or origin; these products are manufactured and distributed with criminal intent; substandard medical products are issued by national regulatory authorities but do not meet national or international quality standards or specifications; These products often have low pharmaceutical active ingredients or dissolution properties, and unregistered or unlicensed medicinal products are those that have not been evaluated or approved by the national or regional regulator for the market in which they are distributed (WHO 2017b, c). Poor quality medicines expose patients, communities and governments to an increased burden of disease, economic loss and drug resistance. Up to 155,000 children die each year from counterfeit anti-malaria drugs, and the same number die from acute pneumonia after being treated with counterfeit and inferior antimicrobials. Estimates of the impact of falsified and sub-standard drugs suggest that the burden is up to 10% of all drugs in developing countries and the economic cost is $10 billion to $200 billion (Relman and Lipsitch 2018; Renschler et al. 2015; WHO 2020a). The issue of illegal drug trade in the local area has a significant connection to the issue of poorly trained drug donors. Unlawful sellers of drugs are a major contributor to the inappropriate use of antimicrobials and the development of AMR in developing countries. More than half of all antimicrobials purchased worldwide are without a prescription. These antimicrobials are sold in many developing countries by traders of illegal antimicrobials in shops, markets, and passenger cars (Belachew et al. 2021).

Lack of efficient diagnostics facilities

Lack of access to quality laboratory facilities, which causes diagnostic ambiguity, subpar clinical judgment, improper antimicrobial usage, and the emergence of AMR, is a significant problem in developing nations (Egyir et al. 2020). It is proven that only 380 laboratories in the sub-Saharan region of Africa were accredited to international standards and that none of the laboratories in 37 of the 49 countries studied were accredited to these criteria (Schroeder and Amukele 2014). Lack of skilled labor, inadequate infrastructure, inadequate (or nonexistent) laboratory equipment, deficiencies throughout the distribution chain, inadequate repair of equipment, ineffective quality-control systems, and lack of government regulation are challenges where laboratories exist (Jacobs et al. 2019; Nkengasong et al. 2018). Lacking guidance from diagnostic laboratory services, which are typically located in urban areas, rural physicians typically resort to the presumptive treatment of patients, blindly prescribing antimicrobials, or referring critically ill cases. Due to this, many individuals experience significant morbidity and mortality (Moran et al. 2019).

Antimicrobial resistance as a worldwide public health crisis

Antimicrobial resistance is one of the greatest threats to global health, food security and development, affecting every person of all ages and in every country. Although naturally occurring, misusing antimicrobials in humans and animals speeds up the process (WHO 2020b). Human antimicrobial consumption, which increases AMR, is projected to increase by up to 200% by 2030 if no policy changes are made (Klein et al. 2018).

Drug-resistant infections are more expensive to treat, may require multiple therapies to be effective, take longer to treat, and are less certain to cure. According to one global worst-case scenario estimate, AMR would increase healthcare spending by up to 25% in developing countries and 8% globally (World Bank 2017). The problem is a major health threat with serious consequences, especially for developing countries (Founou et al. 2017).

More than 900,000 deaths related to AMR and 3.57 million deaths linked to AMR in 2019 were caused by the six main bacteria that cause mortality: *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii,* and *Pseudomonas aeruginosa* (Murray et al. 2022; Richter et al. 2023). The WHO forecasts that by 2050, this number might reach 10 million globally and 4.1 million in Africa (WHO 2021b; WHO Africa Region 2021). In addition, the SARS-CoV-2 pandemic has exacerbated the current global AMR epidemic, mainly as a result of inappropriate and overuse of antimicrobials, immunosuppressive drugs, and prolonged hospital stays (Mirzaei et al. 2020). In the coming years, it is also predicted that increased use of disinfectants such as hand sanitizer and surface cleaners would result in higher rates of pathogenic AMR in bacteria (Bengoechea and Bamford 2020).

The World Bank estimates that by 2050, drug-resistant illnesses may cause a worldwide financial crisis that will cost $1 trillion yearly and push 28 million people into severe poverty (Pulingam et al. 2022; World Bank 2017). The world's highest mortality rate from AMR infection is observed in Africa. The problem is that developing countries do not have enough access to databases to store and retrieve current estimates of AMR. This hampers our understanding of the effectiveness of widely used antimicrobials and the factors that contribute to human resistance. Even if data is routinely collected, access to it is not always guaranteed. They are often collected by hand and rarely integrated or shared with policymakers due to various inadequacies in health, laboratory and surveillance systems (Table 1). African Union leaders committed in February 2020 to address the AMR threat across a wide range of areas, notably human health, animal health and agriculture (Ibrahim et al. 2018).

Rising AMR levels are hampering progress toward many Sustainable Development Goals (SDGs), particularly those centered on health and well-being, reducing poverty, food, the environment, and financial growth (Gajdács et al. 2021). In the interrelationship between human and animal health, crop production, food safety and the environment, an effective fight against AMR requires a concerted approach from all sectors according to the so-called One Health approach (WHO 2021b).

Foods like milk, eggs, and meat can contain antimicrobial residues when animals are given antimicrobials. The various side effects of these residues include transmission of AMR to humans, immunopathological effects, allergies, mutagenicity, nephropathy (due to gentamicin), hepatotoxicity, reproductive problems, bone marrow toxicity (due to chloramphenicol) and even carcinogenicity (sulfamethazine, oxytetracycline, furazolidone). Due to the mobile nature of resistance, the most important negative impact of antimicrobial residues is the spread of AMR to humans (Bacanlı and Başaran 2019).

The threat posed by zoonoses, pandemics and their impact on the environment is given too little attention worldwide (Ramanathan et al. 2021). Despite their well-known role in spreading clinically important infections, insects are among the neglected factors that have hardly been studied as AMR vectors (Rawat et al. 2023).

One of the greatest threats to world health and safety is the spread of infectious diseases. In developing countries, infectious diseases are the leading cause of animal diseases and account for more than 60% of the human disease burden, posing a serious threat to human and animal health. Emerging infectious diseases can be brand new or the evolution of already known infections that originated in humans or other animals. More than 60% of emerging human infectious diseases are zoonotic or animal-borne, with most of them (about 70%) originating from wild animals. These risks, with enormous long-term effects, become more frequent and serious over time (WHO 2022a).

AMR and newly developing infectious diseases including avian influenza, Ebola, Zika, and COVID-19 have recently had a significant negative influence on humanity. Under the One Health initiative, a collaboration between the human, animal and environmental sciences has gained significant importance in addressing emerging public health concerns as the same infections pose a threat to humans and animals (Murray et al. 2022; Ryu et al. 2017). For instance, it is concerning that household cats in South Korea have been found to have HPAI H5N6 infections. Humans and other mammalian animals are at risk from HPAI H5N6 (Lee et al. 2018).

Although the concentration of antimicrobials and the abundance of ARGs in environmental samples are often correlated, in many cases this can be explained simply by differential loads in human excrement, which are a source of both, and not by the selection of resistant bacteria in the local environment at the antimicrobial residues (Ebmeyer et al. 2021). This can lead to anthropogenic ARG transmission, the transmission of infectious diseases from humans to animals.

One health strategies to address the challenge of antimicrobial resistance

One Health is a holistic, integrated, systems-based approach that combines strategies to sustainably optimize the well-being of people, animals and ecosystems (WHO 2023). To promote well-being and address threats to health and ecosystems, the approach mobilizes different sectors, disciplines and communities at different levels of society. It also addresses our shared need to take action on climate change for clean water, energy and air, and for safe and nutritious food (WHO 2021e). AMR cannot be addressed simply by managing the problem in healthcare facilities; therefore it must be confronted from the One Health perspective across human, veterinary, and environmental boundaries (Wang et al. 2018). Interactions between humans, animals, and the environment

Table 1 Death rates involving infection, associated with and attributable to AMR, in SSA in 2019

SSA Region	Deaths attributable to resistance	Deaths rate per 100,000 attributable to resistance	Ref
Western SSA	125,000 (95,400–161,000)	27.3 (20.9–35.3)	Antimicrobial Resistance Collaborators (2022)
Southern SSA	15,300 (11,300–20,400)	19.4 (14.3–25.9)	
Eastern SSA	88,200 (67,000–116,000)	21.4 (16.3–28.1)	
Central SSA	27,200 (19,600–36,400)	20.7 (14.9–27.7	

SSA: sub-Saharan Africa

give rise to possibilities for one group to act as a reservoir for ARG that can go in all directions (WHO 2021f).

AMR transmission not only occurs between humans and humans, but also spreads between animals and plants, animals and humans, environment and animals, and environment and humans. Agricultural practices can potentially lead to the introduction, selection, or replication of AMR organisms in pre-and post-harvest food production systems (Akram et al. 2023). The environment is exposed to antimicrobial residues through human and pet excreta (urine and feces) or direct environmental pollution from aquaculture or crop production (Larsson and Flach 2022).

Although the idea of One Health has been around for a while, recently it has gained attention and evolved due to the more frequent and severe dangers of AMR (Adisasmito et al. 2022). In 2014, WHO in collaboration with FAO and OIE published the first notable paper highlighting the need for the One Health strategy to address AMR in a report describing microbial resistance surveillance. Subsequently, this official partnership between the three organizations enhanced global collaboration and promoted multidisciplinary cooperation between human and animal health combined with food hygiene. AMR has been prioritized for coordinated action by the FAO, OIE, and WHO (Badau 2021).

AMR in the environment can lead to loss of soil biodiversity, and animal or plant diseases. It also increases the use of antimicrobials (negative feedback from original use) for humans, animals and plants, further increasing selection pressure. To better understand the environmental aspects of AMR and to guide science-based decisions and activities, a systems approach like One Health is needed (Aslam et al. 2021; Dortet et al. 2018). AMR can be easily transmitted between and within different ecosystems and populations (Velazquez-Meza et al. 2022). Resistant zoonotic bacteria are found in soil and can infect plants, vegetables, and fruits. Antimicrobial-resistant fungi are known to be produced by the consumption of pharmaceuticals in agriculture and are spread to people through the environment (FAO 2018). Phytopathogens, soil bacteria, and zoonotic bacteria found in the environment and the food chain can all exchange genes through HGT. Resistance to one compound can lead to resistance and multidrug resistance to other structurally related or even very different compounds through HGT, co-resistance, cross-resistance and gene up-regulation. Example: Linezolid, used to decolonize patients before surgery, was rendered resistant by HGT using episomal plasmids carrying the cfr (chloramphenicol-florfenicol resistance gene) (Dortet et al. 2018; Miller et al. 2022).

Another scenario is when a pathogenic bacterium infects a particular patient and is already resistant without knowing when or where the resistance was acquired (Hernando-Amado et al. 2019). The study concluded that the presence of ARGs in clouds is a sign that AMR can travel long distances in the atmosphere. A variety of ARGs can rise at cloud levels found primarily in the free troposphere. Their respective concentrations should vary depending on the sources and geographic origin of the air masses, since once they are absorbed into the atmosphere they are transported efficiently (Rossi et al. 2023).

The issues arising from competing interests and risk–benefit imbalances in different sectors, as well as concerns about AMR, are illustrated through the use of subject matter experts (SME) pharmaceuticals for human and animal therapy. For example, the third generation cephalosporins are used in human and veterinary medicine, i.e., cefotaxime and ceftriaxone for humans and cefpodoxime, cefoperazone and cefovecin for animals. Colistin belongs to the antimicrobial class of polymyxins and has been used in both humans and animals for over 50 years (Collignon and McEwen 2019). Aminoglycosides, tetracyclines, and quinolones are three types of antimicrobial medicines which are often utilized for treating infections in both humans and animals as well as in the production of plants (OIE 2019). Also, classes of antimicrobials critical to human medicine such as broad-spectrum β-lactams and quinolones are prescribed for animals (Bacanlı and Başaran 2019; Jans et al. 2018). Some antimicrobials used in humans and animals like tetracycline, triazoles, and streptomycin have therapeutic uses in plants. In this case, AMR can be easily transmitted between humans, animals and plants. Some countries are using drugs such as colistin, fluoroquinolones and macrolides for animals, which the WHO considers vital to human health (Góchez et al. 2019). This puts bacteria under selective pressure in humans and animals, mutating their genes into ARGs. To alleviate this issue, several One Health strategies are employed.

Awareness creation in society through effective communication, education, and training

Antimicrobial Awareness Week (WAAW), that's increasing its recognition to encompass all antimicrobials, antifungals, antiparasitics and antivirals. Since 2015, the WAAW has been an annual event to raise public awareness of AMR and promote best practices among the public, healthcare professionals and policymakers to halt the emergence and spread of drug-resistant diseases. In 2020, the slogan "Antibiotics: Handle with Care" was changed to "Antimicrobials: handle with care" (Wu et al. 2021) making the term more inclusive.

Effective communication, training and education are key components of any Antibiotic Stewardship Program

(ASP). These should include medical staff from all types of care settings, hospital administrators, patients and the general public. The ASP team often conducts the training. This tuition-free training can be secured for future generations by raising awareness of how antimicrobials should be used to treat common diseases and why improper use can lead to resistance and the loss of effective therapies. The use of didactic lectures at educational events and the distribution of educational or informational brochures and resources are two possible strategies. These strategies are based on the One Health idea. However, there is still a significant information gap between AMR in humans and animals, particularly in developing countries (e.g., Ethiopia). This knowledge gap should therefore be closed by cross-industry knowledge transfer and scientific evidence (EFMHACA 2018).

Farmers should understand how to raise animals, produce fruits and vegetables with no or minimal use of antimicrobials and ideally only use drugs to treat clinically ill individual animals. They must also know how to reduce the need for antimicrobial treatment by improving overall levels of husbandry and minimizing crowded, unsanitary, and stressful conditions that promote the spread of disease in animal and plant populations (McEwen and Collignon 2018). Veterinarians should possess the knowledge, attitudes and behaviors that characterize good antimicrobial stewardship, thereby protecting the health and welfare of their patients, the economic interests of their customers, and the health of the community and One Health (FAO 2021).

It is preferable to include the One Health approach in the curriculum. For example, the Department of Pharmacology, Chicago College of Osteopathic Medicine and Midwestern University, has incorporated topics related to the One Health Initiative into all courses (Prozialeck & Edwards 2018).

Joint effort of various disciplines and sectors

Governments, civil society and the commercial sector must be involved and work together. These efforts should be based on a shared vision and goals toward One Health (WHO 2019). WHO warns that future collective action against AMR will require eight identified components (WHO 2021c).

(a) A governance system that coordinates with all relevant international organizations
(b) Equitable global access to effective antimicrobials
(c) The One Health Approach for working together to reduce the inappropriate use of antimicrobials in food systems, the environment and healthcare
(d) The active participation of civil society organizations
(e) Refusal to be influenced by people with financial conflicts of interest
(f) Well-defined benchmarks for tracking progress and ranking investments
(g) Enough funding to carry out National Action Plans (NAPs)
(h) The acknowledgment of AMR as a component of pandemic preparedness and prevention.

Several legislative measures have been taken to restrict or ban the use of antimicrobials, particularly as antibacterial feed additives for animals and in metaphylaxis and therapy (EU Regulation 2019/6) (EU 2019).

Global and national preparedness to countering AMR through one health

Animal health, food safety, the economy, and the environment are all at risk due to AMR. Resolving and mitigating these risks requires a real connection between broader development issues, including One Health, pandemic preparedness and response, universal healthcare, sustainable food systems, and environmental concerns (WHO 2021b).

Public health and environmental concerns, systems and frameworks, socio-cultural and economic realities, national AMR action plans, and environmentally sound AMR strategies and plans of each country must be considered. Addressing these issues will reduce environmental emissions of chemical and biological pollutants harmful to AMR (Collignon et al. 2018). An environment is a place where AMR can grow and spread (e.g., in contaminated drinking water, recreational waters, effluent from agricultural production, and waste streams from pharmaceutical manufacturing and hospitals) (WHO 2021b).

The COVID-19 pandemic serves as a reminder to better understand and advance all aspects of infectious disease preparedness and prevention, including its environmental elements (Ramanathan et al. 2021). Environmental stakeholders have important roles to play in combating AMR, such as creating robust and realistic regulatory frameworks to limit AMR-relevant emissions into the environment and encourage sustainable production and consumption patterns that balance population growth. This requires a variety of new approaches and innovations for specific industries, financial and business environments, climatic conditions and cultural contexts (Hernando-Amado et al. 2020). Stakeholder activities should focus on four main areas to better prepare for this global situation and reduce environmental concerns associated with AMR:

Enhance environmental governance, planning, and regulatory frameworks

Ensuring compliance with environmental regulations related to antimicrobial manufacturing, water, sanitation and hygiene (WASH) standards, agricultural standards, waste management and infrastructure should be ensured.

Identify and target priority AMR-relevant pollutants

To reduce the burden of AMR by limiting the release of pollutants into urban and rural settings with strategies such as integrated pest management, there is a need to reduce the ecological use of antimicrobials such as fungicides, antimicrobials, and antivirals in plant-based food production systems. Antimicrobial-resistant bacteria and ARG levels can be reduced through wastewater treatment and management at known sources of contamination (such as sewage systems, animal production, hospitals, and pharmaceutical manufacturing sites). Tailored solutions must prioritize the best waste treatment and management alternatives that support regional infrastructure and resources (Graham et al. 2019).

Improve reporting, surveillance and monitoring of antimicrobials

Measuring the impact of antimicrobial pollution on biodiversity and integrating environmental monitoring data (e.g., monitoring of surface water, solid waste and airborne particulate matter) with existing AMR monitoring and pollutant data are critical parts of plans to reduce antimicrobial releases into the environment. Risk assessment and management to determine the probability of occurrence of AMR-related pollution can also be integrated into global standards and monitoring procedures based on other monitoring systems (e.g., stewardship programs) (Hassoun-Kheir et al. 2021).

Systems for the manufacture, sale, use and disposal of unused or expired antimicrobials should also be collected and reported in a transparent and timely manner. There is a need to record releases of antimicrobials, resistant microorganisms and their genetic material into the environment and their impact on biodiversity. The safety of bioproducts (such as biofertilizers, bioplastics, use of biosolids and manure, and plant growth stimulants) and novel agricultural practices should be documented, as should the main sources of pollutants affecting AMR in the environment (UNEP 2022).

In Ethiopia, data on antimicrobial therapy adherence, prescribing, consumption, dispensing and concerning various practice guidelines may be collected on a regular basis to assess the effectiveness of antimicrobial use. The frequency of monitoring antimicrobial use must be planned by each hospital at least once a year. The ASP team can obtain important data for better decision-making through effective surveillance of AMR using patient screenings for certain multidrug-resistant organisms such as carbapenemase-producing Enterobacteriaceae, CPE, methicillin-resistant *Staphylococcus aureus*, MRSA, vancomycin-resistant enterococci, VRE, and extended-spectrum β-lactamases, ESBL, (EFMHACA 2018).

Prioritize financing, innovation, and capacity development

AMR could be addressed by introducing innovative and sustainable finance, which could include removing market-distorting farm subsidies, green public procurement, social and green bonds, and exploring the possibility of incorporating AMR into programs. A compelling economic case must be developed for investments, particularly investments in indigenous resources, in cost-saving or alternative technologies that reduce the environmental risks from AMR (UNEP 2022). Basically, resistance can be related to indirect factors such as gross domestic product (GDP) per capita, public health spending, an aging population, an increase in travel or weak governance (Collignon et al. 2018).

The Ethiopian Public Health Institute (EPHI) is leading AMR surveillance plan with support from the Centre for Disease Prevention and Control (CDC), the American Society for Microbiology, and the Ohio State University Global One Health initiative. To address the need for surveillance system that captures the emergence of resistance, trends, distribution and consumption of antimicrobial agents in different settings, EPHI hosted a three-day workshop in August 2016 to initiate discussions on AMR surveillance. The workshop provided an opportunity to discuss priorities and implementation strategies for monitoring and consensus building, while raising awareness of the importance of AMR among key stakeholders (Ibrahim et al. 2018).

Therefore, by April 2017, Ethiopia had prepared and approved the national AMR surveillance strategy. The strategy aims to build a national surveillance network capable of identifying priority AMR pathogens, analyzing and reporting data, characterizing resistance and providing evidence for the implementation of prevention and control programs. The data management and reporting strategy, steps to establish a national AMR surveillance system and clinical and laboratory stakeholder commitments are all outlined in the plan (EPHI 2017).

However, Ethiopia has encountered difficulties in integrating electronic data collection for AMR surveillance into routine work and laboratory procedures at Sentinel surveillance sites, as well as difficulties in locating high quality microbiological materials on site. Meanwhile, the American Society for Microbiology procured the necessary AMR supplies for EPHI and the Sentinel monitoring stations. To ensure that sufficient and high-quality supplies are available in the future, EPHI has started working with the Pharmaceutical Fund and Supply Agency, Ethiopia's central procurement agency (Hagos 2019; Ibrahim et al. 2018).

For global and national preparedness to address AMR through One Health, one of the lessons learned from the COVID-19 pandemic is the need to simultaneously prevent and address multiple health issues, particularly their environmental components. AMR is already a serious threat to global health and could negatively impact the planet's ability to sustain its environment (Murray et al. 2022).

Surveillance of the AMR under the umbrella of one health

Surveillance of antimicrobial use and AMR in both human and non-human settings is necessary to assess the extent, patterns and health burden of resistance at national, regional and international levels. AMR-One Health surveillance should include appropriate bacteria collected from humans, animals and environments including healthcare facilities, farms, soil, water, food, etc. (Ryu et al. 2019; WHO 2017a).

In order to develop a criterion to identify AMR patients, hospitals and environments, WHO has prioritized the detection of resistant bacteria harboring ARGs by using various novel molecular tools such as real-time PCR, whole genome sequencing (WGS), next-generation sequencing, etc. (Lanza et al. 2018). One Health components that are essential for lowering the global burden of AMR bacteria include the molecular epidemiology and genetic relatedness of AMR at the human-animal-environment interface. To allow AMRs to verify their sufficiency and applicability in the pertinent area, integrated surveillance programs with frequent assessment are needed. In this context, a number of tools are available that define various aspects of surveillance, such as SURVTOOLS (FP7-EU), Network for Evaluation of One Health (NEOH), and Progressive Management Pathway (AMR-PMP; FAO) (Sandberg et al. 2021).

It may not be feasible in the field to use conventional microbiological techniques like cultivating pathogenic bacteria or sequencing isolates since they require additional logistics. An alternate way to address this issue is a pathogen-independent one, such as metagenome sequencing, which is used to find every genetic component in a sample (Lanza et al. 2018). Metagenomics sequencing can be used to identify taxonomies of microbial species and the existence of genes that code for virulence, resistance, and toxin production. It also identifies different mobile genetic elements that can be transferred between different niches (De Nies et al. 2021; Ko et al. 2022). It is a suitable technology that allows for the use of environmental genomic data without culturing samples in order to isolate microorganisms (Liu et al. 2022). It enables us to evaluate the distribution of ARGs and pathogen variety across various One Health niches. AMR has been studied using some sequence-based methods, including shotgun metagenomics, amplicon sequencing, and functional genomics. ARG variations and novel ARGs are frequently found and identified using functional genomics (Collignon and McEwen 2019; Stalder et al. 2019).

More chances exist to manage bacterial infections that are resistant to gene editing and transgenic technologies (Li et al. 2020). The WGS-based genetic similarity between the isolates from different sample sources helps understand the possible transmission pathways between these One Health niches (Griffiths et al. 2017).

New methods have recently been created that make it possible to quickly identify the infection and determine if it is susceptible to various antibiotics. Fast immune chromatography, automated time-lapse microscopy, and matrix-assisted laser desorption ionization (time of flight) are a few technologies that may be useful in this area, (MALDI-TOF MS) mass spectrometry (Florio et al. 2020). These techniques' key advantage is that samples may be used to run them, which immediately cuts down on the time needed for pathogen identification or susceptibility testing. The research that is now available indicates that such techniques will soon be standard laboratory techniques (Aslam et al. 2021). However, there are significant drawbacks to employing these methods, such as the operating expenses, as the reagents utilized in these technologies are highly pricey, particularly for researchers from underdeveloped nations. Additionally, a large number of skilled and trained employees are needed to use these technologies (Baer et al. 2021; Maurer et al. 2017). Regarding this, several databases are available online like ResFinder, AMRFinder, CARD and ARG-ANNOT (McDermott & Davis 2021).

Conclusions

Antimicrobial resistance occurs when the drug loses its ability to prevent or treat infections in humans, animals, and plants. In developing countries, factors such as the use of antimicrobials without a prescription, poor access to quality antimicrobials, lack of awareness, lack of AMR policies and monitoring systems, inadequate laboratory infrastructure, etc. can trigger AMR. Another scenario in spreading AMR is the use of same drugs for human, animal and plants. For example, the 3rd generations cephalosporins are used in human and veterinary medicine, Colistin is used in both humans and animals, and drugs like tetracycline, triazoles, and streptomycin used in humans, animals and plants. Through misuse, overuse, or unnecessarily high consumption of broad-spectrum antibiotics and the above factors, the bacteria develop mutations in their genes and develop a selection mechanism for survival. The altered genes are transmitted either vertically from parent to offspring or horizontally between different bacterial cells by transformation, transduction, or conjugation. Drug-resistant infections are more expensive to treat, may require multiple therapies to be effective, take longer to treat, and are less certain to cure.

To promote well-being and address threats to health and ecosystems, the One Health approach mobilizes different sectors, disciplines and communities at different levels of society to work in collaboration. AMR cannot be addressed simply by managing the problem in healthcare facilities; therefore it must be confronted from the One Health perspective across human, veterinary, and environmental boundaries. Agricultural practices can potentially lead to the introduction, selection, or spread of AMR in pre-and post-harvest food production systems and the environment is exposed to antimicrobial residues through human and animal excreta. In developing counties where human, animal and foods are living in single room, AMR inter-transmission is common and hence One Health is very crucial.

One Health strategies such as raising awareness in society through effective communication, education and training, and joint efforts across disciplines and sectors are important. In One Health, detection and diagnostic tools such as metagenomics, polymerase chain reaction, whole genome sequencing and metadata recording are critical.

It holds particular promise for developing countries like Ethiopia, where complex economic, social, and political issues are wreaking havoc. The problem could not be solved by the development of human or veterinary diagnostic tools and drugs alone. It requires a joint, well-structured and organized teamwork of health experts for humans, animals and the environment. Humans cannot be healthy while animals are sick. Animals cannot be healthy while plants are sick. All or some organisms cannot be healthy while the environment is sick. Therefore, we strongly recommend the implementation of the One Health Initiative to mitigate the impact of AMR.

Finally, we would like to recommend that more work is waiting for AMR-One Health in developing countries. The data are very scarce and policy implementation regarding AMR is threatening. It is therefore advisable that academics, researchers, healthcare professionals and government agencies take appropriate action to combat AMR under the umbrella of the One Health Initiative. Nobody is safe until everyone is safe. We also suggest that it would be helpful for countries to incorporate the One Health Initiative into their national curricula.

Abbreviations

AMR	Antimicrobial resistance
ARGs	Antimicrobial resistance genes
ASP	Antibiotic Stewardship Program
EFMHACA	Ethiopian Food, Medicine and Healthcare Administration and Control Authority
EPHI	Ethiopian Public Health Institute
EU	Eurpean Union
FAO	Food and Agriculture Organization
GDP	Gross domestic product
HGT	Horizontal gene transfer
OIE	Office International des Epizooties
UNEP	United Nations Environment Programme
WAAW	World Antimicrobial Awareness Week
WGS	Whole Genome Sequencing

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