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REVIEW ARTICLE

Managing Antimicrobial Resistance from Medical and Veterinary Health Systems Perspectives to Achieving Universal Health Coverage in the African Region

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Abstract

Antimicrobial resistance (AMR) is a threat to global health security and may reverse the gains in preventive medicine. This is worsened by the fact that development of resistance out-paces that of new antimicrobials. The factors driving the development of AMR range from health systems to socio-economic and environmental factors. These include poor antimicrobial stewardship, poor access to quality drugs, prescribing antimicrobials without susceptibility laboratory tests, use of antimicrobials in crop, animal production and aquaculture farming. Others are lack of coordinated medical and veterinary health systems strengthening, poor universal health coverage and practice of one health. The burden of the problem is of public health importance especially in Africa where there is high incidence of poverty, high incidence of out-of-pocket health expenditure, lack of basic social amenities and weak health systems with poor collaboration. The impact of AMR includes increased burden on the healthcare system, hospital admission, cost of patient treatment, poor clinical outcomes and impact on food security, among others. In view of the interplay of various systems and factors in the development and emergence of AMR, there is need for multi-sectoral and interdisciplinary approach at global, regional, national and local levels for its prevention and mitigation. Strengthening of health systems from the medical and veterinary perspectives and universal health coverage are critical in the fight against AMR. The relevant stakeholders include political leaders, community leaders, health professionals, academics, and research institutions, federal and state ministries of health, agriculture, education and Nongovernmental organisations among others.

Keywords: Africa, Antimicrobial resistance, Health systems, Universal Health Coverage

Conflict of interest: None declared

Introduction

The increasing health threat from emerging infectious diseases and Antimicrobial Resistance (AMR) require an urgent global response, especially in Africa for reasons such as weak medical and veterinary health systems (HS) and high poverty level, among others. These could reduce access to appropriate, quality antimicrobials and subsequent emergence of AMR. Antimicrobial resistance has been described as a global crisis by the United Nations (UN) General Assembly, World Health Organisation (WHO), world leaders of G7 and G20, World Bank (WB), African Union (AU) , European Union (EU); and it is one of the greatest threats to public health requiring urgent global response (1,2,3). It is a trans-boundary problem in which the organisms require no international passport (4). AMR threatens all countries in different ways and to varying extents; and despite scanty information, the data available showed evidence of increasing trends of AMR in the African region and the rest of the world (5, 6). This paper discussed antimicrobial resistance, HS and universal health coverage (UHC), their interactions and the potential of applying the principle of universal health coverage to prevent/ mitigate the problem of AMR (**Figure 1**).

Methods

This paper is a narrative review using searches of peer-reviewed articles published between 1999 and 2020 in databases such as Pubmed, Medline, African Journal online (AJOL), Bioline international, Popline and google scholar; and grey literatures such as reports and research briefs. The words used for search were Africa, Antimicrobial resistance, health systems and universal health coverage.

Results and Discussion

Antimicrobials and antimicrobial resistance

Antimicrobials are drugs used for the treatment of infectious agents such as bacteria, viruses, fungi, parasites and have played prominent role in human and veterinary medicine, agriculture and environment (7). They are global public good which have improved health care, saved lives and enhanced economic gains (8, 9). Antimicrobials are cornerstone on which the HS is standing on, not only for the basic treatment of infections, but also for medical and surgical procedures (10, 11). However, the emergence of resistant microorganisms has compromised their effectiveness (12). AMR is defined as the development of resistance in a microorganism to an antimicrobial agent to which it was previously sensitive (13). Access to quality antibiotics which is a subset of antimicrobials used to treat bacteria is very essential in the treatment and prevention of resistance. In Africa, AMR has been documented to be a problem for HIV and the pathogens that cause tuberculosis (TB), typhoid, meningitis, gonorrhea; Bovine TB, Pseudomonas oryzae and Pseudononas syringae infections (1,14 ,15). Sixty percent of pathogens harmful to humans are of animal origin; humans and animals share the same bacteria (9).

Drivers of antimicrobial resistance

Many factors are contributing to the emergence and spread` of AMR globally and in Africa. These include the overuse and misuse

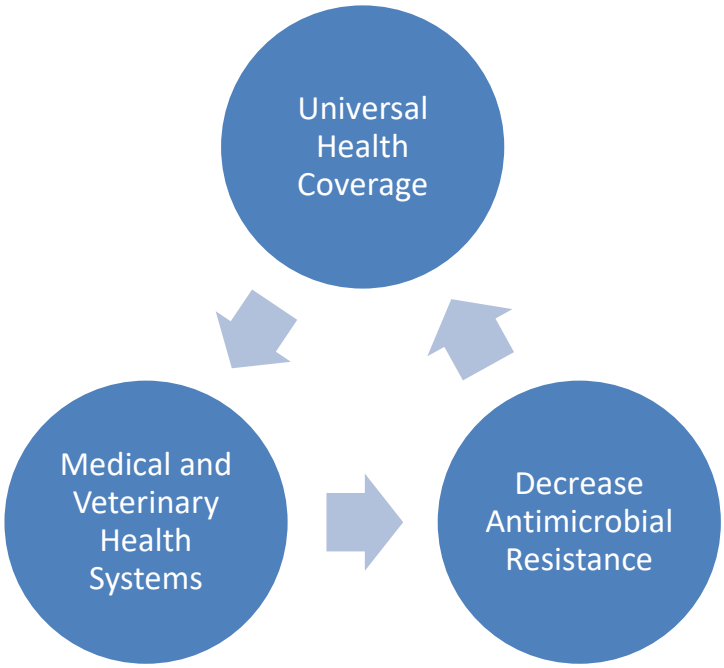

Figure 1: Chart showing the links between universal Health Coverage, Health Systems and Antimicrobial Resistance.

of antimicrobials, sub-optimal infection control, use of antibiotics as massive depot preparation in animal production with no observe of withdrawal periods, antimicrobial agents use for growth promotion in animal husbandry, use of substandard and/ or counterfeit drugs in both medical and veterinary practices, poor capacity to conduct antimicrobial susceptibility testing, among others (1, 16, 17, 18, 19). The transmission of AMR is accelerated by impaired access to potable water, limitations in public health prevention programs such as immunization and sanitation (1). Vaccination of humans and animals is a very effective way to prevent them from becoming infected, thereby reducing the need for antibiotics for the infections that do not have existing vaccines (20). The development of AMR and its spread to other organisms via mobile genetic elements (plasmids and transposons) has been amplified by industrial discharges (pharmaceutical, agricultural) and human wastes contaminating the environment (21). In addition, antimicrobials are used to treat human, animal and plant diseases, depending on the species treated and particular drug used, 10- 80% of the drug used is absorbed or metabolized, while the remainder are excreted as active compounds through urine and faeces into the environment (21). Manure and waste water are used as fertilizers in farms and sub-therapeutic antimicrobials used for treatment can serve as selective forces in AMR emergence (21). Antimicrobial resistant genes and bacteria with resistance to one or more drugs have been detected in surface waters, in soils, in animal feeds and on edible plants globally (21). Food is likely to be quantitatively the most important potential transmission pathway from livestock to humans, although direct evidence linking AMR in humans to food consumption is lacking (22). The use of antibiotics in chicken could cause resistance in humans; and MRSA in animals have been linked with that in humans (23, 24, 25, 26, 27). The globalizations of trade in food products, conventional and medical tourisms facilitate the spread of resistant bacteria (9). Socioeconomic status has also been shown to have an influence on what antibiotic agents are prescribed and association with resistance and the linkages between poverty and AMR (28, 29, 30). Poor people are less likely to seek for medical prescription when indicated and may not afford complete treatment with adequate dose of antimicrobials (30).

The burden of antimicrobial resistance

The economic burden of AMR is difficult to calculate due to insufficient data and the need to account for externalities especially in Africa (31). However, estimates of the impact of AMR on the US economy are exceedingly high, including $20 billion in direct health care costs with additional indirect costs as high as $25 billion, 2 million illnesses and 23000 deaths per year(32). The WB projects that 24 million people could fall into extreme poverty by 2030 because of AMR and most would come from low and middle income countries. Globally, AMR is estimated to account for more than 700,000 deaths per year and if current trends continue, it will cost approximately 10 million lives per year and over US$100 trillion in lost output globally by 2050 (4). It has been estimated that about 4,150,000 deaths will be attributed to AMR in Africa by 2050 (4, 13, 33).The increase in AMR could lead to a reduction in options available to treat infectious diseases, support

chemotherapy, surgery, and this will have a significant impact on the HS and economies (13). Infections with resistant organisms have been associated with increased hospital stay, increased morbidity and mortality, use of additional drugs, laboratory tests and increased treatment cost (34, 35). This has financial implications for the individuals, families, communities and the HS (13). This has increased poverty as it has been documented that millions of Africans fall into poverty due to high out of pocket health payments (36). AMR could lead to loss of productivity from the spread of diseases to other animals and death of the animals, thereby threatening the sustainability and security of food production and the livelihood of farmers.

Drug related causes of AMR and health systems

Poverty has been cited by WHO as a major force driving development of AMR (37). In developing countries factors such as inadequate access to effective drugs, unregulated dispensing and manufacture of antimicrobials related to cost are contributory (37). While in America, poverty-driven practices such as medication-sharing, use of "leftover" antibiotics, the purchase and use of foreign-made drugs of questionable quality are likely contributing to AMR; this has also been reported in Africa (38). In many HS, widespread inappropriate use of antibiotics combined with inadequate access especially for the poor contributes to the problem of AMR (5). Poor collaboration between the human and veterinary/animal health sectors is also a problem. Little data exist about the individual practices of veterinarians in Africa and most antibiotic prescriptions are used during animal production. Veterinary antibiotics can be purchased on the open market just as human antibiotics and the lack of separation of antibiotics used for animals and that for humans, which have negative public health consequences. Lack of stringent penalties on manufacturing and distribution of substandard and counterfeit drugs in Africa is also a challenge (39).

What has been done in response to AMR?

The WHO 2015 Global Action Plan on AMR underscores the need for collaboration between human, animal, food and environmental sectors (7). Also, the WHO 2018 competency framework for health workers' education and training on AMR has four main AMR domains, namely building awareness of AMR, appropriate use of antimicrobials, infection prevention and control and diagnostic stewardship (40). In Africa, the Africa Centre for Disease Control and Prevention (Africa CDC) has established the AMR Surveillance Network (AMRSNET) which is a network of public health institutions and leaders from human and animal health sectors who will collaborate to measure, prevent, and mitigate harms from resistant organisms. AMRSNET's four goals are: improve surveillance of AMR organisms among humans and animals; delay emergence of AMR; limit transmission of AMR and mitigate harm among patients infected with AMR organisms (1). The Tripartite collaboration between WHO, Food and Agricultural Organisation (FAO) and the World Organisation for Animal Health (OIE) has provided critical leadership to foster concerted efforts aimed at combating the threat of AMR at a global level in recent years but remains seriously underresourced (41, 42). Nigeria, being the most populated country in West Africa has to take

the lead in tackling AMR using the 'One Health' approach, which acknowledges the links among humans, animals and the environment as the corner stone of its plan (39). The government has focused on good leadership, multidisciplinary approach, enforcement of regulations, public education and community participation on tackling the growing AMR problem (39).

The medical and veterinary health systems

Health system consists of all organizations, people and actions whose primary intent is to promote, restore or maintain health (43). A good HS should be "STEEEP", namely safe, timely, effective, efficient, equitable and patient-centred. The WHO Health System framework describes HS in terms of six core components or "building blocks", which are leadership/governance, health workforce, financing, service delivery, health information system and access to essential medicine, antibiotics inclusive. Therefore, to preserve antibiotic effectiveness, interventions need to be implemented throughout the whole HS and the whole of society (11).

Universal Health Coverage

Universal Health Coverage which is the access by all who need all basic health care services at a cost that will not expose them to financial hardship. It has the advantage of equity, quality, efficiency, accountability, sustainability and resilience. UHC include financial risk protection, access to essential healthcare services, access to safe, effective, quality and affordable essential medicines and vaccines for all. The role of UHC is vital in order to have access to these essential medicines in Africa in particular, where majority of people pay for healthcare with out-of-pocket expenditure (35, 36). It ensures access by all people, to all quality services at cost not exposing them into financial difficulties, and it is central to improved access to quality drugs e.g. antimicrobials. Financial access is crucial in view of the high poverty level and burden of infectious diseases in Africa (35). An estimated 11 million people become poor each year and one-third of Africans in need of healthcare do not have access because of financial barrier (36, 44). The UHC ensures that every citizen gets at least the minimum health package by the system. Health system could have structured financing mechanism in which the government pays for the people and the one in which the people contribute. However, a pooling financing mechanism (from government or insurance) could help in risk sharing and resources allocation for majority of the citizens. The National Health Insurance Scheme (NHIS) is the best way to finance the HS whereby both government and individual have responsibilities for health and the mechanism gives people better access to healthcare. However, the NHIS in Nigeria mainly captures the formal sector (about 10% of the population) (45). Many countries in the region have 3 key financing sources namely, donor funding, OOP payment and tax-based government financing. OOP payments have increased in nearly all countries, and the regional average has increased from US$15 per capita in 1995 to US$38 in 2014 (36), and OOP spending for health care services in Nigeria is among the highest in the world with 72% [39]. This could lead to poor access to quality healthcare and quality antimicrobial which will result in AMR. Out-of-pocket payment is the simplest financing mechanism, and because it does not ensure equity and financial risk protection, it is universally

agreed to be the worst way to finance HS (46). Here the health services are according to ability to pay not need. The UHC as an approach that is linked to financing mechanism, it has health, political and economic benefits (46), and can provide an ideal platform to manage AMR through adequate provision and rational use of antimicrobials (**Table 1**). The health system attributes and the UHC actions for addressing AMR include equity, quality, efficiency, accountability, sustainability and resilience. Universal Health Coverage can build system governance and coordination capacities that are highly relevant to tackling AMR (47). Government can take informed decisions and wisely allocate health investment in areas such as training of health workers, strengthening of medical and veterinary systems, improved health information, effective infection prevention and control program, vaccines and evidence-based antibiotic stewardship program, research and development (26, 33, 48). For the any UHC to be successful, the relevant stakeholders such as political leaders, community leaders, health professionals, academics, and research institutions, federal and state ministries of health, agriculture, and education and Non-governmental organisations need to work together.

Health Financing

In the Abuja declaration of April 2001, the Heads of States of the AU countries pledged to set the target of at least 15% of the annual budgets to improve the health sector. However, only four countries met the Abuja target of 15 percent of general government spending in 2014. Limited commitment of domestic resources is often reflected in shortages of critical inputs namely- manpower, materials, money and minute (4Ms). Financial protection is generally low in Africa, requiring most patients to pay for health services from their own household income (OOP payments). Out-of-pocket payment for health services predisposes person or families to catastrophic health expenditure and poverty. In addition, it does not allow pooling of resources and risk sharing that is beneficial to the sick persons and government.

Access to essential medicines

Sub-standard and counterfeit antibiotics are widely available in Africa and have a substantial negative impact on the medical and veterinary health systems. They facilitate AMR and worsen case-fatality. Patients with infectious diseases that are not properly treated could develop complications requiring second-line medications that are very expensive; and sometimes may result in poor health outcomes. This can also happen in the veterinary hospitals/clinics. Nigeria is among the 10 countries projected to have increased antibiotics use in veterinary medicine by 2030 (25).

Leadership/governance

Accelerating progress toward UHC in Africa is within reach but will require political leadership and a clear strategic vision (36). The quality of leadership and stewardship varies at all levels of the health sector, from the top positions in the health down to officers' in-charge of hospitals or health centres. Laws and policies play critical roles in framing, enabling, and protecting public health. The AU and Africa CDC have been playing important role. Issues such as regulations for antimicrobials in food and feed, strengthening of anti-

Element of Health Systems	Measures to tackle antimicrobial resistance
Service delivery	-Provision of clean water, sanitation, immunization, infection prevention and control -Facilitate rational drug use through diagnostics and primary health care - increase investment in veterinary services and animal health
Health workforce	-Invest in professional education, training, certification and development as well as regulation of professionals. - Joint scientific meetings and conferences by medical and veterinary professionals and other stakeholders
Health information systems	-Strengthen monitoring and surveillance across networks focusing on laboratories and set standards for diagnostics.
Access to essential medicines	-Ensure antimicrobials are accessible, but not used irrationally. This requires linking access with ensuring responsible use -Use alternatives to antibiotics such as probiotics, prebiotics, organic acids, exogenous enzymes and essential oils among others as growth promoters in animal production
Health financing	-Consider antimicrobial resistance a risk to both the sustainable financing of universal health coverage and the individual's ability to pay for higher cost of treatment -Approach financing of universal health coverage through an antimicrobial resistance-lens -Delink health worker income and profit of companies and institutions from the volume of antimicrobials sold.
Leadership/governance	-Strong political leadership, advocacy and accountability -The impact of antimicrobial resistance goes beyond health care, and systems changes should therefore be applied to the agricultural and environmental sectors - Regulations on antimicrobial use and prevention of infections.

Table 1: Entry-points for integrating AMR into Universal Health Covering using the Health Systems elements (Adapted from reference 43)

microbial policies, engaging civil society organisations and standard treatment guidelines for human, terrestrial and aquatic animals, plants and environment are very crucial (1,41).

Health workforce

Health professionals are the most critical input in the delivery of health services and functioning of any HS. Sufficient human resources with adequate education and skills are needed for AMR surveillance and control in both human and animal health sectors (1). Africa CDC has identified the need to promote stewardship programs to increase the proportions of physicians and veterinarians adhering to prudent antibiotic use guidelines, which will help delay emergence of AMR and improve outcomes among patients already infected with AMR organisms (1).

Service delivery

Health care services should be people-centred, qualitative, target the poor and marginalized, including those in hard-to-reach areas (35) which will improve access to basic services to the majority. However, infrastructure in most government facilities in some African countries is poor; hospital wards, outpatient clinics, health centres and health posts, along with their water and electricity supplies and sanitation are usually in need of repair, renovation or expansion. Enhancing capacity of the health care workers will improve the quality of the health services, better health status of the people and animal and reduced incidence of sickness.

Health information systems

The critical need for timely, relevant and reliable medical and veterinary data to support evidence-based decision making is very important. Evidence based information is required to facilitate behavioural changes on appropriate use of antimicrobials and safeguard human and animal health (41). Health data is very essential for planning, delivery of evidence based health care services, research and tracking of HS (42). Real time and reliable data will help in the planning of the medical and veterinary services, identification of gaps and optimization of services. Updated antibiogram results will help in rational use of antibiotics and reduced misuse, which will decrease the emergence of AMR in medical and veterinary health sectors.

The one health concept

One Health is a collaborative effort of multiple disciplines working locally, nationally, and globally to obtain optional health for people, animals and our environment (47). One health is a public good that has the potential to mitigate the negative externality of AMR (47). The Canadian Science center for Human and Animal Health is the first organization worldwide to house in one facility the laboratory for human and animal diseases research (47). Studies have shown that implementing one health especially in low income countries will save lots of money for the veterinary and medical health systems (49). This money can be used to enhance surveillance and improve capacities in medical and veterinary HS. Surveillance systems are the foundation for a better understanding of the epidemiology of AMR and the key for tackling this public health threat (33, 50).

Conclusion

Universal Health Coverage is an important approach to combat AMR through medical and veterinary HS strengthening as AMR is a threat to social, economic, health and development. Also tackling AMR will require relevant stakeholders and concerted, multi-sectoral and multi-disciplinary approach at global, regional, national and local levels that is sustainable.

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