Feasibility of Combating Antimicrobial Resistance using One Health Approach

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ABSTRACT In recent years, antimicrobial resistance (AMR) has assumed global health importance. Inability of current antimicrobial agents available to treat common and life-threatening infections is gradually pushing humanity to dark ages of post antibiotic era. It is no longer a medical problem since global community considers it as a development and economic issue. The Sustainable Development Goals articulate a commitment to launch well-coordinated multi-sectoral actions to combat AMR. Apart from developing new and affordable antimicrobial agents, which are both expensive and time consuming, the rational and reduced use of antibiotics is also a key element of any strategies to minimize impact of AMR. Huge quantities of antimicrobial agents are used in a veterinary sector, mainly as growth promoters. These are instrumental in giving rise to resistance in pathogens for critically important antimicrobial agents, thus putting human health at grave risk. A comprehensive One Health approach that addresses the use of antimicrobials in humans, animals and environment is the solution to comprehensively address the growing menace of AMR across the world, especially in developing countries.

Introduction

Antimicrobial resistance (AMR) is unresponsive to the standard doses of antimicrobial agents in treatment of a disease. Of late, common and life-threatening infections like pneumonia, gonorrhoea, and post-operative infections, as well as HIV, tuberculosis, and malaria are increasingly becoming untreatable because of AMR. Recognizing the risk posed by burgeoning antimicrobial resistance to the achievement of the ambitious Sustainable Development Goals (SDGs), on 16 September 2016, at the unprecedented session of the United Nations General Assembly (UNGA), world leaders, through a political declaration made a strong commitment to combat, on priority, growing menace of antimicrobial resistance across the world. They advocated taking a broad, coordinated and multi-sectoral approach to address AMR by engaging human health, animal health, environment and agriculture with the broad objective of prolonging the efficacy of currently available antibacterial drugs or antibiotics, as commonly called[1].

The political declaration associated with SDGs[2] articulates sustained action against AMR. It states *"we will equally accelerate the pace of progress made in fighting malaria, HIV/AIDS, tuberculosis, hepatitis, Ebola and other communicable diseases and epidemics, including by addressing growing antimicrobial resistance and the problem of unattended diseases affecting developing countries."*

Spurred by UNGA and SDGs, the countries have also reaffirmed their commitment to develop national action plans on AMR, based on the *"Global Action Plan on Antimicrobial Resistance"* – the blueprint for tackling AMR developed in 2015 by WHO[3] in coordination with the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE). Subsequently, more than 80 countries have developed their respective national action plans to combat AMR and submitted to World Health Assembly before May 2017, but this has just been an easy part. The harder part appears in the efficient implementation of National Action Plan (s). AMR is an extremely complex issue that warrants strong and sustained multi-sectoral approach with active contributions by all stakeholders. It requires sound and solid leadership with sustained funding.

Emergence of AMR as a global challenge

Almost 20 years ago, AMR was considered purely a medical problem. In less than two decades, it has become not only a global health challenge but also a burgeoning economic, developmental and political challenge. It is not involved only intergovernmental agencies like FAO and WHO, where AMR is being talked about, but in the past 2-3 years, various development and political establishments including World Bank, G7, G20, G77, EU, ASEAN, etc. have also expressed their concerns on this issue and articulated commitments to combat it through the efficient coordination and the One Health approach that encompasses humans,

animals and environment. In South-East Asia, ASEAN is expected to come up with a region-specific declaration against AMR in November 2017.

Currently, AMR is estimated to kill around 700,000 people every year. If no concrete actions are taken, the number of annual projected deaths due to infections with resistant pathogens by 2050 shall be a staggering 10 million. This number shall be greater than deaths from cancers and road side accidents put together. Most of these deaths are found in the developing countries. Thus, the global increasing cost in health care would finally be reached at USD 1 trillion[4].

Economic impact of AMR shall be devastating. A loss of USD 100 trillion is projected and the Global GDP shall be pushed down by 3.5%. World Bank estimates that 28 million people are likely to be pushed into poverty as a direct consequence of the diseases caused by resistant pathogens[5] (World Bank report). In addition, global exports will see a decline of 3.8%. Livestock production shall reduce by 7.5% throughout the world thus impacting the food security[5].

Genesis of AMR

Microorganisms in their quest of survival, continuously undergo changes in their genetic apparatus. Some of these genetic changes bring about changes that thwart the action of antibiotics. This is a natural unstoppable phenomenon. However, the resistant strains get selected, and become dominating population subsequent to their interaction with antibiotics. Greater is the selection if quantity of antibiotics is big and application is irrational. Prolonged misuse, abuse and overuse of antibiotics select resistant pathogens and provide them a survival and proliferation advantage. It is now obvious that the excessive use of antibiotics, in any settings, is the biggest driver of AMR. While extensive use of antibiotics in the health sector is well known, much more antibiotics are globally used in the veterinary sector than in the human sector. It has been estimated that, while in 2010, more than 63,000 tonnes of antibiotics were used in animals, it is expected that this number would exceed 100,000 tonnes by 2030 indicating a 63% increase[6]. Against a use of 3.3 million kilograms (kg) of antibiotics in humans in the United States of America, more than 8.9 million kg is consumed in animals every year[7].

Antibiotics consumption in animals is not limited to their therapeutic use. These are used for metaphylaxis (Administration of antimicrobials to animals when perceived to be in contact with animals diagnosed with disease), prophylaxis (Mass administration of antimicrobials to animals to prevent disease when risk is established) and for growth promotion (Administration of antimicrobials to animals to boost feed efficiency and increase weight gain). Global data shows that maximum consumption of antibiotics in the animal health sector is for the growth promotion of animals by various mechanisms including mixing with animal feed. This is primarily to meet the growing demand of protein-rich food in countries where their economy is growing that leads to a higher demand of nutritious food of animal origin. FAO has demonstrated this gradual but sustained growth in meat production (Fig 1).
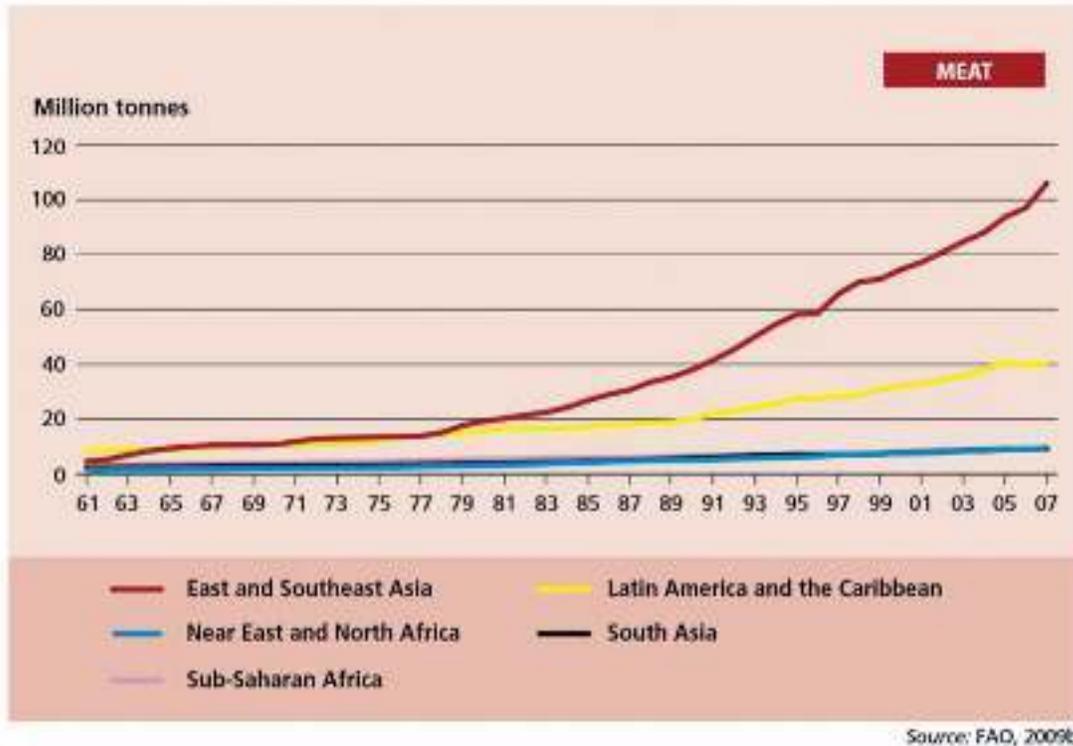
Fig. 1   Exponential increase in meat production in different regions of the world

This increase is matched with an increase in the consumption of antibiotics in several developing countries and shall reach almost 100% in Brazil, India, Russia, China and South Africa (BRICS countries) in next two decades[6].

Impact of AMR in animals is a serious human health risk

Several antibiotics commonly used to treat human infections are, in contrast, not necessary for animals. WHO has classified few antibiotics as critically important antibiotics (CIA). These include the 3rd and above generations of cephalosporins, glycopeptides, polymyxin, macrolides, and quinolones. Since humans and animals share several pathogens, emergence and proliferation of resistant pathogens, the animal community thus reaches humans through food, direct contact and environment. Some of these pathogens demonstrate resistance to the last resort antibiotics in life threatening human infections. Emergence of transferable colistin (one of the CIAs) resistance in *Enterobacteriaceae* is a result of the extensive use of this antibiotic in pigs-rearing in China. The resistance is firstly reported in 2016[8] and has been found by CDDEP spreading to many countries in different parts of the world (Fig 2). This implies a serious warning to protect global health by restricting or phasing out use of such critical drugs. The extensive use of such antibiotics in organized poultry farms in India has also been recently shown to culminate in the emergence of widespread resistance to several pathogens[9].
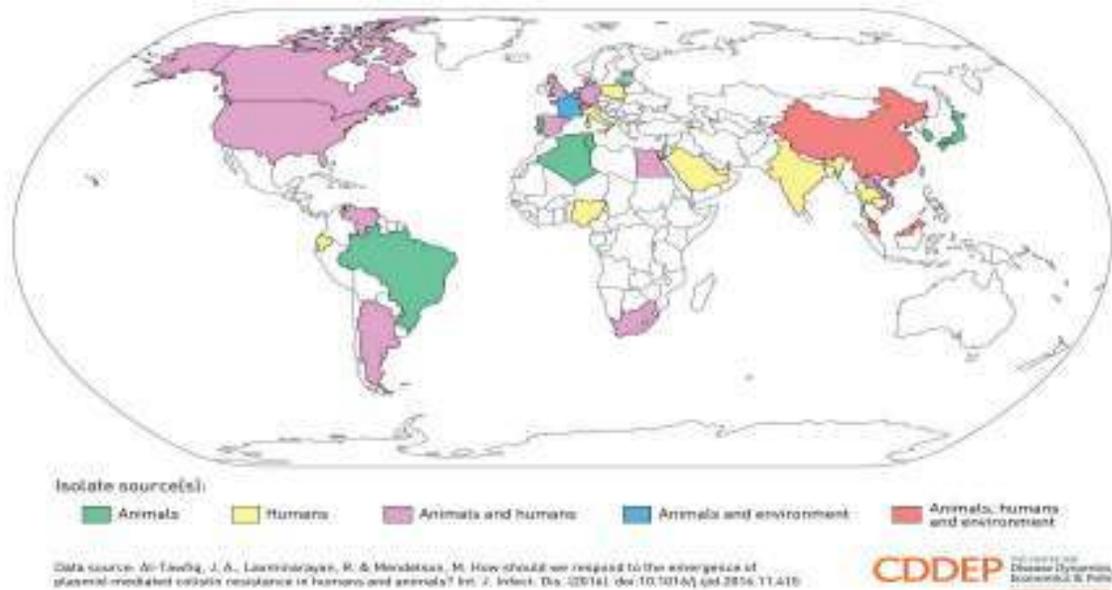
Fig. 2 Countries reporting plasmid-mediated colistin resistance encoded by *mcr-1* (Source: CDDEP)

Combating AMR-multi-sectoral one health approach

Combating AMR has a common-sense approach with following four key components

1. Discover new drugs faster than emergence of resistance

2. Rationalize the use of available antimicrobial agents

3. Prevent emergence of resistance by reducing selection pressure with appropriate control measures including infection control

4. Reduce disease burden

Discovery of new antibiotics is a time consuming and expensive proposition with an estimated investment of USD 1 billion over a period of 10-12 years. The final product, if used irrationally, shall soon become ineffective to treat infections. This has deterred many manufacturers from venturing into this endeavor. Reduction in disease burden and implementing infection control measures (in both human and animal settings) are also important measures to prevent AMR.

Owing to the fact that antibiotics use is the greatest driver of AMR, all efforts need to be made to reduce and rationalize the use of antibiotics in all settings especially for the growth promotion in the animals. Accordingly, all global commitments have advocated the use of One Health approach.

One Health approach recognizes the interdependence of humans, animals and envi-ronment especially for human health. It also recognizes that co-existence of animals, humans

and environment is essential. It indicates that the improvement of human health likely depends on animal health and safe environment. It is well established that 60% of all existing human infectious diseases are zoonotic. At least 75% of emerging infectious diseases in humans (including Ebola, influenza, MERS CoV etc.) have animal origins, and 80% of the agents with potential bioterrorist use are zoonotic pathogens. Unrestricted use of antibiotics in animals is a critical factor that promotes AMR.

Elements for implementation of One Health

Implementation of One Health requires several key elements with few salient activities, as shown in Table 1.

Table 1   Key elements and activities for implementation of One Health approach

Key element	Activities
Policies	Program & Person
	Legislations
	Regulations
Institutions	Joint Planning
	Strategies
	Operational Plan
Individuals	Awareness
	Advocacy
	Participation

National efforts to implement One Health approach shall warrant having national commitment in the form of adequately funded policies which can be translated into efficient programmes, run by skilled human resource through legislative approach and enforceable regulations. The planning for the activities has to be jointly undertaken by all the sectors (human, animal and environment) and based upon practical strategies that should be converted into an operational action plan. Community participation and support to this programme are essential. Efficient implementation of this approach shall result in not only an improved human health but also a safe environment and food security.

AMR containment is currently high on national and international political, development, economic and health agendas. Drug resistance is a key global issue. While addressing issue of AMR through a One Health approach, it is certain that various other components of One Health will also be benefitted. Multi-sectoral approach is, thus, the ultimate key to combat this burgeoning problem.[10]

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