Antimicrobial Resistance in India: The Road Ahead

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Abstract

Antimicrobial resistance (AMR) is a global public health challenge, requiring immediate actionable strategies to prevent the next pandemic due to untreatable multi- and pan-resistant microorganisms. The antibiotic overuse and misuse with poor infection prevention and control are the major reasons for accelerated resistance to antimicrobials. The problem of AMR is widespread across humans, plants, food, animals, and environment and does not recognize any geographic

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borders. AMR is like a ticking time bomb that requires urgent, comprehensive, coordinated, collaborative actions between human health, animal health, and environment sectors based on "One Health approach" for deferring this disaster.

In recognition of this crisis, the Global Action Plan on AMR was developed and endorsed by the 68th World Health Assembly in 2015, followed by adoption by other international bodies. In alignment with the global action plan, India developed its National Action Plan on AMR (NAP-AMR) in 2017. The NAP-AMR is a comprehensive plan that addresses the strategies and priorities for AMR containment across all sectors encompassing all dimensions of antibiotic use and disposal. Several initiatives have been undertaken to implement NAP-AMR, but the gains have yet not been consolidated due to highly complex and competing national priorities. The plan is highly resource intensive and requires integrated, cohesive governance between human, animal health, and environment to bring out any perceivable change.

Keywords

Antimicrobial resistance · Global action plan · National action plan · One health approach · Antibiotics

1 Introduction

Antimicrobial resistance (AMR) is a phenomenon in which microorganisms stop responding to antimicrobial agents (antibiotics) intended to inhibit/kill them. Antibiotics are meant to kill microbes, and microbes fight back to evade antibiotics by different strategies and in due course become tolerant/resistant to the effect of antibiotics. Resistance to antibiotics is not only restricted to the older and much more frequently used antibiotic classes, but the resistance is increasing at alarming rates among the newer and more expensive drugs like carbapenems and colistin. Available data indicate alarming rates of AMR across multiple pathogens of clinical importance with almost one fourth of all isolates studied in India being resistant to multiple antibiotics (World Health Organization, 2020; Laxminarayan & Chaudhury, 2016). AMR is an equally devastating threat with much higher magnitudes and almost similar patterns of resistance in animal population due to higher animal biomass (Van Boeckel et al., 2019). Antibiotic residues, AMR pathogens, and resistant genes from humans, food-producing animals, agriculture use, and from pharmaceutical manufacturing units find their way into the environment through sewage, hospital wastewater, rivers, and surface and ground waters (Pareek et al., 2015). This leads to antibiotic pollution with AMR pathogens/genes seeding into environment, and subsequent recycling in food chain (Pareek et al., 2015).

AMR is a natural biological unstoppable phenomenon directly linked to antibiotic use and misuse. Resistance in microorganisms does not occur suddenly. It is the outcome of long-time misuse of antibiotics in different settings. Accumulation of resistance in one bacterium over the period makes it multidrug-resistant organism

(MDR) or as is called as "superbug" in layman term. Cross-resistance against other antibiotics and metals provides greater lethality to the microorganisms. The detection of superbugs or MDR pathogens reflects just the tip of the iceberg, consequential to long-term neglect of rational use of antibiotics in various sectors. All antibiotics have the potential to select drug-resistant bacterial populations with varying frequencies depending upon class of antibiotic, dose administered, and the bacterial strain specificities. Not only overuse but underuse of antibiotics due to lack of access in many settings is also a perpetuator for AMR. Once developed, AMR is largely irreversible or may reverse very slowly to susceptibility status if antibiotic use is withheld for a very long time.

AMR is a complex problem. It is not only a technical challenge but has several other dimensions. It is a regulatory issue, an educational problem, has behavioral dimension, and carries huge economic and social impact. It needs a multiprong attack. Engagement and ownership of all sectors with "One Health approach" is essential to address this challenge.

2 AMR: A Global Public Health and Economic Challenge

AMR is a global problem as infections caused by the antibiotic-resistant pathogens are much more difficult to treat than those caused by antibiotic-susceptible pathogens and result in increased morbidity, longer stay in hospitals, and forced use of expensive diagnostic tests/toxic drugs. These infections are also associated with worst clinical outcomes and consume much more healthcare resources (Table 1).

Global estimated mortality data due to AMR have emerged, but developing country-specific information on mortality, morbidity, and economic losses is yet not available. Among Asian countries, in Thailand alone, more than 38,000 people are being killed annually by antibiotic-resistant pathogens with a loss of US$ 1.3 billion/year (Thamlikitkul et al., 2015). It is estimated that globally ~ten million deaths will occur annually with a cumulative loss of US$ 100 trillion to the global economy by 2050 (O'Neill, 2014). The O'Neill report has also highlighted the impact of AMR on human development, including deaths, hospitalization, and

Table 1 Impact of antimicrobial resistance on human health

Longer illness
Longer treatment duration
Higher mortality
Treatment with expensive drugs
Greater use of diagnostics
Increased burden on health system
Nullify technological advances
Transmission of drug-resistant organisms in community
Impact on economy and global human development

food security (O'Neill, 2014). In one world, a catastrophe is waiting to happen because of our inactions.

Unfortunately, this war is increasingly being won by the resistant pathogen and the world is now approaching a "post-antibiotic era" where humanity will not be able to manage even small wounds and infectious diseases will again become major killers. The well-established and life-saving advances in complex medical surgeries, viz., transplantation, cardiac repairs, etc., shall be negated because of the post-surgery untreatable infections due to resistant pathogens.

Post-antibiotic era is not far ahead at the current pace of pan-resistant microorganisms spreading across the globe and not many new antimicrobials are likely to be developed in near future due to their cost, low return on investment, short shelf life, and long development period (Bhatia & Walia, 2017; Bhatia & Narain, 2010).

It is well known that the development of a new antibiotic class will take an investment of more than US$ 1 billion over a time span of more than a decade. These efforts do not ensure appropriate return on investment because of rapid emergence of resistance. According to a World Bank report, AMR shall be responsible for a fall of up to 3.5% in global exports, with diminishing of livestock production by 7.5% and likewise an increase in healthcare-related costs of US$ 1 trillion by 2050. If left uncontrolled, AMR shall push 28 million people into poverty (The World Bank, 2016).

Global leaders and leading inter-country organizations (FAO, WOAH, WHO, UNEP, OECD, G7, G20, G77, ASEAN, etc.) have recognized that AMR has serious implications not only on human health but more so on economy, food security, and a serious negating influencer for overall human development (WHO, 2016).

3 Key Drivers of AMR

Extensive, irrational, and indiscriminate use of antibiotics is the biggest driver of AMR, and this common thread for the emergence of AMR pathogens runs across various sectors. Antimicrobial use is in turn dependent on sanitation, hygiene, access to clean water, vaccination coverage, and quality healthcare services (CDDEP et al., 2021). Prevalence of AMR pathogens varies depending upon levels and volumes of the antimicrobials consumed in humans, animals, and environment.

Antimicrobials are inappropriately consumed in human health not only for treatment of infections but also for prophylaxis, treatment of self-limited, and noninfective diseases both in community settings and hospital-admitted patients (Versporten et al., 2018; Center for Disease Dynamics, Economics, & Policy et al., 2021). Antibiotics are prescribed without adhering to standard treatment guidelines and a large number of factors like high patient attendance (resulting in less counseling time for appropriate antibiotics use), unjustified patient demand, lack of diagnostics, poor sanitation, hygiene and infection control practices, fear of losing patients, unethical practices, and not keeping pace with advances in antibiotic prescribing practices are main factors for irrational prescribing practices. Self-medication, over-the-counter availability of antibiotics,dispensing by pharmacies and registered medical practitioners, and easy access to higher generation antibiotics,

broad-spectrum antibiotics and irrational antibiotic fixed-dose combinations, sub-standard antibiotics, also contribute to overuse of these precious molecules and thus emergence of AMR (Morgan et al., 2011; Laxminarayan & Chaudhury, 2016).

All classes of antimicrobials important for human medicine are used in much larger quantities in animals in veterinary practices and animal husbandry and factors driving antibiotic use in animals are more or less similar to human use. Antimicrobial agents are also extensively used in otherwise healthy livestock and poultry to overcome the issues of inadequate biosecurity and sanitation in farms and provide prophylaxis to animals against infectious diseases that may either kill them or stunt their growth (Klein et al., 2018). Besides, antimicrobials are added in low doses for growth promotionand improved feed conversion efficiency to promote faster growth in food animals (Van Boeckel et al., 2019). The use of antimicrobial agents as growth promoters has been successfully discontinued in Western countries. It still continues as a major intervention in developing nations where it is considered a cheap alternative to an improved biosecurity system. In India, economic prosperity and population growth have resulted in increased demand for animal protein with a massive increase in egg and broiler production, resulting in over-reliance on indiscriminate antibiotic use as a growth promoter in farms (Ministry of Animal Agriculture and Farmers welfare, 2018). Fish production systems have also become much more intensive to meet the growing demand with India becoming the largest producers of aquaculture products globally, along with China and Vietnam (Bostock et al., 2010). In parallel to increased demand of food/food products of animal origin, antibiotic consumption has also doubled between 2000 and 2015 in animals in India (Klein et al., 2018).

4 Responding to AMR Threat

In 2015, 68th World Health Assembly (WHA) endorsed the global action plan to tackle AMR (including antibiotic resistance) as the most urgent response to spiraling drug resistance trends (WHO, 2015). The goal of the global action plan (GAP-AMR) is to ensure successful prevention and treatment of infectious diseases as long as possible, with effective and safe quality-assured medicines used in a responsible way, and accessible to all those who need them. The WHA resolution 68.7 has also set a target that all WHO member states should develop respective National Action Plans on AMR (NAP-AMR), aligned to the principles outlined in the GAP-AMR by May 2017. International development partners, mainly the World Health Organization (WHO), World Organisation for Animal Health (WOAH), and the Food and Agriculture Organization of the United Nations (FAO), also recognized AMR as the top priority on their respective agendas and called all its member states to develop their nation-specific action plans to combat AMR within 2 years (WHO, 2015; World Organization for Animal Health, 2015; Food and Agriculture Organization of the United Nations, 2015). United Nations General Assembly in September 2016, in an unprecedented special session, recognized AMR as an immediate challenge and called for commitment by global leaders toward an aggressive and highly coordinated intercountry, multisectoral “One Health approach” (WHO, 2016).

4.1 One Health Approach

One Health is a simple, validated, powerful, integrated, and holistic approach advocated by the WHO, WOAH, and FAO, where human health, animal health, and environment sectors work together in a coordinated way to prevent the emergence of AMR and its spread (WHO, 2015; World Organization for Animal Health, 2015; FAO, 2015). To advocate the use of "One Health approach" in national health programs and provide guidance on its implementation, a tripartite agreement between these three organizations has been in vogue since 2010 (WHO, 2017a). The key elements of the implementation framework for One Health approach for AMR are shown in (Table 2). FAO in 2020 has developed a national framework to implement One Health to assist countries in initiating the implementation of One Health activities for AMR as well as the growing challenge of zoonoses.

It is crucial to bring about a change in the narrative in national response to zoonoses, improving food security and ensuring environmental integrity so that AMR can be effectively countered. The success of "One Health" is quite unlikely if it remains a purely governmental endeavor. Awareness, engagement, and active participation of individuals and civil societies shall augur well for its success (Bhatia et al., 2019; Bhatia, 2019). The engagement of top political leadership and the international development partners with intersectoral collaboration is essential to accomplish the benefits (Bhatia, 2019).

5 AMR Containment in India

Efforts for AMR containment in India started taking shape in 2010 with the establishment of National Task Force for AMR Containment with enactment of National Policy on containment of AMR in 2011 (Ministry of Health and Family Welfare, 2011). "Jaipur Declaration on AMR," which calls for comprehensive action against the irrational use of antibiotics, was adopted in September 2011 by India, along with the health minister of all member states of the WHO South-East Asia

Table 2 Key elements of implementation framework for One Health approach for AMR

Political commitment
Policy formulation
Sustainable financing
Program development
Knowledge sharing
Institutional collaboration
Capacity enhancement
Engagement of civil society
Active participation of the communities

Adapted from Food and Agriculture Organization, National Framework for One Health, New Delhi, 2021

Region WHO, 2011). The "National Programme on Containment of Antimicrobial Resistance" was launched under the 12th five-year plan (2012–2017) with the aim to regulate antimicrobials usage in humans and animals with requisite labeling requirements in food, along with the establishment of a laboratory-based surveillance system in the country (National Centre for Disease Control, 2012).

5.1 National Action Plan on AMR, India

AMR has been identified as a national priority by the Government of India, and the customized National Action Plan on AMR (NAP-AMR) was developed in 2017 in alignment with GAP-AMR (MoHFW, 2017). The NAP-AMR is built on an efficient multisectoral, multidisciplinary, and multipronged "One Health approach" incorporating strategic activities for human health, animal health, and environment sectors with the ultimate aim of combating AMR for global health security. NAP-AMR aims to reduce the impact of AMR in India by establishing and strengthening governance mechanisms and enhancing capacity of all stakeholders to work toward combating AMR.

The plan incorporates six strategic priorities, out of which five are aligned with the Global Action Plan on AMR and the sixth priority highlights India's leadership, commitment, and collaborations at the international level to implement AMR containment at the ground level. (Table 3) outlines the six strategic priorities outlined in NAP-AMR (MoHFW, 2017).

Each of the strategic priorities with defined focus areas is briefly discussed below.

5.1.1 Strategic Priorities

Priority 1

This strategy focuses on improving awareness and understanding of AMR through effective communication, education, and training, and has two focus areas:

1. To raise awareness among all stakeholders through information, education, and communication
2. Education and training to improve the knowledge and behavior of professionals in all sectors

Table 3 Strategic priorities under India's NAP-AMR (2017–2021)

To improve awareness and understanding of AMR through effective communication, education, and training
To strengthen knowledge and evidence through surveillance of AMR
To reduce the incidence of infection through effective infection prevention and control
To optimize the use of antimicrobial agents
To promote investments in AMR activities, research, and innovations
To strengthen India's leadership in AMR through international collaborations

Adapted from National Action Plan on Antimicrobial Resistance, MoHFW, 2017

This strategic priority aims to increase awareness among the users and providers regarding the emergence of AMR due to unnecessary antibiotic use and its socio-economic impacts. The first and foremost requirement before implementing any communication program is to understand and assess the level ofunderstanding and knowledge about the antibiotic use and AMR among the general public and other stakeholders to design comprehensive programs.

Besides improving general awareness, there is an urgent need for rigorous, regular, restructured, standardized education and training programs specifically tailored for policymakers, regulators, doctors, nurses, pharmacists, veterinarians, animal farmers, agriculturists, and environmentalists for upgradation of their knowledge, skill, and aptitude regarding the use of antibiotics.The plan envisages revision of curriculums in schools, colleges, and medical and veterinary schools with incorporation of basic and advanced learning about antibiotics and AMR. In addition to training, deep insight and brainstorming are required to bring in human factor engineering to inculcate sustained behavior modification for effective implementation of correct practices.

Priority 2

This priority focuses on strengthening knowledge and evidence through surveillance and has two focus areas:

1. Strengthening laboratories in human, animal, food, and environment sectors
2. Ensuring surveillance of AMR in human, animal, food, and environment sectors

Generation of quality-assured microbiology data to understand the trends in pathogens implicated and antibiotic susceptibility patterns is of paramount importance to design evidence-based interventions to combat AMR. This priority aims to strengthen the microbiology laboratories for pathogen identification and antimicrobial susceptibility testing with generation of robust quality-assured surveillance data in humans, animals, food, and environment (in wastewaters generated from healthcare settings, factories, and farms). The plan also envisages collection, compilation, analysis, and information management of AMR surveillance data in a standardized and coordinated manner at central, state, and district levels across all sectors.

Priority 3

Strategic priority 3 focuses on reducing the incidence and spread of infections by improving sanitation, hygiene, and infection prevention and control in

1. Healthcare
2. Animal health
3. Community and environment

This priority aims to promote sanitation, hygiene, and infection control practices in healthcare, veterinary practices, animal husbandry, dairying, aquaculture, food,

environment, and community to reduce the transmission of infections. Simple evidence-based interventions in the form of hand hygiene, biosecurity, and cleanliness drives can play an unparalleled role in reducing the spread of infections, thereby decreasing antibiotic use and emergence and spread of drug-resistant pathogens.

Priority 4

This priority focuses on optimizing the use of antimicrobial agents in health, animals, and food by

1. Strengthening regulations, ensuring access, and surveillance of antimicrobial use
2. Antimicrobial stewardship in healthcare
3. Antimicrobial stewardship in animal health and agriculture

Antibiotic use is the key driver for AMR, and this strategic priority focuses on optimizing antibiotic use based on evidence-based treatment guidelines and locally generated antibiograms in all sectors using antimicrobials in any form. Developing and strengthening the regulatory framework for rationalized antibiotic use for humans, animals, and food industries with enforcement of regulations and standards for preventing environmental contamination from waste effluents is critical to reduce the spread of antibiotic-resistant pathogens/genes. Ensuring uninterrupted access to quality-assured antimicrobials wherever indicated is an equally important prerogative for effective timely treatment and control of infection transmission. Surveillance of antimicrobial use with measurement of total antibiotic use/consumption, patterns, and rationality of antibiotic use allows for tracking and comparison of consumption statistics across different settings with designing interventions to regulate irrational prescribing.

Antimicrobial stewardship programs in healthcare facilities, animal facilities, agriculture, and food processing units are essential to ensure safe, effective, economic, and rational use of antimicrobials to reduce with increased life span of existing antibiotics.

Priority 5

This priority aims to promote investments in AMR activities, research, and innovations through

1. New medicines and diagnostics
2. Innovations to develop alternative approaches to manage infectious diseases
3. Sustainable financing to ensure adequate resources for containment of AMR

The focus of this strategy is to promote operational research and support innovations to find implementable solutions to contain AMR across human, veterinary, and environment sectors. The thrust is to identify research priorities and innovations for new antibiotics, alternatives to antibiotics, vaccines, new diagnostic modalities, and novel infection prevention and control remedies in human and animal health to tackle AMR. Identification of financial implications with resource mobilization for

sustained funding for AMR interventions is foremost for continued research, innovations, and implementations of interventions in all sectors.

Priority 6
This strategy focuses on strengthening India's leadership in AMR through

1. International collaborations
2. National collaborations
3. State-level collaborations

The prime focus of this strategy is to promote India's leadership and commitment through inter−/intra-country collaboration and coordination for AMR-related activities. Strengthening of national collaborations integrated with vertical disease control programs and implementation of action plan at ground level by development of state action plan is the ultimate requirement.

Implementation of NAP-AMR requires the establishment of relevant governance mechanisms with clear lines of accountability to strategize the outcomes across all settings. Stringent monitoring using descriptive, qualitative, and quantitative metrics for outcome measures is critical for the evaluation of the initiatives undertaken.

5.1.2 Initiatives under NAP-AMR, India

The major initiatives that have been undertaken under NAP-AMR toward combating AMR are summarized below.

5.2 Awareness, Education, and Training

Campaigns to raise awareness about antibiotic use and harms resulting from the misuse of antibiotics have gained momentum with sensitization of general public and school children amalgamated with the "World Antibiotic Awareness Week," which is observed every November (World antibiotic awareness week, 2019). Mass media campaign to raise awareness about Swachh Bharat Abhiyan initiative, redline campaign to identify drugs that need dispensing against a prescription from a licensed doctor, and prime minister radio address in Mann ki baat on faulty and unnecessary antibiotic use have provided a kick start to the program (Swachh Bharat Mission, 2014).

Customized education and training programs have gained impetus with the development and dissemination of guidelines, and standard operative procedures on various aspects of AMR, by the National Centre for Disease Control (NCDC), Indian Council of Medical Research (ICMR), Indian Network for Fisheries and Animal Antimicrobial Resistance (INFAAR) based on World Health Organization (WHO), and Centre for Disease Prevention and Control (CDC) guidelines. Capacity building through offline and online training programs has gained impetus for rational prescribing practices, basic identification and susceptibility testing in bacteriology, surveillance of antibiotic consumption and AMR, quality assurance, data capture,

and data management by several national-and state-level professional bodies and civil societies.

5.3 Strengthen Knowledge and Evidence Through Surveillance of AMR

AMR surveillance networks have been established and progressively strengthened with hand-holding of participating laboratories to generate quality data to determine the magnitude and trends of AMR for priority bacterial pathogens in both human and animal sectors.

ICMR and NCDC have started AMR surveillance networks to capture AMR data of priority pathogens. These organizations are supporting teaching and training programs, and development of resources (standard operating procedures) for isolation and antimicrobial susceptibility testing besides supporting laboratory infrastructure.

ICMR initiated the Antimicrobial Resistance Surveillance Research Network (AMRSN) in 2013 to generate a nationally representative reliable data on AMR to guide treatment strategies and rationalize AMSP in India (ICMR, 2013). The network started with six reference labs located in four tertiary care medical institutions each for 6 priority pathogens and 16 regional centers in tertiary care hospitals. The NCDC also initiated a National AMR Surveillance Network in 2017 for capturing AMR, which currently has around 29 sites across the country. The NCDC network sites have also started capturing AMU data. The NCDC as the national coordinating center for AMR surveillance is reporting aggregated AMR surveillance data to the Global Antimicrobial Surveillance System (GLASS) to contribute toward global understanding of the AMR trends (WHO, 2020).

INFAAR was established and operationalized as a joint Indian Council of Agricultural Research (ICAR) and FAO's initiative to generate structured, quality data on AMR in fisheries and animal health sector in order to strengthen knowledge and better understanding of AMR (FAO, 2017). The network has been expanded to include a total of 18 ICAR and 3 university members. ICAR-National Institute of Veterinary Epidemiology and Disease Informatics, Bengaluru (NIVEDI), is responsible for coordinating the overall technical and data management operations of the network, and ICAR-National Bureau of Fish Genetic Research, Lucknow (ICAR-NBFGR), collaborates with ICAR-NIVEDI in coordinating technical activities of labs from fishery sector.

5.4 Infection Prevention and Control

Initiatives like Swachh Bharat Abhiyan and Kayakalp award scheme have accelerated the efforts toward universal sanitation with safe management of solid and liquid waste across the entire nation with equivalent focus at the community and healthcare level (Swachh Bharat Mission, 2014; MoHFW, 2015). Sustained IPC activities have been recognized as a core component toward certification of health facilities by

many international and national healthcare organizations like Joint commission International (JCI), National Accreditation Board of Hospitals (NABH), and National Quality Assurance Systems (NQAS). Hand hygiene day is observed nationwide on 5 May every year as the most effective infection prevention method.

National guidelines for infection prevention and control in healthcare facilities, implementation manuals, and assessment frameworks have come into existence for effective dissemination of knowledge and translation at ground level (MoHFW, 2020). National Patient Safety Implementation Framework has also identified infection prevention and control as a strategic priority for patient safety (MoHFW, 2018–2025).

ICMR-AIIMS HAI surveillance, India, network has come into existence with the involvement of ~40 sites pan India to strengthen the national capacity for surveillance of HAIs.This network aims to develop trained workforce by strengthening HAI surveillance using standardized criteria, along with the generation of reliable AMR data (HAI surveillance, India, 2020).

5.5 Optimizing Antibiotic Use

Antimicrobial stewardship has been recognized by ICMR and NCDC as the backbone for optimizing antibiotic use and combating AMR. Treatment guidelines for antimicrobial use in common clinical syndromes and National Treatment Guidelines for Antimicrobial Use in Infectious Diseases have been released by ICMR and NCDC, respectively, to streamline antibiotic prescribing practices (ICMR, 2017; MoHFW, 2016). WHO has updated and published Critically Important Antimicrobials list (CIA) for human medicine (sixth revision, 2018) and Essential Medicines List (20th Edition, 2017) with categorization of antibiotics into Access, Watch and Reserve category (AWaRe) to improve the quality of antibiotic prescribing based on indications for use and potential for resistance development (WHO, 2017b, 2018). National Essential Diagnostics List with access to diagnostic tests from primary healthcare to district level has been rolled out and is being implemented toward integration of diagnostic stewardship with AMS activities (ICMR, 2019).

Measurement of antimicrobial consumption (AMC) using standardized tools is essential to design any AMS intervention.World Health Organization (WHO) Defined Daily Dose (DDD) methodology is an aggregate method to capture antimicrobial consumption and allow comparison within and across the facilities.Capacity building for AMC estimation has begun. National workshops on surveillance of antibiotic consumption are being organized for laboratories enrolled in NCDC Network across India with attempts to integrate antimicrobial use with AMR to establish a relationship of antimicrobial use with resistance.

Several regulations have been strengthened to streamline antimicrobial prescribing in humans, animals, and food industry. Schedule H1 came into existence to check over-the-counter indiscriminate use of 47 drugs, including several antimicrobials. The Food Safety and Standards Authority of India (FSSAI) under Food Safety and Standards (contaminants, toxins, and residues) Regulations 2011 laid the (a) limit of antibiotic and other pharmacologically active substances in the fish and

fisheries products; (b) antibiotics prohibited in fish farming system with (c) antibiotics limits in honey (FSSAI, 2011). Besides, a recent amendment (March 29, 2019) in the 2011 regulation has also specified the tolerance limits for 43 antibiotics and veterinary drugs for foods of animal origin (FSSAI, 2019). Also, the Bureau of Indian Standards 2007 laid the poultry feed specification with the prohibition of systemic use of antibiotics like chloramphenicol, doxycycline, tetracycline, nitrofuran, and furazolidone as food additives for growth promotion. Drugs and Cosmetics Rules, 1945, 2013, lay down the requirement of labeling the medicine container for the treatment of food-producing animals with the withdrawal period of the drug. The Central Pollution Control Board has recently drafted standards for antibiotic residues in pharmaceutical industrial effluent and common effluent treatment plants.

5.6 Investments in AMR Activities, Research, and Innovations

WHO published a list of priority pathogens for which new antibiotics are urgently needed, and the Indian Priority Pathogen List aligned with WHO global priority pathogen list has been released under DBT's Mission AMR to guide research, discovery, and development of new antibiotics (WHO, 2017©). Global Antibiotic Research and Development partnership (GARDp) in collaboration with WHO was launched in May 2016 to address global public health and needs of LMICs to target products that industries are not likely to develop to ensure new antibiotics are affordable to all and pilot use of alternative incentive models with delinking the cost of research and development from volume-based sales and prices.

5.7 Collaborations

The essence of One Health is coordination, collaboration, and communication between several stakeholders to plan and work together to achieve the shared objectives of combating AMR. Health is a state subject under the Indian Constitution, and all states and UTs need to develop their own state action plan on AMR depending on their situation and challenges in coordination and collaboration with all stakeholders. Kerala, followed by Madhya Pradesh and Delhi, has rolled out its state action plan and is striving to roll out operational plans to implement it at ground level.

5.7.1 Barriers to Implementation

Although attempts are ongoing for the implementation of NAP-AMR, in India but the gains have not been perceptive due to many barriers that are more or less alike in several developing countries because of its complexities and various competing national priorities.

Some of the barriers hampering implementation (Bhatia, 2018a; Queenan et al., 2017) include long-time ingrained practices of silo and sector-specific approaches

Table 4 Barriers to the implementation of One Health approach

Financial constraints
Disintegrated governance between human, animal health, and environment
Ambiguity about the concept and scope of one health approach
Underestimation of economic benefits
Discordance between professional on ways ahead
Inadequate training and capacity-building activities

with disintegrated governance between human, animal health, and environment. Besides, there is ambiguity about the concept and scope of "One Health approach," underestimation of its economic benefits, discordance between professionals on ways ahead, inadequate training, and behavior modification initiatives (Table 4).

6 Way Forward: AMR and Universal Health Coverage

It is evident that a resource-intensive stand-alone AMR containment program shall not be feasible in contemporary times. One of the possible alternatives is to pillion-ride another approach/program, which is already a national priority. One such endeavor and possible entry point for AMR plan implementation may be synchronizing it with Universal Health Coverage (UHC) by 2030, which has already been recognized as a sustainable development goal (United Nations General Assembly, 2012; Sustainable Development Goals, 2015).

UHC can provide an ideal enabling platform since it can support several sensitive and specific AMR interventions (Bhatia, 2018b; Tayler et al., 2019). UHC is the aspiration that all people obtain quality promotive, preventive, curative (including treatment of infections), rehabilitative, and palliative healthcare without suffering financial austerity. AMR containment program also aims at ensuring the prevention and treatment of infectious diseases with efficacious, quality-assured medicines easily accessible to those who need them. Both initiatives have to run in unison with an objective to bring equity, quality, efficiency, accountability, sustainability, and resilience in order to strengthen the health system. Integration of UHC and AMR by national governments and key stakeholders carries a tremendous potential to enhance economic growth and in turn neutralizing the major impact of AMR of pushing people into avoidable poverty (WHO, 2018).

7 Conclusion

AMR is not only a patient-oriented issue but is the biggest threat to the control of infectious diseases faced alike by the developed and developing world (Bhatia, 2018a). The unjustified, inappropriate antibiotic use in humans, animals, and agriculture needs intensive scrutiny with deliberations to curb it as an urgent global and national priority. Combating and countering AMR requires continuous uninterrupted

funding, worldwide collaboration, and national efforts toward rational use of antimicrobials with a concentrated focus on preventing infectious diseases with appropriate infection control measures and good animal husbandry techniques rather than using antimicrobials for prophylaxis and growth-promoting agents.

There is an urgent need to generate the resources needed to create newer diagnostic and therapeutic tools to effectively diagnose and manage infectious diseases without undue reliance on antimicrobials. It is a battle that must be fought aggressively and won; otherwise, inaction of today may culminate in a horrendous post-antibiotic era of tomorrow. Collaborative honest implementation of "One Health approach" with inviolable political commitment at the highest level is a prerequisite and the key to success (Bhatia, 2019). A strong political will and determination to contain this complex challenge, sustained funding, and an efficient programmatic well-coordinated "One Health approach" are validated and globally accepted practices. These need to be implemented across the country to minimize the impact of AMR on human development and preserve the efficacy of antimicrobial agents for the next generations.

The world must collaborate with India in strengthening its efforts to combat AMR and also in building capacity of other developing countries. Given the presumed high burden of AMR, availability of sufficient skilled human resource, numerous well-equipped institutes, and growing awareness of the implications of AMR on the national economy, especially cost to health system and export potential of animal products, India is the ideal country for greater technical support by the global community to reap abundant benefits with potential global implications in the context of AMR.

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