COMBATING ANTIMICROBIAL RESISTANCE – A ONE HEALTH APPROACH

Abstract

AMR (Antimicrobial Resistance) is a multidimensional problem that endangers both human and animal health. Improving global surveillance of antimicrobial resistance and decreasing consumption of antibiotics in humans and animals can contribute reducing antimicrobial resistance. The One Health approach is a comprehensive strategy that recognizes the interconnectedness of human health, animal health, and environmental health in the fight against AMR. Understanding the exact burden of the AMR is a challenging task. In the year 2017, Union Ministry of Health and Family Welfare started India′s National Action Plan (NAP) for creating Awareness for antimicrobial resistance with goals of raising awareness, boosting surveillance, improving infection prevention and control, undertaking research and development, supporting investments, and collaboration among different sectors to combat AMR.

AMR spread through the triad of environment, animal and man. Resistant microorganisms and genes are spreading very rapidly and widely through food chains and environment.

In accordance with the Global Action Plan for Anti- Microbial Resistance has been implemented throughout India over six years in a phase wise manner to fight against AMR. The necessity of the hour for significant community engagement is to promote awareness and advocacy regarding AMR. Enhanced surveillance and strategies based on evidence, interdisciplinary collaboration, judicial antimicrobial use, new research must be implemented through

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regional, national and international policies. In this chapter, threats of AMR and steps to tackle this menace of AMR with the help of One health approach have been discussed along with future perspectives of intersectoral involvement and engagement.

I. HISTORY AND CONCEPT

As all of us know Rudolf Virchow, MD, (1821-1902) is known as the "Father of Pathology". In the 19th century he mentioned that there are no dividing lines between animal and human medicine. Later Calvin W. Schwabe, DVM, MPH (1927-2006) mentioned the term One Medicine in his textbook Veterinary Medicine and Human Health in the year 1965.In subsequent years the concept of One Health came. Initially, zoonotic illnesses were discussed in relation to One Health.

One Health's major goal is to attain optimal health and sustainability for humans, animals, and the environment at the same time. We just encountered the COVID 19 pandemic in the twenty-first century. Other pressing issues include developing and re-emerging infectious illnesses, climate change, pollution, habitat loss, human encroachment on animals, and antimicrobial resistance. (1),(2)

In an interview with Down To Earth, Roderico H Ofrin, WHO India's representative, discussed WHO's involvement in combating antibiotic resistance in India. When it comes to public health, at local, regional, national, and international levels, he emphasizes the significance of a cooperative, multi-sectoral, and transdisciplinary "One Health" approach. It is a big challenge to address the various sectors like animal health, agriculture, environment and food. Therefore, One Health approach can be implemented to collaborate these sectors with human health and to address silent pandemic like antimicrobial resistance. WHO India has worked in partnership with all health partners, including the Indian offices of the United Nations Environment Programme (UNEP) and the Food and Agriculture Organization (FAO).

II. ANTIMICROBIAL RESISTANCE (AMR)-A GLOBAL THREAT

AMR is a multidimensional problem that endangers both human and animal health. Improving global surveillance of antimicrobial resistance and decreasing consumption of antibiotics in humans and animals can contribute reducing antimicrobial resistance. In a review (3) it is also mentioned that 10 million annual AMR related deaths might occur by the year 2050.

As per the Review on Antimicrobial Resistance, (3) Improving global drug resistance detection and lowering human and animal antibiotic use are two crucial stages in reducing the needless use of antibiotics in agriculture and their release into the environment. It is also mentioned that if the current trends continue, there might be up to 10 million annual AMR-related fatalities from a variety of infections by the year 2050. The United Nations dedicated their 71st General Assembly in 2016 addressing the issue of AMR. A resolution was made by the members of the house and it was emphasized that the main cause of AMR is the improper use of antibiotics in human health, animal health, agriculture, poultry, food, and aquaculture. Furthermore, that resolution highlighted AMR as an urgent issue that needed to be tackled urgently all around the world. (4)

Understanding the exact burden of resistance is a challenging task. It is because in many areas surveillance is limited and statistics are unavailable.(5)India′s National Action Plan(NAP) for creating Awareness for antimicrobial resistance was released in the year 2017

by Union Ministry of Health and Family Welfare. Goals of National Action Plan include raising awareness, boosting surveillance, improving infection prevention and control, undertaking research and development, supporting investments, and collaboration among different sectors to combat AMR.

The NAP's objectives include increasing awareness, increasing surveillance, enhancing infection prevention and control, conducting research and development, increasing investments, and collaboration to battle AMR.(6)

III. THREAT OF AMR SPREADING THROUGH TRIAD OF ENVIRONMENT, ANIMALS, MAN

Global AMR dispersion is influenced by a number of factors, including intensive food production, globalization of food distribution, international travel (which might spread resistance genes), changing climates, increasing population density or growth, and urbanization. The global burden of ABR may be attributed to a number of factors, including the overuse of antibiotics in humans and animals (food, pets, aquatic environments), antibiotics sold without a prescription over-the-counter, increased international travel and trade, migratory birds, refugees, climate change, inadequate sanitation and hygiene, and the release of antibiotic residues or non-metabolized antibiotics into the environment.

According to a study, almost 80% of marketed antibiotics in the United States are used as growth supplements or to manage animal infections. In 2010, the global map of antibiotic usage projected that 63 151 tonnes of antibiotics were used in livestock. (7) Antibiotics are widely available without a prescription in India, leading to indiscriminate use. In the lack of true drug legislation and law enforcement, unethical enterprises' distribution of counterfeit or inferior antibiotics also contributes to rising resistance.

Additional research and development are essential for the latest antimicrobials. It is imperative to create innovative treatments while preserving the effectiveness of existing ones. Furthermore, resistant microorganisms and genes are spreading widely throughout the environment and food chains. In Asia, piped water often faces significant coliform contamination, and antibiotic resistance genes have been detected in numerous drinking water supply systems across different regions. The indiscriminate use of antibiotics in cattle and aquaculture, whether for treatment or growth promotion, has hastened the emergence and dissemination of foodborne pathogens resistant to antibiotics. (9) Recognizing the interconnection of human, animal, and environmental factors is vital for managing antimicrobial resistance, in line with the One Health concept. Relying solely on antimicrobial resistance surveillance in hospitals is insufficient.

The introduction of antibiotics into medical treatment has significantly transformed the conditions for the emergence and spread of resistance by imposing exceptional selection pressures, particularly on the microbiota of humans and domestic animals. This selective pressure has facilitated the movement and horizontal transfer of a wide range of antibiotic resistance genes (ARGs) to various bacterial species. Antibiotic resistance represents a natural phenomenon encoded by microbial ARGs that has evolved over billions of years. Well before the initial clinical use of antibiotics, environmental bacteria carried ARGs that contributed to the development of resistance to newly approved antibiotics. Antibiotics,

antibiotic-resistant bacteria (ARB), and antibiotic resistance genes (ARGs) constitute the three primary elements of antimicrobial resistance (AMR), all of which are categorized as emerging environmental contaminants.

The environment is now widely recognised for its contribution in the rise of global spread of antibiotic resistance due to the extensive presence of antibiotics, antibiotic resistant bacteria, antimicrobial resistant genes (ARGs). The pooling and proliferation of ARGs through aquatic environment and their transfer to clinically relevant bacteria is well documented, with several studies linking clinical isolates of multidrug-resistant pathogens to environmental water bodies and continued emergence of new highly resistant bacteria. Antibiotic resistance genes (ARGs) have been recognized as emerging pollutants that are widely distributed and accumulated in most of aquatic environment.

Most of studies emphasized only overuse of antimicrobials in human and animals. But antimicrobial resistance produced and transferred in the environment is generally overlooked by scientists. Moreover, determinants of AMR in the environment differ greatly in different regions of the world.

Escherichia coli, which is the cause of several infections, develops resistance through various mechanisms. Colistin is regarded as a last-option antibiotic for treating infections caused by E. coli. Plasmid mediated mobile-colistin-resistant (mcr) genes are regarded as a serious hazard to public health. The main reservoir of E.coli are human, pigs and poultry birds. A meta -analysis from 2022 summarizes the findings in two categories: clinical research, which only included isolates from hospitals, outpatient clinics, or laboratories, and community-based studies, which included isolates from healthy humans, hens, or pigs. E. coli with mcr-mediated colistin resistance (mcrMCRE) was present in 54 nations across five continents with a prevalence of 6.51%; With the exception of mcr-2, Asia reported the greatest diversity of mcr-variants (eight of nine). With estimated prevalence rates of 15.8% and 14.9%, respectively, hens and pigs were shown to be the primary reservoirs of mcr globally. Less prevalent populations included healthy people (7.4%) and clinical isolates (4.2%). By adopting the necessary control strategies, this knowledge can be used to decrease the occurrence of zoonotic transmission. (8)

Although the area has had consistent social and economic growth, a huge section of the population still lives in poverty. Resistant diseases and genes circulate more quickly amongst people and in the environment when there is inadequate housing and sanitation. (9)

A study was carried out in Cardiff and New Delhi in 2010. Fifty tap water samples and seventeen seepage samples were gathered for this investigation in New Delhi, whereas seventy sewage effluent samples from Cardiff Wastewater Treatment Works were collected in Cardiff and tested for the blaNDM-1 gene. No sample from Cardiff included the gene, while 51 out of 171 seepage samples and two out of 50 drinking-water samples from New Delhi did. This investigation demonstrated the existence of NDM-1 β-lactamase-producing bacteria in New Delhi ambient samples (10).

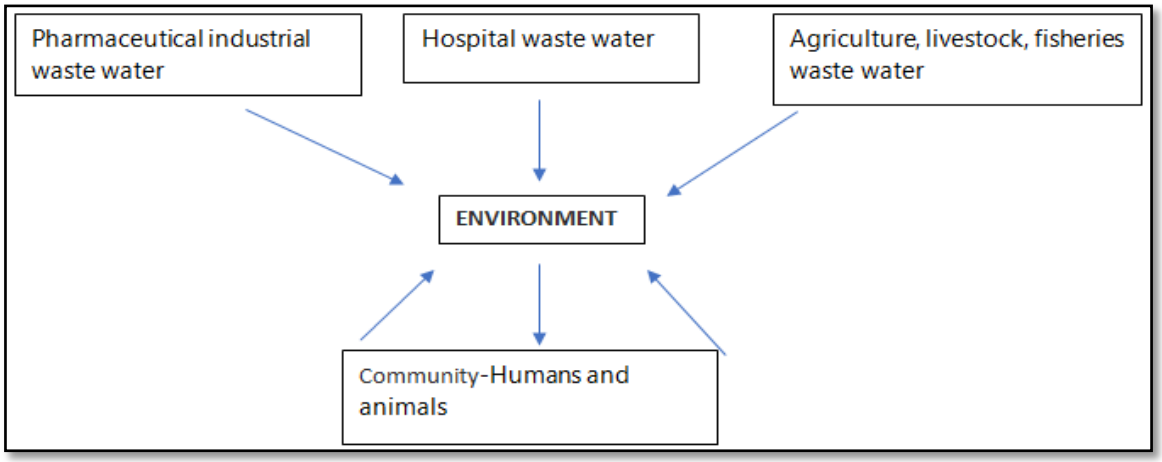
In 2015, India was one of the top antibiotic consumers, with a defined daily dosage (DDD) of 4,950 per 1,000 population. Antibiotic use in veterinary animals, both medicinal and nontherapeutic, is expected to rise by 18% by 2030. There are numerous mechanisms by

which antibiotics, ARBs, and ARGs in solid and liquid waste infiltrate the environment. Antibiotics, ARB and ARG are found in wastewater from hospital and healthcare facilities, pharmaceutical industries, animal food and veterinary industries. (11)

As per a study done in South India STP (Sewage treatment plant) is one of the most significant points where environmental contamination by bacteria resistant to antibiotics occurs. Hospital wastewater inflows significantly increased the prevalence of E. coli that is resistant to antibiotics in South Indian STPs, although treatment methods and sampling times had no impact on this. (12) To stop the environment from becoming contaminated with bacteria that are resistant to antibiotics, hospital wastewater must be treated before being released into the main stream.

IV. STEPS BEING TAKEN TO COUNTER THE THREAT OF AMR

Existing traditional wastewater treatment technologies, such as the activated sludge process (ASP), do not assure that antibiotics, ARBs, and ARGs are completely removed from wastewater. Similarly, the created sludge finds its way to agricultural land, where it eventually spreads resistance in the ecosystem. Once released into the ecosystem, these pollutants are difficult to remove. In 2017, India's AMR action plan regulated antibiotic use for humans and animals, as well as addressed AMR transmission from all possible sources and containment.



1. **Key sources of antibiotics, ARB, and ARG contamination the environment:** The Indian government implemented a discharge regulation for 121 antibiotics in the effluents of bulk drug production businesses, formulation industries, and common effluent treatment plants (CETP) handling pharmaceutical wastewater in 2020. (11)

   In accordance with the Global Action Plan for Anti-Microbial Resistance (GAP-AMR), the National Action Plan for Anti-microbial Resistance (NAP-AMR) has being implemented throughout India for over six years. Ministries of Health and Family Welfare, Agriculture and Farmer Welfare, Environment, Forestry, and Climate Change are major stakeholders in AMR. Additionally, the continuous AMR surveillance conducted by INSAR, NCDC, and ICMR networks is essential. Each state has a varied stage of development for its State Action Plan for Antimicrobial Resistance. Kerala, Madhya

Pradesh, and Delhi are the three states that have published and are putting into practice their state action plans.

- State Action Plan to combat Antimicrobial Resistance in Delhi (SAP-CARD)
- Madhya Pradesh State Action Plan for Containment of Antimicrobial Resistance
- Kerala Antimicrobial Resistance Strategic Plan

Since health is a state issue, all Indian states and Union Territories (UTs) should prepare State Action Plans for Containment of Antimicrobial Resistance, or SAPCAR.WHO India has provided support to the Union Ministry of Health and Family Welfare (MoHFW) in the creation and execution of SAPCAR in Delhi, Madhya Pradesh, and Kerala. Using these states' experience, other states and Union territories are trying to develop their own state action plans on AMR. With support from the WHO Country Office for India, the MoHFW formed the Intersectoral Coordination Committee, Technical Advisory Group, and Core Working Group on AMR.

In collaboration with MoHFW and the Kerala government, the WHO arranged the First Regional Workshop on Developing SAPCAR for the Southern States and UTs in 2020, coinciding with the establishment of the Delhi Declaration on AMR, the National Action Plan on AMR, and SAPCAR in three states. Any state's framework for monitoring treatment outcomes, prioritizing effective evidence-based initiatives, and conducting AMR surveillance are essential for assessing AMR.

There are already three state-level AMR surveillance networks in Maharashtra, Kerala, and Delhi, with plans to add more in the future. Furthermore, WHO India is supporting a 'One Health' AMR pilot project in the Krishna area of Andhra Pradesh in collaboration with MoHFW. Even with the achievements, there are still issues in containing and tracking AMR. These include a lack of systems and personnel specifically designed to address the AMR agenda, shifting and competing priorities in health and development, ownership and involvement of 'One Health' AMR stakeholders, funding AMR initiatives within the constraints of government budgets, supporting the implementation of existing laws and regulations, monitoring, and evaluation. Bihar recently introduced the State Action Plan (SAP) to combat antimicrobial resistance.

The necessity of the hour for significant community engagement is to promote awareness and advocacy regarding AMR. Enhanced surveillance and strategies based on evidence must be implemented. Strick vigilance over use of antimicrobials in human, animal, poultry sector is utmost important. Treatment of wastewater discharges from pharmaceutical industries and healthcare industries is very crucial.

V. FUTURE PERSPECTIVES

The concept of One health emphasises the need for a more integrative effort by all the major stakeholders since AMR enters our food chain stealthily and affects each one of us directly or indirectly. AMR in the food chain not only reduces overall productivity, health risks, food insecurity, higher healthcare costs, as altering the climate. An intersectoral approach would be the best way to mitigate this menace of AMR. Therefore, the farm-to-plate continuum should adopt a comprehensive One Health strategy that takes into account not only the issue at hand but also every aspect of the AMR menace as a whole.

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