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Antimicrobial Resistance (AMR): Emerging Global Public Health Concern

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Antimicrobial Resistance (AMR): Emerging Global Public Health Concern

Abstract:

Antimicrobial Resistance (AMR) poses a critical global health threat, with the potential to cause 10 million annual deaths by 2050. This paper examines the causes of AMR, including inappropriate antibiotic use, rising GDP levels, problematic prescribing patterns, and use in agriculture. It highlights the geopolitical divide between the Global North and South in addressing AMR, emphasising disparities in infrastructure and funding allocation. The study proposes policy recommendations such as global collaboration, national antibiotic policies, banning over-the-counter antibiotic sales, and adopting a "One Health" approach. It stresses the urgency for concerted global efforts to combat AMR, calling for improved antimicrobial stewardship, surveillance, and prevention measures to mitigate this growing crisis.

Introduction:

Antibiotics, antifungals and antivirals - together constitute the essential antimicrobials. These medical regimens are often called "magic bullets" against infections and are deemed the most remarkable medical discovery of the 20th century. The introduction of antibiotics, in particular, has saved millions of lives. Its use has been diversified over the decades - from animal husbandry to crop production. Antimicrobials prevent, treat, and cure infections affecting a broad spectrum of living beings - humans, livestock, aquaculture, and crops. The newest threat to life on earth is not another meteorite but rather the ineffectiveness of these lifesaving substances. Many antimicrobial medications are ineffective because the microorganisms called 'superbugs' (United Nations Environment Programme, n.d.) have become resistant to them.

Antimicrobial resistance or AMR occurs when bacteria, fungi, viruses or parasites become resistant primarily to traditionally used treatments to which they were previously vulnerable. AMR is an inevitable evolutionary process observed in all organisms. Organisms undergo genetic mutations to safeguard against environmental selection pressure (Centers for Disease Control and Prevention [CDC], n.d.). The World Health Organisation (WHO) prioritises AMR as

one of the top 10 global public health concerns humanity will face in the near future. This was declared at the UN General Assembly on AMR in 2016 when the UN solicited nations to draw up individualised National AMR Action Plans (United Nations General Assembly, 2016).

However, despite this clarion call, drug resistance led to about 4.95 million deaths globally in 2019, with a considerable portion of this coming from low- and middle-income countries (LMIC) - especially sub-Saharan Africa (Antimicrobial Resistance Collaborators, 2022). This devastating death toll is far higher than the annual global deaths caused by HIV/AIDS (8.64 lakhs), tuberculosis (1.5 million) and malaria (6.43 lakhs). Recent estimates point out that not addressing the AMR issue will effectively lead to over 10 million deaths annually by the year 2050 (O'Neill, 2016). It is estimated that the current levels of antibiotic usage in poultry and cattle have risen to catastrophic levels across continents. It is predicted to increase by 67 per cent by 2030 in developing countries (Boeckel et al., 2015). This brewing issue has also led to a significant increase in the world's financial burden from healthcare. If unaddressed, AMR is estimated to lead to a global GDP shortfall of $3.4 trillion annually in the next decade, potentially pushing 24 million people into poverty (World Bank, 2017). LMICs will bear a significant burden of this in terms of both the disease burden and its economic implications.

AMR also exacerbates existing inequalities in society - the most vulnerable being women, children, refugees, migrants, people employed in specific sectors (healthcare, agriculture, etc.) and those living in poverty.

Causes:

The WHO and other AMR surveillance systems have pointed out various factors that are leading to AMR - rise in human and animal populations, expansion of globalisation, international trade, high demand for animal feed and easy availability and access to antimicrobials in developed and developing nations (Lutgring et al., 2017). They can be broadly classified under four categories - i). Environmental factors (mass travel, population growth, unhygienic conditions, ineffective control schemes, etc.); ii). Drug-related factors (substandard drugs, counterfeit drugs, easy availability, etc.); iii). Patient-related factors (self-medication, subtherapeutic dosages, poor

compliance, poverty, etc.); iv). Physician-related factors (improper prescription, inadequate dosages, lack of updated knowledge, etc.). Below are a few of the widely recognised factors driving AMR -

1. Inappropriate Use of Antibiotics - Epidemiological studies have shown that long-duration exposure to subtherapeutic antimicrobials in livestock creates the ideal environment for bacteria to develop resistance-related genes. These genes can be transmitted to the human gut microbiome through the environment or contaminated food. Global surveys have also revealed many misconceptions regarding what an antibiotic can do - a significant portion of people, especially the uneducated, believe that antibiotics are easy cures to viral infections such as the flu or common cold (Chokshi et al., 2019). The spread of AMR is further facilitated by the over-the-counter (OTC) availability of antibiotics. Abuse of antibiotic drugs can be attributed to the lack of a clear and actionable antibiotic policy and other standard treatment guidelines, which are frequently observed issues in developing countries. This also occurs when physicians prescribe unnecessarily lengthy drug courses, sometimes for the sake of financial incentives provided by pharma companies (Noor et al., 2023). In other cases, it takes place to satisfy patients' expectations (CDC, 2022).

2. Rising Gross Domestic Product (GDP) Levels - The explosion in the usage and prescription of antibiotics has been attributed to the rise in the GDP of developing countries. This has brought with it an improvement in quality and access to healthcare in the LMICs, which positively correlates to the consumption of antibiotics. Klein et al. estimated that between 2000 and 2015, antibiotic consumption worldwide increased by 65 per cent.

3. Problematic Prescribing Patterns -The inappropriate use of antibiotics is a significant driver of AMR. This includes prescribing antibiotics when they are not needed, selecting the wrong type of antibiotic, administering incorrect dosages, or prescribing courses that are too short or too long. According to the USA's Centre for Disease Control and Prevention (CDC) report of 2017, about 30 per cent of hospital patients were administered antibiotics without adequate testing for extended durations (CDC, n.d-a.). The situation was observed to be much worse in nursing

homes, where about 3/4th of antibiotic prescriptions were either inappropriate or incorrect, with wrong durations and wrong dosages (CDC, n.d.-b).

4. Lack of Futuristic Antibiotics in Sight - There is a paucity of required futuristic antibiotics, which merits urgency from global pharma firms to develop new novel antibiotics. However, despite repeated emphasis by the WHO, there needs to be more such antibiotics. Only 8 of the 51 newly researched and developed antibiotics can be categorised as innovative drugs useful to combat antibiotic-resistant bacteria (World Health Organization, 2017). The rest of them are re-engineered versions of old drugs. Consequently, the bacteria is also expected to grow resistant to these new drugs. In this context, management of drug-resistant tuberculosis, pneumonia, urinary tract infections, etc., are getting jeopardised due to a lack of treatment options. As a result, people of old and extremely old age have become highly vulnerable to life-threatening diseases (Chang et al., 2015). Regulatory restrictions and economic liability are significant constraints for pharma firms in producing new antibiotics. This has led to a dire situation where close to 18 major pharma companies have abandoned their antibiotic production and moved to prioritise profitable segments of chronic diseases (Ventola, 2015).

5. Antibiotics in Agriculture and Animal Husbandry - antibiotics in all types of farming, especially livestock farming, have increased in most developing countries, primarily to address the growing demand for animal protein (Van et al., 2020). Nearly 70 per cent of medically necessary antibiotics are sold for animal use in the USA. This is of particular concern because the types and modes of working of antibiotics employed for veterinary practices are similar to those prescribed to humans (Frost et al., 2019). This, in turn, has led to AMR due to the increased presence of antibiotic residue in livestock products such as meat, fat, liver, milk and eggs. Antibiotics are also used randomly, unprescribed for treating livestock diseases, growth promotion, improving feed conversion efficiency and disease prevention (Food and Agriculture Organization , n.d.). These practices are observed highly in the case of developing countries due to a lack of regulatory oversight and dedicated government policies controlling the same. Another aspect of this rise is the increasing consumption of animal protein, adding to the transmission of AMR from animal sources to humans (Woolhouse et al., 2016).

6. Growing Global Migration and Travel - Growing evidence suggests that the emergence and spread of drug-resistant bacteria are facilitated by human movement. Ease of travel for both humans and livestock, as well as goods, has led to easy dissemination of AMR across the globe. When tourists return to their home countries, they knowingly or unknowingly carry infections by AMR organisms. Evidence suggests that AMR bacteria can persist for close to 12 months inside a person's body after travelling to a highly endemic AMR region, thus amplifying the risk of transmission (McCubbin et al., 2021).

7. Knowledge Asymmetry - There is growing evidence that the public and healthcare workers have knowledge gaps regarding the correct use of antibiotics and the mechanisms leading to AMR (Carter et al., 2016). Constant surveillance is a prerequisite to establishing the magnitude of the AMR burden and implementing strategies to prevent it. Unfortunately, empirical data regarding the status of antibiotic usage in humans, animals, and agriculture is lacking worldwide. Surveillance helps bring out important information that is useful in drafting interventions to prevent AMR. This existing knowledge gap must be bridged to encourage all stakeholders to cooperate.

8. AMR in the Environment - While AMR is an evolutionary process, it has been exacerbated since the industrial age due to human activities and biological and chemical pollution. When antimicrobials are released into the environment, they can contact resistant microorganisms, or new AMR can occur. Places that receive large amounts of pollutants, such as lakes, rivers and oceans, are more likely to harbour AMR organisms and lead to their spread (Kelly et al., 2009).

The Geopolitics of the Global North and Global South:

AMR is a problem that requires resolutions at the national level, as well as coordination and agenda-setting at the global level. Here comes the catch - the priorities and needs of the Global North and Global South are so fundamentally different that they threaten to undermine the goal of mitigating AMR. For example, a study investigating the effect of numerous interventions to reduce AMR found that the most significant reduction was brought upon by infrastructure

interventions (Collignon et al., 2018). This included improvements in sanitation, adequate water access, electricity and urbanisation. This is further substantiated by the study of sewage, which found that AMR genes per sample were highest in Africa, South America and Asia (Hendriksen et al., 2019). Countries with lower Human Development Index scores, as measured by the World Bank, tended to have a higher prevalence of antimicrobial resistance genes in their sewage systems. Conversely, countries ranking higher on the Human Development Index generally showed fewer AMR genes in their wastewater. Apart from infrastructure interventions, vaccinations and Water, Sanitation & Hygiene (WASH) measures were found to be most effective in combating AMR for the Global South.

The danger of the Global South falling short of funds to mitigate AMR is real, as the focus of global funding from the North is more towards research and developing new novel antibiotics. For example, the UK government is funding a £265 million Fleming Fund programme to support improving laboratory infrastructure in a few LMICs. Minimal global funds go towards vaccination, infection prevention and boosting WASH measures (Global AMR R&D Hub, n.d.). The inequality between the Global North and Global South is further evident, as the Global North procures nearly 2/3rd of all the global pharmaceuticals. In contrast, antibiotic production predominantly takes place in China and India, with an increasing risk of contamination of water sources due to antibiotic residue discharge from the pharmaceutical manufacturing processes (Boston Consulting Group & Wellcome Trust, 2022).

The upcoming UN General Assembly AMR High-Level Meeting in September 2024 is an essential opportunity to raise concerns regarding the existing and exacerbating inequality between the Global North and Global South and the risks of such a divide.

Policy Recommendations:

1. Global Measures - There is a need to establish collaboration between international agencies, NGOs, CSOs and governments. Early warning and surveillance networks must be set up globally with interconnected operations. More dedicated laboratory facilities are needed to detect and report AMR pathogens and map their spread. This should be further strengthened using

international tracking systems to - control the global trade of counterfeit drugs, fund research and development of new medicines and vaccines and focus funding on the specific requirements of nations.

2. National Level Strategies - Nations need dedicated "Antibiotic Policies" with transparent enforcement and accountability measures. This should include both human and veterinarian components. A decentralised surveillance, monitoring and evaluation system with a centralised command portal is a need of the hour. Increasing funds for domestic research and development of new drugs and antibiotics using the genetic map of the endemic population is required as a targeted solution.

3. Banning OTC Availability of Antibiotics - There must be strict regulation and enforcement of a ban on dispensing antibiotics OTC. Registered pharmacists should ensure compliance with prescriptions. This can be done through awareness campaigns for both pharmacists and patients.

4. Focus on Infection Prevention and Control - This evidence-based approach protects patients and healthcare workers from avoidable infections from drug-resistant pathogens. This includes healthcare workers' compliance with hospital infection control and antibiotics policies and timely notification of drug-resistant cases to the surveillance teams.

5. R&D of New Drugs and Vaccines - As pathogens rapidly resist emerging new classes of antibiotics, focusing on futuristic drugs and vaccines is necessary. This ensures excellent investment in operational research through industry-academia collaboration at national and international levels (World Health Organization, n.d.).

6. Community Engagement - The propagation of AMR is a biological process that relates to numerous everyday activities of people - home and animal hygiene, livestock maintenance, waste disposal, etc. Further, communities often have their understanding and perception of antimicrobials, which can be used and targeted to safeguard that community from AMR. This involves including people and understanding their unique experiences.

7. "One Health Approach" - The WHO introduced the "One Health" approach in 2008 to achieve better global public health outcomes. It is an integrated approach that is collaborative, multisectoral, and multidisciplinary, working with people at the local, national, and international levels to attain optimal health outcomes for people, animals, and the environment. It includes the One Health Initiative Task Force (OHITF), which works on AMR. The foundation of One Health is based on communication, coordination and collaboration among human, animal and environmental professionals. This can play a crucial role at the global level to mitigate the issue of AMR.

Way Forward:

The evolution of AMR of pathogens is a continuous phenomenon. The dire condition, booming over the past two decades, has created a grave risk for global public health and is now being addressed as one of the gravest dangers of the 21st century. The diseases that could once be treated with tried and tested drug regimens are now causing deaths. Considering the rapidly resistance-evolving pathogens, the future development of novel antibiotics looks bleak.

Combating AMR requires a concerted global effort from all stakeholders, including governments, NGOs, policymakers, researchers, healthcare professionals, pharmaceutical companies, agricultural leaders, and the public. This collaborative endeavour aims to decelerate the ongoing trends in AMR and minimise its health and economic burdens.

Developing and implementing a comprehensive antimicrobial stewardship program in healthcare facilities is crucial. This involves creating detailed guidelines for antibiotic use, ensuring healthcare providers adhere strictly to these protocols, and regularly monitoring and adjusting practices to optimise antimicrobial use and minimise resistance. Surveillance, monitoring, evaluation, minimising OTC antibiotics and their use in food feed, increasing access to vaccines and diagnostic services, and enforcing strict legislation are vital steps in mitigating the AMR problem.

Prevention remains the best cure to reduce AMR infections and their global spread. While restoring the efficacy of existing antibiotics is difficult, we need to ensure their rational use. At the same time, it is crucial to focus on developing new effective antibiotic molecules, trusted alternatives to antibiotics, and technological breakthroughs for quick diagnosis and vaccine development, like in the case of COVID-19.

While there have been several attempts to address AMR and the required interventions and coordinated global and regional-level action, they have yet to yield the desired results, primarily due to a lack of political will. If not addressed urgently, within a few years, we might face dire setbacks in the medical, social, and economic sectors, and all our essential achievements in modern medicine, such as heart and other organ transplantations, chemotherapy, etc., will be jeopardised unless practical and long term global coordinated efforts are immediately undertaken.

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