

The Impending Global Challenge of Antimicrobial Resistance: A Call for Urgent Action

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INTRODUCTION

Antimicrobial resistance (AMR) is a critical global health issue driven by antibiotic misuse and overuse in various sectors, leading to the emergence of resistant microorganisms and represents an impending pandemic. Against the backdrop of COVID-19 pandemic, conflicts, and the escalating impact of anthropogenic climate change, the emergence and rapid escalation of antimicrobial resistance (AMR) represent one of the most significant and imminent global public health threats of the 21st century.(1) As bacteria, viruses, fungi, and parasites increasingly evolve resistance to drugs that once treated infections effectively, the 'superbugs' such as Methicillin-resistant Staphylococcus aureus (MRSA) and extremely drug-resistant tuberculosis, bacteria that are difficult to treat have emerged. This has brought humanity to the brink of a post-antibiotic era, where re-emergence of common infections is being noted. With resistance on the rise, surgical procedures like organ transplants and cesarean sections, cancer treatments where antibiotics are crucial, and management of life-threatening infectious diseases such as pneumonia, TB, HIV, and malaria are at risk of

becoming dangerous due to the high potential for untreatable infections. (2)

The World Health Organization (WHO) has declared AMR a top 10 global health threat, with estimates suggesting that with current trends continuing drug-resistant infections could cause 10 million deaths annually by 2050. This would reduce global GDP by 2-3.5%, with low- and middle-income countries facing the worst economic impact of AMR alongside societal costs, including increased morbidity, mortality, and loss of productivity.(3) AMR deaths in India have higher death tolls than other major diseases like neoplasms, respiratory infections, tuberculosis, enteric infections, diabetes, kidney diseases, and maternal and neonatal disorders. Despite this looming crisis, responses to AMR have been fragmented and insufficient.

Tracing the Roots and Emerging Trends

Recent trends reveal that AMR is accelerating faster pace than previously anticipated. Additionally, the global burden of AMR is disproportionately high in countries with inadequate healthcare infrastructure, poor regulatory frameworks, and limited access to diagnostics. The discovery of multi-drug-

resistant (MDR) and extensively drug-resistant (XDR) bacteria, particularly in low- and middle-income countries, has raised concerns about the potential for uncontrollable outbreaks. One of the most significant drivers of antimicrobial resistance is the over-the-counter, quack-prescribed irrational use of antimicrobial agents. Besides, non-therapeutic use of antimicrobial agents in the veterinary and fishery sectors also affects anti-microbial resistance development which has found its way to humans through the food chain. The COVID-19 pandemic has further exacerbated the situation, as the widespread use of antibiotics to treat secondary bacterial infections in COVID-19 patients has led to an increase in resistant strains.

Drug Resistance in Bacteria

WHO 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report state concerning levels of resistance among key bacterial pathogens. Across 76 countries, *Escherichia coli* showed a 42% median resistance rate to third-generation cephalosporin, while *Staphylococcus aureus* had a 35% resistance rate to methicillin. In 2020, about 20% of urinary tract infections caused by *E. coli* displayed reduced susceptibility to standard treatment regime with ampicillin, co-trimoxazole, and fluoroquinolones. *Klebsiella pneumoniae*, also demonstrated high resistance levels to critical antibiotics, leading to increased reliance on last-resort drugs like carbapenems. However, resistance to carbapenems is now an emerging issue. The Organization for Economic Cooperation and Development (OECD) estimates that resistance to last-resort antibiotics could double by 2035 compared to 2005 levels, showcasing the urgent need for improved antimicrobial stewardship and broader surveillance efforts.(4)

Drug Resistance in Fungi

Drug-resistant fungal infections are on the rise, with a major concern being the emergence of multi-drug-resistant *Candida auris*, an invasive fungal infection. The WHO has developed the Fungal Priority Pathogens List to address this

growing issue, following a thorough global review of drug-resistant fungi.

Drug Resistance in HIV, Tuberculosis, and Malaria

HIV: HIV drug resistance (HIVDR) transmitted during infection or acquired through inadequate treatment adherence or drug interactions has led to higher rates of HIV transmission, as well as increased morbidity and mortality.

Tuberculosis (TB): TB is a significant contributor to antimicrobial resistance, particularly in the form of multidrug-resistant tuberculosis (MDR-TB), and extensively drug-resistant tuberculosis (XDR-TB), representing a public health crisis, with only about 40% of those with drug-resistant TB receiving treatment in 2022.

Malaria: Drug-resistant parasites pose a serious threat to malaria control efforts. The emergence of partial resistance to Artemisinin-based combination therapies (ACTs) that are the first-line treatment for uncomplicated *Plasmodium falciparum* malaria complicates treatment choices.

Drug Resistance in Neglected Tropical Diseases (NTDs)

The development of drug resistance against treatments for neglected tropical diseases (NTDs) poses a critical threat to global efforts aimed at controlling, eliminating, and eradicating these diseases, which disproportionately affect vulnerable populations.

Plasmid Mediated Resistance

Horizontal gene transfer through plasmids exacerbates AMR. Colistin resistance through the *mcr-1* gene spreads to different bacterial species, especially in areas having extensive use of Colistin in agriculture.

Turning the Tide: Strategic Actions to Combat Antimicrobial Resistance (AMR)

The challenges posed by AMR are daunting, but recent developments offer cautious optimism. Public health interventions play a crucial role in this effort. The proliferation of genomic surveillance, investment in

alternative therapies, and coordinated global efforts indicate that progress is being made. However, sustained investment in research and development of new antimicrobials, diagnostics, and vaccines is crucial.

Additionally, reducing the inappropriate use of antibiotics and improving infection prevention and control across all sectors will be vital to slow the spread of AMR. Global Policy Initiatives have emerged to combat AMR. The World Health Organization (WHO) has developed the Global Action Plan on AMR, with countries being encouraged to create national action plans. The World Bank and the United Nations have also supported international collaborations aimed at reducing antimicrobial misuse, particularly in low- and middle-income countries where healthcare infrastructure may be limited. Ultimately, a multifaceted, One Health approach that addresses the intersection of human, animal, and environmental health will be essential in effectively combating antimicrobial resistance.⁽⁵⁾ As we move forward, collaboration between governments, healthcare providers, researchers, and industries will play a pivotal role in preserving the efficacy of antimicrobials and protecting public health.

Key strategies include Surveillance and Monitoring to track the spread of AMR and identifying emerging resistance patterns is essential. Data-driven approaches can inform targeted interventions and policy decisions. The World Health Organization's Global Antimicrobial Resistance and Use Surveillance System (GLASS) is a critical initiative that collects data on antimicrobial use and resistance patterns worldwide. Surveillance efforts are not confined to human medicine but extend to the veterinary and agricultural sectors, where antibiotic overuse has led to the emergence of resistance in zoonotic pathogens.⁽⁶⁾

Alongside, Antibiotic Stewardship Program implementation in healthcare settings to optimize the use of antibiotics and reduce unnecessary prescriptions is critical.

Antimicrobial stewardship (AMS) is an organisational or healthcare-system-wide approach for promoting and ensuring judicious use of antimicrobials to preserve their effectiveness.⁽⁷⁾ Hospital-based ASPs have proven to be effective in decreasing inappropriate antimicrobial use by 30-40%. Recent studies have shown that ASPs can reduce the incidence of drug-resistant infections and improve patient outcomes. Community-level Stewardship finds its place in outpatient settings, where misuse of antibiotics in prescriptions is often provided for self-limiting conditions. Educational campaigns and regulatory measures to control the over-the-counter sale of antibiotics have been integral to reduce unnecessary prescriptions.

Investing in research and development of new antibiotics, vaccines, and alternative therapies is vital to stay ahead of evolving pathogens. Public-private partnerships can accelerate the development of innovative solutions. Government must enforce stricter regulations on the sale and use of antibiotics in both human medicine and agriculture. International collaboration is also needed to address the global nature of AMR. Engaging communities in the fight against AMR through education and awareness programs can empower individuals to take responsible actions, such as adhering to prescribed treatments and avoiding the misuse of antibiotics. World Antibiotic Awareness Week (WAAW), initiated by the WHO since 2020, has become a critical platform for educating the public, healthcare providers, and policymakers on AMR prevention and encourage best practices among all to curb the evolution and spread of antimicrobial-resistance. A cornerstone of public health interventions against AMR is infection prevention and control (IPC). Effective IPC measures can substantially reduce the transmission of resistant pathogens in both healthcare and community settings.

A Call for Collective Action to Overcome Antimicrobial Resistance (AMR)

The global nature of AMR requires international collaboration and coordinated

policy initiatives. Public health interventions are increasingly guided by global frameworks, such as the WHO Global Action Plan on Antimicrobial Resistance, which encourages nations to adopt a One Health approach that looks at human, animal, and environmental health as a whole. Recognising that AMR does not respect borders, the One Health approach integrates efforts across sectors such as human health, veterinary medicine, and environmental science.(7) Reducing antibiotic use in food-producing animals, for example, has been a major focus of public health interventions.

India's Roadmap to Combat AMR

Antimicrobial resistance (AMR) poses a major threat to human health around the world. In India, AMR poses a significant challenge due to the high burden of infectious diseases and widespread use of antibiotics. The Indian government has taken steps to combat AMR, including the launch of the National Action Plan on AMR in 2017. Following the launch of the Global Action Plan (GAP) on AMR and the request for member states to adopt National Action Plans (NAP) on AMR, India published its NAP on AMR in 2021.(8) India has begun the process of formulating the NAP AMR 2.0. The National Centre for Disease Control (NCDC), in partnership with the WHO Country Office for India and the United States Agency for International Development's Infectious Disease Detection and Surveillance (IDDS) project, has initiated a series of national expert consultations to draft this updated plan. India has consistently worked to combat antimicrobial resistance (AMR) and reduce the misuse of antibiotics through various initiatives, including the Jaipur Declaration, the implementation of Schedule H1, the launch of the Redline campaign, the establishment of surveillance systems like the National Antimicrobial Resistance Surveillance Network (NARS-Net) and the Antimicrobial Resistance Surveillance and Research Network (AMRSN), along with other policy and regulatory measures.(9) However, there is a need for greater implementation and enforcement of regulations, particularly in rural areas where access to healthcare is limited.

The role of academic institutions in India cannot be overstated. They must lead the way in AMR research, training healthcare professionals, and developing innovative solutions tailored to the Indian context. Collaboration between government agencies, academic institutions, and the private sector is crucial to advancing these efforts.

CONCLUSION

A coordinated, urgent action is essential to prevent an AMR catastrophe. This requires a holistic "One Health" strategy that considers the interconnection between human, animal, and environmental health. A multifaceted strategy having robust antimicrobial stewardship, heightened surveillance, improved infection prevention, and investment in research and development for new therapeutics and diagnostics is the call of the day. Simultaneously, efforts must focus on limiting the inappropriate use of antimicrobials in healthcare involving both human and veterinary field, and agricultural settings, as these practices fuel the rise of resistant pathogens.

The gravity of this challenge demands political will, sustained funding, strict legislation, and global cooperation. Countries must implement and enforce national action plans that align with the WHO Global Action Plan on AMR. Furthermore, the global community needs to support low- and middle-income countries, that often lack the infrastructure that are necessary for effective AMR surveillance, diagnosis, and treatment. Public health campaigns must intensify efforts to educate healthcare professionals and the public about the prudent use of antimicrobials. In the absence of urgent, global intervention, the progress of modern medicine will be undone by the silent pandemic of antimicrobial resistance. The battle against AMR is far from over, and the stakes could not be higher. This moment is to reaffirm our commitment to safeguarding the effectiveness of antimicrobials and protecting global health. Act now!

AUTHORS CONTRIBUTION

All authors have contributed equally.

CONFLICT OF INTEREST

There are no conflicts of interest.

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The authors haven't used any generative AI/AI assisted technologies in the writing process.

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