



# Antimicrobial Resistance: Prevention and Control of the Global Crisis

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## Abstract

**Background:** Over the recent decades, increasing Antimicrobial Resistance (AMR) has emerged as a huge public health problem worldwide. Left inadequately addressed, it may end up with a situation resembling pre-antimicrobial era with emergence and re-emergence of infectious diseases that had been brought under control or eradicated. The quantum of resultant morbidity and mortality and economic fallout can be massive.

**Objective:** An overview of the ongoing approaches directed at prevention and control of AMR at different levels.

**Design:** A critical review of the English medical literature on AMR with special reference to its prevention, control and containment.

**Results:** AMR is a natural phenomenon. However, its spread is boosted by irrational antimicrobial use. The malady needs to be fought on a war-footing with restrengthened emphasis on inculcating awareness amongst people at large and the stakeholders such as doctors, nurses and paramedics to shun abuse of antimicrobial agents. In keeping with the WHO's Global Action Plan, in the year 2017 India launched its own National Action Plan which is well-structured, relevant to India's circumstances and comprehensive. However, its appropriate implementation and execution at ground level warrants a big "push" developing newer antimicrobials should be a top research modality to circumvent the ineffectiveness of the existing antimicrobials.

**Conclusion:** Result-oriented endeavors towards containment of the global problem need further strengthening. Check on the irrational use of antimicrobials is mandatory to the success of various components of the programs. Furthermore, researchers need to develop newer antimicrobials on priority.

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**Keywords:** Antimicrobial resistance; COVID-19; Extensively drug resistance; India's National Action Plan; Multidrug-resistance; Newer antibiotics; Pandrug resistance; Who's Global Action Plan

## Introduction

Today, Antimicrobial Resistance (AMR) ranks amongst the 10 leading global public health problems [1,2]. Though a natural phenomenon, it is accelerated by irrational antimicrobial use in variable ways [1-4]. This causes bottlenecks in appropriate treatment of the infectious diseases. Additionally, AMR increases the risk of transmission and worsening of the infection. There is even a likelihood of re-emergence of the eradicated or controlled infectious diseases as well as high morbidity and mortality [2-4]. The currently prevalent, COVID-19 pandemic with senseless use of antimicrobials, including antiviral drugs, has further compounded the magnitude of AMR crisis [5].

The present communication aims at sharing a state-of-the-art update based on available information in the English medical literature on prevention and control of AMR with special reference to the Indian subcontinent.

## AMR in a Nutshell

### Basics

AMR occurs when a pathologic microbe no longer responds to the antimicrobial agent that was previously effective in it [1-4]. Major mechanisms involved are:

- Barrier to uptake of the drug

- Modification of the drug target
- Inactivation of the drug by an enzyme such as beta-lactamase, and
- Active efflux of the drug [6].

These mechanisms need not always be native to the microorganism. These can readily be acquired from another microorganism.

ADR is a natural phenomenon usually related to mutations by the pathogenic bugs. Irrational use of antibacterial, antiviral, antifungal and antiparasitic antimicrobial drugs facilitates its development.

AMR is categorized as

- Multidrug Resistance (MDR),
- Extensively Drug Resistance (XDR) and
- Pandrug Resistance (PDR) [7,8].

AMR causes endless difficulties in appropriate treatment of infectious diseases with both health-related and economic implications. Majority of the Antibiotic-Resistant (ABR) infections are by MDR pathogens. Amongst these, about 40% of infections are by Gram-negative bacteria like *Pseudomonas*, *Aeruginosa*, *Escherichia*, and *Klebsiella* pneumonia that are resistant to even last-line antibiotics such as carbapenems and colistin [9]. Colistin (polymyxin E) re-emerged as a last-hope pharmacotherapy [10] a couple of decades back against MDR Gram-negative pathogens due to the development of XDR. In recent years, resistance towards colistin too is begging to develop and the drug losing its shine.

**Burden**

Like any public health issues, patient-based sustainable AMR surveillance is warranted for obtaining information on AMR burden and its impacts. However, as yet, current estimates of the global burden of AMR continue to be handicapped by lack of dependable data [9,11].

Nevertheless, there is enough evidence that AMR is responsible for a massive chunk of morbidity and mortality from infectious diseases worldwide. It is estimated that AMR infectious diseases claim a minimum of 50,000 lives annually in the United States and European countries alone [1,2]. Though authenticated precise figures in this context are not yet readily available, AMR burden is expected to be much more in resource-limited countries like India.

According to conservative estimates, global AMR burden appears to be comparable to that of tuberculosis, malaria, HIV/AIDS and influenza combined together.

There is a need to assess AMR burden during the currently prevalent COVID-19 pandemic [12].

**AMR and COVID-19**

Before the COVID-19 pandemic took off from Wuhan City of Peoples Republic of China in November 2019, AMR was dubbed as one of the 10 top global public health challenges and a priority for action. Subsequently, evolving dynamics due to COVID-19 in wake of extensive antimicrobial usage (frequently without justification), are likely to have further increased the burden of AMR [5,9,15,16].

**Broad principles of AMR prevention and control:** Broadly speaking, AMR may be prevented by the following simple means:

1. Preventing infections through
  - Good personal, community and environmental hygiene
  - Immunization/vaccination
  - Balanced, nutritious and healthy diet
  - Immunity-strengthening/boosting measures: Diet rich in fruits and vegetables, active lifestyle, avoiding smoking and excessive alcohol, adequate sleep, etc.
2. Rational use of antimicrobials
  - Avoiding over prescription
  - Avoiding self-medication
  - Avoiding underdosing/overdosing
  - Avoiding half-hearted therapy.

AMR is significantly boosted by the irrational use of antimicrobial drugs and poor infection prevention, treatment and control. Naturally, it is mandatory that steps are taken at all levels of society to contain it.

Mercifully, the WHO continues to be eminently proactive in developing ways and means to contain this malady that has assumed pandemic proportion. In collaboration with its allied organizations and governments of the various countries, it has launched various initiatives, especially its landmark, Global Action Plan (vide infra).

Ever since 2015, WHO has been observing every November the World Antimicrobial Awareness Week (WAAW) with such themes as “Boosting global awareness of AMR”, “Promoting best practices among the public at large, health workers and policy makers”, “Minimizing the further emergence and spread of AMR bugs”, and “Handle with care: United to preserve antibiotics”.

The activity is contributing to sensitizing people at large and healthcare professionals about this malady and fighting AMR through rational antimicrobial therapy.

Further, the initiative, Antimicrobial Stewardship Program [17], is already on the move worldwide through its activities need further spearheading and a big push.

**WHO’s Global Action Plan on AMR**

In 2015, in order to contain the crisis of AMR, WHO and allied organizations formulated a Global Action Plan with certain objectives (Table 1).

Table 1 lists the five major objectives of the GAP.

The broad guidelines for different categories of stakeholders are:

**At individual level**

- Antibiotic use only when prescribed by a certified health professional
- Never demanding antibiotics if your doctor says you don’t

**Table 1:** The five strategic objectives of “Global Action Plan on AMR.”

1. To improve awareness and understanding of antimicrobial resistance.
2. To strengthen surveillance and research.
3. To reduce the incidence of infection.
4. To optimize the use of antimicrobial medicines.
5. To ensure sustainable investment in countering AMR.

need them

- Always follow your health worker's advice when using antibiotics
- Never share or use leftover antibiotics
- Prevention of infections by
- Regularly washing hands
- Avoiding close contact with sick people
- Practicing safer sex
- Keeping vaccinations up to date
- Preparation of food hygienically, following the WHO five keys to safer food, namely keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials.
- Choosing foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals.

#### At policy-makers' level

- Ensuring a robust national action plan to tackle antibiotic resistance is in place.
- Improving surveillance of antibiotic-resistant infections.
- Strengthening of policies, programs and implementation of infection prevention and control measures.
- Regulation and promotion of the appropriate use and disposal of quality medicines.
- Availability of information on the impact of antibiotic resistance.

#### At health professionals' level

- Prevention of infections by ensuring clean hands, instruments, and environment clean.
- Prescription and dispensing of antibiotics strictly as per current guidelines.
- Reporting of antibiotic-resistant infections to surveillance teams.
- Counseling of patients about correct antibiotics intake, antibiotic resistance and the dangers of misuse.
- Guiding patients about actions aimed at preventing infections.

#### At healthcare industry level

- Development of new antimicrobials, vaccines, diagnostics and other tools.

#### At agriculture sector level

- Giving antibiotics to animals under veterinary supervision.
- Avoiding use of antibiotics for growth promotion or to prevent diseases in healthy animals.
- Vaccinating animals.
- Promotion and application of good practices at various steps of production.

- Processing of foods from animal and plant sources.

### India's National Action Plan on AMR

Formulated in 2017 by India's ministry of Health and Family Welfare [17], this comprehensive plan, covering essentials of the WHO's GAP, has a thrust on the following six strategic priority areas:

1. Awareness and understanding through education, communication and training,
2. Strengthening knowledge and evidence through surveillance,
3. Infection prevention and control,
4. Optimized antimicrobial use in health, animals and food,
5. AMR-related research and innovation
6. Strengthened leadership and commitment at international, national and sub-national levels.

Notably, in the true spirit of the "One Health" approach, the India's plan stresses on the need for handling AMR across multiple sectors like human health, animal husbandry, agriculture and environment. Though hailed as a commendable plan, its execution at ground level has been called into question by some experts [14].

### Newer Antimicrobial Drugs: Need of the Time

Let's concede and reconcile that, despite the laudable remedial endeavors of the WHO and its affiliate agencies and governments of various countries, the AMR crisis is likely to stay in a considerable measure as a threat to modern pharmacotherapy. The fresh resistance is very likely to continue to emerge and proliferate at new sites.

According to WHO [19] an overwhelming chunk of the antimicrobials in development offer limited clinical benefit over existing antimicrobials. In actuality, about 82% of the recently approved antibiotics are derivatives of existing antibiotic classes that are known to have established drug-resistance. It is but natural to anticipate rapid emergence of drug-resistance to them.

Understandably, there is a growing need for developing newer antimicrobials, particularly the antibiotics [18], against MDR Gram-negative bacteria in hospitals and against community-acquired microbes such as causing tuberculosis, gonorrhea and urinary tract infections.

### Summary and Conclusion

AMR, a top public health problem across the globe, poses a massive challenge to the mankind. If not tackled on priority, it may lead to situations where infectious disease is left with no effective antimicrobials, the so-called "pre-antimicrobial era", thereby having a field day and ending up with widespread morbidity and mortality. Notwithstanding the fact that AMR is a natural phenomenon, its spread is accentuated by irrational antimicrobial use. The malady needs to be fought on a war-footing with special emphasis on inculcating awareness among people at large and the stakeholders such as doctors, nurses and paramedics to shun abuse of antimicrobial agents. There is also the need for developing new antimicrobials. In keeping with the sentiments of the WHO's GAP, in 2017 India launched its own National Action Plan. Though the Plan is comprehensive and ambitious, its execution in actuality has not been up to the mark, needing reorientation at ground level. In view

of the anticipated further change in dynamics of AMR following the abuse of antimicrobials during the ongoing COVID-19 pandemic, surveillance activities need to be expanded. Finally, there is a pressing need for focused research to develop new antibiotics and other antimicrobial drugs.

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