

Policy Brief: Anti-Microbial Resistance In India: Are Magic Bullets Eroded

Vishal Tikhute¹

¹Pragati Creations, India

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Abstract: Antimicrobial resistance (AMR), also known as drug resistance, occurs when microorganisms such as bacteria, viruses, fungi, and parasites evolve in ways that render the medications used to cure the infections they cause ineffective [1]. When the microorganisms become resistant to most antimicrobials, they are often referred to as “superbugs” [1]. AMR is a major public health concern because a resistant infection may kill, can spread to others, and imposes a huge cost on individuals and society [1]. Therefore, this policy brief presents a situational analysis of AMR and advocates for a multi-disciplinary approach to control AMR in India. The most recent and relevant publications on AMR in India were reviewed and analyzed to recommend a comprehensive health policy framework. The study recommends an innovative health policy framework for avoiding emergence, supporting research and development (R&D) for new drugs, and encouraging multi-sectoral coordination. Further amendments to the existing health policy with a targeted approach to prevent the growing epidemic of AMR are required. Failure to do so may cause irreversible damage with high morbidity, mortality, and disability in India.

Introduction

The antibiotics have represented a great revolution for humankind, the development after the World War II of a magic bullet (the antibiotic molecule), as imagined by Paul Erlich, the pioneer of chemotherapy, with the property to kill or inhibit the growth of microorganisms by hitting the microbial structures with low toxicity for host cells and tissues, has determined a new era in the treatment and prophylaxis of infectious disease and in the quality of human life [2].

The antibiotic era revolutionized the treatment of infectious diseases worldwide [3]. Antimicrobial usage has brought remarkable improvements in human life. Administering antimicrobial right from birth (especially for pre-term and low birth weight neonates) has increased life expectancy at birth, it has greatly reduced death rates due to communicable diseases [3], injuries and most importantly reduced incidences of fatal diseases like cholera, diphtheria, pneumonia, typhoid fever, plaque, tuberculosis, typhus, syphilis, etc. to an extent of complete eradication [3], [4].

However irrational use of antimicrobial has introduced new forms of public health challenges [1], [5] – resistance to ages long invented antimicrobial by evolving microbes; where microbes do not respond to antibiotic dosage and continues to threaten human life [1], [5]. Practices like over prescription of Antimicrobial, lack of counselling before prescribing them, and improper dosage taken by patients thanks to temporary relief are making situation worse than before [6]. Besides, fear of frequent epidemics of veterinary diseases like bird flu; as a result, on large scale Antimicrobial are administered to chickens in large poultry houses [7]. Similar situation does exist in pig farms, where irrational use of Antimicrobial indirectly releases resistant microbes into food chain [7], [8]. There is need to regulate – private partners, drug distribution systems of chemists, and provide capacity building to employees in poultry and pig farms to use Antimicrobial as per need and that only if prescribed by veterinary doctor.

Antimicrobial Resistance is a Global Threat

Advancement in contemporary medicine and surgery could not be possible without use of anti-microbial drugs [5]. They have remarkably reduced the number of cases with infections and have made it possible to introduction of complex medical interventions [9]. Replacing damaged body parts or organs, advanced surgery and care of premature or low birth weights children are some of the procedures endangered by increasing spread of resistant organisms [9]. Antimicrobial resistance (AMR) is a natural phenomenon, which due to irrational use has been accelerated in last few decades [10]. Figure 1 presents the key facts about anti-microbial resistance. Irrational use includes unnecessarily prescribing antimicrobials in low dosage than required, it also includes use of antimicrobials in unhygienic hospital settings [11]–[13]. High use of antimicrobial in the animals used for food consumption such as in poultry and pig farms is supportive for growing AMR, as it has been a global practice to introduce antimicrobials on large scale to livestock [12]. By 2030, world-wide it is estimated that the consumption of antimicrobials in the livestock sector is increase by 66.7 per cent [14]. International transportation and trading have accelerated the spread of resistant micro-organisms [11], [13], [15]. Besides, research and development of new generations of antimicrobial drugs has almost stopped [5], [16]–[18].

Health and Economic Burden

Antimicrobial resistance (AMR) augment the health problems as well as brings huge economic loss in the form of significant reduction in productive days of work by employee who are severely ill [5]. The most common resistant microbes found across India are presented in Table 1. These microbes with higher resistance rate are responsible for high morbidity and mortality due to severe infections. Further, patients infected with resistant microbes are more likely to receive therapies that are inadequate or receive the appropriate therapies in low dosages than recommended [10]. With this risk of spreading that infection increases to other organs and to entire body as well [10]. Patients infected with resistant microbes are more likely to die than those who are infected with regular microbes. Patients infected with resistant microbes. World-wide, Antimicrobial resistance (AMR) causes around 700,000 deaths annually [5], [9], [10], [19], [20]. If such pace remains there, then resistance rates increase by 40% as a result 9.5 million deaths will be there annually [19], [20].

AMR increases the cost of healthcare. Patients infected by resistant microbes needs advanced and costly care and are more probably to get admitted to a for serious health consequences [19], [20]. Aggressive antimicrobial therapies and additional laboratory tests adds extra expenditure is due excessive cost on nursing and medical care cost, as well as many other things [15], [20]. As first line drugs do not work even for common ailment, physicians need to prescribe costly second or third-line of antimicrobial drugs [10]. The situation will become worse if current picture of increase in antimicrobial resistance (AMR) remains same.

Antimicrobial resistance (AMR) cost more to society. as with more drugs are required to administer with higher cost than usual first line drugs, this will collectively increase the cost of entire healthcare [20]. Increase in cost is directly associated to treatment failure, ill-health and also it results in loss of income due to death and disability [20]–[22]. Indirect cost on seeking health care adds more to the loss in productivity as patient may remain in hospital for longer period which keep him or her away from work [23]. If no effective strategies are put in place, it may result in deaths and disability among citizens in productive age group. This will adversely affect the total GDP.

Responding to the Rise of AMR

Antimicrobial resistance (AMR) is a major public health concern for India where the burden of infectious diseases is high and consumption of antibiotics is huge and un-regulated [24]. In this regard there is need to devise interventions focused to tackle excessive or irrational use of antimicrobials and limits transmission of resistant microbes into humans, as well as R & D, are needed to control the health as well as economic burden caused by Antimicrobial resistance (AMR). This policy brief recommends the following strategies to prevent consequences of AMR in India:

1. Avoiding emergence
2. Avoiding spread
3. Encouraging R & D
4. Innovative policie
5. Multi-disciplinary approach
6. Restricting OTC

Recommendations

1. *Avoiding emergence.* Effective interventions for rationalising antimicrobial consumption include stewardship programmes to educate healthcare personnel and prevent excessive use of Antimicrobial, awareness campaigns, as well as enhanced immunisation programmes [15]. Price policies and behavioural approaches (e.g. delayed prescriptions) are increasingly considered as potential tools to decrease unnecessary consumption [15].

2. *Avoiding spread.* Large scale implementation of strategies for early detection of resistant microbial infections and enhanced hospital-based care with complete course of treatment can effectively preventing and control transmission in larger population [25]. Local physicians through CME can be trained to properly consult patients to take full course of antibiotics, they can also be trained to handle resistant cases (i.e. by referring them to higher centre of care) [26], [27]. Another strategy to increase complete use of antibiotics can be implementing the five WHO principles on hand washing, coupled with goal setting, incentives or accountability [15].

3. *Encouraging R & D.* With limited research and development pharmaceutical industries in India have been marketing for ages old antimicrobial drugs – most of which have developed resistance and proved to be in-effective [1], [5], [28]. There is need to boost expenditure on research that will develop plants based indigenous antimicrobial drugs to prevent or cure infectious conditions [29], [30]. Also, there is need to invent newer treatment regimens that can be more effective and simultaneously more cost-effective than antibiotics use [31].

According to several research studies, particularly the one conducted in Boston, after three billion years of bacterial evolution, the world's infecting bacteria had almost no antibiotic resistance genes, but a half century of antibiotic use then spread many into more than a quarter of them [32]. People or animals receiving Antimicrobial as well as countries that use more Antimicrobial have been found to have more antibiotic resistant bacteria [33]. From all we know, the progression of antibiotic resistance would appear to be ultimately some cumulative function of how many bacteria have encountered an antibiotic [34].

4. *Innovative policy supporting intersectoral coordination.* The existing national policy on antimicrobial resistance has been formulated in 2011 [35]. Antimicrobial resistance is a serious threat to global public health that requires action across all government sectors and society and is driven by many interconnected factors [5]. Single, isolated interventions have limited impact and coordinated action is required to minimize the emergence and spread of antimicrobial resistance [1]. Therefore, it is crucial to alter the existing policy to encourage inter-sectoral coordination between different ministries concerning health like – ministry of chemical and fertilisers which regulates the pharma industry, ministry of health and family welfare which monitors the quality and cost of drugs. However existing policy do not encourage practice of inter disciplinary work. Hereby we recommend the due policy change in that will ultimately favours the inter sectoral coordination and also encourages the linkages between the existing research and development and drug procurement through proper channel. Also considering cost component, there is strong need to re-design pharmaceutical policy that will provide free and quality drugs, so that over the counter drug purchase can be controlled and this will be a greater measure to combated anti-microbial resistance.

5. *Multidisciplinary approach to control progression of antibiotic resistance.* Antimicrobial resistance (AMR) is a global health and development threat [5]. It requires urgent multi-sectoral action in order to achieve the Sustainable Development Goals (SDGs) [5]. To control this serious public health issue and to save human and animal lives; multi-disciplinary approaches across health care settings as well as

environment and agriculture sectors are required [36].

Use of Antimicrobial in food animal production in inappropriate over dosage has aggravated the issue [8]. Also use of antimicrobial should be limited for the treatment of severely infected animals' birds and should not be used for non-therapeutic purposes like - convert feed to muscle [37], growth promotion [38], or to cope up with load on transportation and situation of crowding and poor hygiene [37], [38]. Wherever possible other modes of preventing infection should be adopted. Third generation cephalosporins, fluoroquinolones, other antimicrobial used for controlling diseases, should be limited for treating refractory infections in individual animals [5]. Policy recommendations from FAAIR can be adopted to limit antimicrobial administration to animals only on prescription by a veterinarian [39]. To assess the human health risk and inform public health policy, quantitative data on antimicrobial use (in-depth measurements) in agriculture should be made available by pharmaceutical manufacturers, importers and end users [8], [40], [41]. Regulatory agencies should consider the ecology of antimicrobial resistance –the processes of spread and complex interactions between bacteria – both pathogens (disease causing) and non-pathogens (commensals), food animals, humans, and their environments [39]. Surveillance programs for antimicrobial resistance should be harmonized to permit integrated analysis of human and animal data [39].

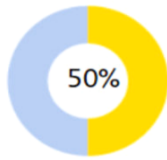
6. Restrict over the counter purchase (OCT) of drugs and controlling hospital acquired infections. India has one of the highest rates of antimicrobial resistance (AMR) worldwide [42]. Despite being prescription drugs, antibiotics are commonly available over-the-counter (OTC) at retail pharmacies [42]. Further rampant urbanization and unregulated industrialization have failed to provide quality of life to the overall human population [43], resultantly most of Indians live in poverty. All these factors contribute to the lack of knowledge about proper use of medicines among urban poor population and inadequate guidance to use antibiotics by physicians.

Some of the unhygienic practices at hospitals and health care facilities also contributes to AMR due to hospital acquired infections [36]. Therefore, restricting OCT by pharmacists and a few precautions for hospital-based workers such as —practicing simple control measures such as the hand hygiene changing gloves after examining the patient, can be monumental in controlling the spread of resistant bugs, as well as hospital-acquired infections [37], [44]. There are few studies that shows that only 30 per cent of doctors and health workers do hand wash after they examine each patient [45]; this increases the spread of resistant microbes to other ill patients with poor immunity. The current policy brief therefore recommends the policy change in existing guidelines that assures the standard operating procedures are being practiced among health care workers in health care facilities that ultimately controls hospital acquired infections and spread of resistant microbes.

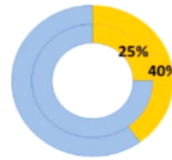
Figures and Tables

Figure 1. Key facts about anti-microbial resistance

Key facts



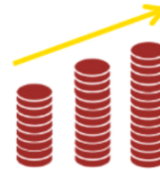
Antibiotic-resistant bacteria are highly prevalent. Up to **50% of infections in All countries may be resistant** to first-line antibiotics



Globally **25%** of countries have **national policies** to tackle AMR and **40%** have **infection and control programmes**



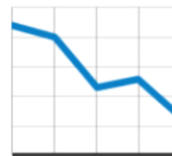
Patients with AMR have **2-3 times higher mortality and risk of complications** (e.g.: local progression of disease and sepsis)



AMR treatment costs **additional 10-40K USD** per patient and **extra 23 billion USD** for **healthcare systems**



About **50,000 deaths** may be caused each year by antibiotic-resistant infections



Even by accounting for extra healthcare costs, by **2050 up to 2.9 trillion USD of GDP** could be **lost** at different regions of world just due to AMR, at current resistance rates

Source: OECD 2015

Table 1. Antibiotic resistance rates of various organisms in India

Location (year of study)	Organism	Resistance rate (%)
Delhi (2007)	V. cholera 01 [46]	96
Kolkata (2007)	MBL producing bacteria [47]	43.3
Lucknow (2007)	Klebsiella spp [48]	98.28
Puducherry (2008)	Staphylococcus isolates [49]	72.34
Nagpur (2009)	MRSA [50]	4.16
Various centers across India (2010)	P. aeruginosa [51]	42.6
Mangalore (2010)	Enterococcal strains [52]	16.67 to 42.86

Note: Table derived from Kumar, et al (2023). [28] Sources for individual studies are mentioned as superscript in the column for respective organism. MBL = Metallo-beta-lactamase.

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