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Antimicrobial resistance: A public health challenge

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ABSTRACT

Antimicrobial resistance has become a global concern. Though an evolutionary phenomenon, it is promulgated by faulty human behaviours. It is a growing concern ever since first reported in 1940s. Today, a plethora of newer generation antimicrobials have become ineffective against previously susceptible organisms. This is a huge challenge for health care managers all across the globe, compounded by the "discovery void" in the field of development of new antibiotics. If proper steps are not taken presently, the lurking fear of reaching a therapeutic dead end will become a reality. This paper aims at describing the pandemic of AMR from a public health perspective and suggesting strategies to deal with it in an effective and collaborative manner.

Introduction

Antimicrobial resistance (AMR) is defined as resistance of microorganisms to an antimicrobial against which they were originally sensitive. Though a natural evolutionary phenomenon, it is accelerated by the misuse of antimicrobial medicines and poor infection control practices. Newer and newer antibiotics have been challenged with the threat of resistance over past few decades. The global spread of AMR is lubricated by increased mobility of patients or carriers and hence, that of the resistant bugs. AMR is a major threat to the gains made in public health with a potential of even reversing such gains. It affects a myriad of stakeholders such as individual patients, healthcare providers, pharmaceutical industry and society at large. A concentrated effort at all levels of health care is the need of the hour to tackle the menace of AMR.

A growing concern

Resistance to sulphonamides and penicillin was reported as early as 1940s followed by resistance to other antimicrobials subsequently. Today, almost all major infectious diseases of public health concern are faced with the scourge of AMR.

The WHO estimates that in 2011, out of the total 12 million TB cases worldwide, 630,000 were MDR. Extensively drug-resistant TB has been identified in 84 countries.[1] As the world contemplates on dealing with resistance to antimalarials such as chloroquine and sulfadoxine–pyrimethamine, *Plasmodium falciparum*'s resistance to artemisinin derivatives is already knocking on the doors in South East Asia.

The incidence of hospital-acquired infections caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) or multidrug-resistant Gram-negative bacteria is steadily rising all over the world. Shigella is showing

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a widespread resistance to Ciprofloxacin, the only antibiotic currently recommended by WHO for treating infections by it. For gonorrhoea oral cephalosporins are reckoned as "last-line" of defense, against which resistance is increasing worldwide. By 2012, virtually all circulating Influenza A viruses in humans were resistant to amantadine and rimantadine.[1]

The "Plasmid encoding carbapenem resistant metallo beta lactamse", known as the New Delhi superbug, was detected in December 2009 in a Swedish patient in India. Within a few months, it was reported from many countries. Apart from the above, Vancomycin Resistant Enterococci (VRE), Extended Spectrum Beta Lactamase (ESBL) producing Enterobacteriaceae, Carbapenem resistant *Klebsiella* (CRK), pan drug resistant (PDR) *Pseudomonas* and *Acinetobacter*, antifungal resistant fungi and antiviral resistant viruses are playing a havoc in treatment facilities around the world, causing deaths and delaying healing.

Antibiotics are inseparable from medical procedures such as heart surgery, diabetes related chronic infections, post organ transplantation, aggressive immune-modulating therapy for auto-immune diseases such as rheumatoid arthritis, as well as for several malignancies. With changing lifestyles and ageing populations, chronic diseases which are currently treated through surgery, are ought to rise that would be impossible without effective antibiotics.

Suggested cause of this pandemic

In India, studies suggest that antibiotics are often prescribed in irrational ways such as incorrect indication, dose, frequency, or duration. Overprescribing and overuse are seen in all settings: public and private hospitals.[2] Literature reveals that 45–80% of patients with symptoms of acute respiratory infections and diarrhoea are likely to receive an antibiotic when the cause is viral.[3,4]

Antibiotics are also over-used in agriculture, livestock rearing and fishing industry. Resistant bacteria can be transferred to humans through contact with livestock, through the food chain, and through wastewater from these operations, as well as wastewater from hospitals and pharmaceutical plants.

The phenomenon is also affected by the misconceptions, that antibiotics are a panacea for all infections, among physicians as well as in the general populace.

Key public health issues relating to AMR

AMR hampers the control of infectious diseases

AMR delays treatment, rendering patients infectious for longer time, increasing the risk of spreading resistant microorganisms to others. From the public health perspective, the patient acts as a reservoir of infection for a longer period thus putting at risk more members of community and health care workers. The longer duration of illness and treatment increases health-care costs and the economic burden to families and societies. A 2010 study in Vellore compared the overall cost in patients when empirical antibiotic therapy is effective (causative bacteria being susceptible) compared with those in whom it was ineffective (bacterial resistance to the empirical antibiotic). The median cost of treatment in the 'susceptible' group was Rs. 8437 while that for the 'resistant' group was Rs. 13,652. Apart from this direct increase in cost of higher antibiotics, associated expenses like longer ICU stay, repeated Lab culture and sensitivity tests and ward charges put even more financial burden on the patients or the health care system. Overall, an individual had to spend around Rs. 20,959 more if he/she belonged to the 'resistant' group.[5]

As of August 2013, an Indian agricultural worker (majority of national workforce) earns a daily wage of Rs. 224 as per Labor Bureau, Govt of India. A difference of Rs. 20,959/- per patient in overall cost between resistant and susceptible groups therefore translates to approximately 90 days of income. According to WHO, the death rate for patients with serious infections treated in hospitals is about twice that in patients with infections caused by non-resistant bacteria.

AMR threatens a return to the pre-antibiotic era

Many infectious diseases risk becoming untreatable and uncontrollable, which could derail the progress made towards reaching the targets of the health-related United Nations Millennium Development Goals set for 2015. A report from WHO SEARO shows that shortly after the emergence of multidrug resistant *Salmonella typhi* in this region, death rates approaching 10% were reported, close to 12.8% of the pre-antibiotic era.[1]

We now face a dramatic challenge resulting from two combined problems. First, microorganisms are becoming extremely resistant to existing antibiotics. Resistance can be combined with virulence, acting as a potentially deadly duo, as observed in the recent large epidemic outbreak of *Escherichia coli* 0104:H4 in Europe in 2011. Second, the antibiotic pipeline has become extremely dry, especially for Gram-negative bacteria. The fear of clinicians facing a therapeutic dead end in the treatment of several bacterial infections might soon become a reality. This worrisome situation will lead us back to the pre-antibiotic era of the 1930s and early 1940s.

No new antibiotic discoveries

Our present generation antibiotics are the result of scientific discoveries that happened decades ago. A timeline of dates of discovery of distinct classes of antibiotics (and not those of market introduction) illustrates that there have been no successful discoveries of new classes of antibiotics since 1987.[6] A major reason for the same may be that chronic illness medications like those for hypertension and diabetes form more lucrative business propositions for the pharmaceutical companies as compared to newer antibiotics, because of their prolonged usage in a given patient and no issues of resistance. Also, smaller pharmaceutical companies cannot afford the cost of meeting complex requirements for clinical trials involving antibiotics. This compromises the development of many promising new agents.

AMR poses a significant challenge to Primary Health Care

Majority of the Indian population, especially in the rural areas and urban slums, is dependent on grass root Government