

Editorial:**Antimicrobial resistance - have we scored a self goal?**

With limited resources in India, emerging antimicrobial resistance (AMR) is a grave underrated threat staring at the health care professionals in their battle against infectious diseases. Further, by virtue of the size of our population, the infectious disease burden of easily preventable diseases like pneumonia, meningitis and diarrhoea is being compounded by AMR resulting in increased annual health costs including increase in disability-adjusted life years. Though AMR is a global phenomenon, this is a greater problem in our country due to unregulated use of antibiotics. Multidrug-resistant (MDR) bacteria increase the cost of treatment by prolonging hospitalization in an already ailing patient.¹

In fact, it needs to be appreciated that unregulated use of any drug in the veterinary discipline also has an impact on human life directly or indirectly by altering the ecosystem. This aspect was never considered in the full perspective it deserved till recently. The unregulated use of antibiotics in the veterinary discipline has been aptly emphasized by an innovative study observing large scale abuse of antibiotics in the poultry sector used for human consumption in the national capital region of Delhi.² Though AMR is gaining the attention of all stakeholders (health care professionals, hospital administrators and policy makers) in India, an important catalyst for increased awareness about AMR was the ‘discovery’ of New Delhi metallo- β -lactamase-1 (NDM1). Over the years, this ‘headline news’ in the international and national media was splashed all over the world bringing ‘negative’ publicity for our country.^{1,3}

The newly released World Health Organization (WHO) document on “Antimicrobial resistance: Global report on surveillance 2014” has presented a comprehensive surveillance data of AMR from 114 countries out of 129 member states of WHO. The country-level data was mainly obtained from sites in European and American continent. The obvious reason being robust surveillance programs followed as a protocol in their health care settings. The data pertained for a selected set of nine bacteria-antibacterial drug combinations of public health importance.

The key findings include more than 50% resistance to third generation cephalosporin reported for *Escherichia coli* and *Klebsiella pneumoniae*. The consequence of these alarming observations implies that carbapenems have to be administered to treat these patients. Carbapenems are expensive antibiotics and have obvious economic implications in a resource-limited setting like India. Furthermore, the more startling observation in this surveillance report that *Klebsiella pneumoniae* resistant to carbapenems has also been reported up to 54% isolates, thereby further underlying the gravity of the situation.⁴ Similarly, more than 50% of isolates were reported methicillin-resistant *Staphylococcus aureus*. As a result, therapy for suspected *Staphylococcus aureus* infections would have to include the newer antimicrobial agents like linezolid, which need a more stringent monitoring of their side effects. Of course, increasing cost of therapy is an obvious offshoot of this dilemma.⁴



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The overall implications of this report signify that the treatment of common community-acquired infections like urinary tract infections, pneumonia and wound infections would become more complicated both therapeutically and financially. The important message from this WHO report, which has declared AMR a major global threat, for health care professionals is 'loud and clear' thereby meaning that if the situation is alarming in these developed countries with stringent control on the use of antimicrobial drugs, the situation in resource-limited nations like India would be worse if not the same.

As far as Indian scenario of AMR is concerned, observations lately reflect a dismal picture. NDM-1 is a relatively recently discovered metallo-beta lactamase (MBL). This novel MBL belongs to the carbapenemase group. NDM-1 was first observed from a foreign patient in isolates of *Klebsiella pneumonia* and *Escherichia coli* on his return to his parent country. The patient was treated in a New Delhi health facility.⁵ Later this carbapenemase has been reported from 40 countries encompassing all continents, except South America and Antarctica.⁶ Carbapenems are among the few useful antibiotics against MDR extended beta-lactamase (ESBL) producing gram-negative bacteria, especially Enterobacteriaceae.⁷ This led to widespread concern regarding the loss in efficacy of this very useful antibiotic group. In fact, NDM-1 was also reported from drinking water and seepage drainage systems from New Delhi resulting in panic as well as introspection in the scientific community.⁸

Recently, novel RmTF enzyme has also been found in association with NDM-1 in Enterobacteriaceae group, which has additional resistance to tigecycline and colistin. The fact that these two drugs which are the last resort in the fight against serious bacterial infections are also becoming resistant should be a cause of concern to all clinicians.⁹ In last few years, studies have also demonstrated high rates of resistance of pathogenic common gram-negative including *Acinetobacter*, *Pseudomonas*, *Salmonella* and *Escherichia coli*. Some of these organisms are known to cause life threatening nosocomial infections¹⁰⁻¹². Varied MDR resistance patterns have been reported in uropathogenic *Escherichia coli* from Kolkata in hospitalized patients.¹³

Over the last two decades, resistance to *Salmonella typhi* has increased exponentially. MDR *Salmonella typhi* strains to ciprofloxacin and ceftriaxone has been reported in patients with enteric fever. The first line antibiotics for enteric fever like ampicillin and cotrimaxazole have already become resistant for use in *Salmonella typhi* infections.^{14,15} High resistance to fluoroquinolones in *Salmonella typhi* has already been reported, thereby limiting the armamentarium for treatment of enteric fever.¹⁶ The WHO document has also confirmed the worldwide presence of resistant strains of nontyphoidal *Salmonella* causing diarrhea.⁴

Staphylococcus aureus, especially methicillin-resistant staphylococcus aureus (MRSA) has always been the Achilles heel in the treatment of serious nosocomial infections. In fact, when MRSA was increasing globally, vancomycin was introduced to tackle this problem. Thereafter, vancomycin-resistant enterococci have become a major predicament.¹⁷ In the intensive care unit of the largest government tertiary care hospital in North India, almost a quarter of patients were infected with *S aureus*.¹⁸ The quantum of the problem with the systemic antibiotics can be assessed by a simple fact that resistance is developing in a topical antibiotic for MRSA. Mupirocin has been an excellent drug for treatment of skin and soft tissue infections as well as eradication of nasal carriage of MRSA, especially in health care personnel. Recently, it has been observed from south India that

screening for mupirocin resistance in MRSA is warranted as these pathogens are developing resistance to this topical antibiotic also.¹⁹ It is extremely obvious that the problem of evolving AMR cannot be tackled by developing newer antibiotics. The pathogens with their ‘Darwinian’ instincts evolve through metamorphosis to ensure their survival!

Broadly, to overcome the crisis situation in AMR, three levels of intervention are urgently required at the microlevel and macro level of health care. The microlevel intervention includes at the level of the clinician and health care facility whereas the macrolevel includes government policy, operational research and medical education.²⁰

As it is said “Charity begins at home”, clinicians need to realize that the immediate ‘solution’ to the exponential evolution of AMR is the appropriate use of antibiotics with a rational approach. Unfortunately, antibiotics are prescribed as ‘fast food’ cure for many infectious diseases (many are viral in etiology) without introspecting the long term implications of this approach. Inappropriate use of antibiotics in improper dosages have a double whammy effect. Not only they increase the development of resistance, they also increase the health expenditure. This is akin to scoring a self-goal used in the football parlance which was the sporting event of the world this year!

Each health care facility should have an antibiotic surveillance programme under an active infection control committee and microbiology department. This will help the clinicians in prescribing appropriate antibiotics to their patients. Moreover, antibiotic usage should also be audited in the health care facility (wards, intensive care units and outpatient departments). Based on the surveillance, antibiotic policy (hospital antibiogram) should be a mandatory requirement in a health care facility. The role of specimen culture (blood, urine, any other relevant fluid or site) and antibiotic sensitivity testing needs to be ingrained in our patient care ethos so that the antibiotic therapy can be tailored as per the culture and sensitivity testing report.

It is also important to appreciate that stringent guidelines and policies need to be notified by the government, otherwise the usage of antibiotics remains in the realm of “empirical” therapy without any scientific basis. Recently, the National Policy for Containment of Antimicrobial resistance has been proposed.²¹ Of course, a stringent implementation of this policy is important for its success. As the use of antibiotics in livestock and poultry is also increasingly being appreciated in the development of AMR in our country, guidelines to regulate their use also needs to be incorporated in our laws in a robust manner.

Another initiative to tackle the menace of AMR at a national platform has been a joint meeting of the medical societies in India, eminent policy makers from central and state governments, representatives of World health organization, National Accreditation Board of Hospitals, Medical Council of India, Drug Controller of India and Indian Council of Medical Research held at Chennai last year and has come to be known as “Chennai declaration-A roadmap to tackle the challenge of antimicrobial resistance”.²²

Global Antibiotic Resistance Partnership (GARP), funded by the Bill and Melinda Gates Foundation, is an important initiative to delay the spread of AMR in five low-and middle-income countries (India, Kenya, South Africa, Vietnam and China). A critical path is proposed for the recommendations being formulated by this group in India.²

Operational research in non-conventional antibiotics is another exciting field in its nascent phase. Nanotechnology using silver nanoparticles is an effective antimicrobial agent and is being tried to tackle AMR.²³

Moreover, the importance of AMR needs to be incorporated in a more structured fashion during the medical training of all types of health care professionals, especially in undergraduate and postgraduate training of doctors.

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