## ANTIMICROBIAL RESISTANCE: ARE WE READY TO FACE THE CALAMITY?

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It was a busy day when I received a call from the administration of the hospital that the external auditors are enquiring about a patient's record who was given sixty four injections of Meropenem in December 2017. I was surprised how this got highlighted as it was almost two years old record. The treatment chart was traced which was of an 18 years old male, hawker by profession with extended drug resistance (XDR) Salmonella infection. The cost incurred for this therapy was 140,000 Rupees. What's an XDR organism? How one get it? And what will happen if we get more patients like this? were the simple questions by the auditor. Never concerned with the associated mortality and morbidity he was focused on his domain and was worried that without finances it will not be possible and this will increase the cost of care many fold.

Antimicrobials discovery has revolutionized the whole medical practice and are considered one of the strongest weapons to combat life-threatening infections. Not only humans but animal and plant health also changed dramatically. Unfortunately, this precious resource was not taken care of properly and the feeling of safety with this powerful tool is lost. We now live in an era where chances are very high that one might be having a resistant organism which can spread to other people resulting in antibiotic resistant infections.

Antimicrobial resistance (AMR) is defined as the microbial ability to beat or overcome the medications that are supposed to destroy or suppress these microbes. Currently, it is feared as a greatest threat to public health worldwide. Though, AMR, is a naturally occurring phenomenon, but it is the misuse of antibiotics in animals and humans which is fuelling the process. If no preventive measures are taken in time, it can reach to

any environment and affect any human being, animal or plant, of any age, in any country.

The mechanisms used by micro-organisms to produce resistance against antibiotics can be classified into the following 04 categories: 1) reducing the permeability and penetration of antimicrobials into the cell; 2) once gained entry into the cell, their expulsion using efflux pumps; 3) modification or degradation of antimicrobial agents and hence their inactivation; and 4) changes in the targets for antimicrobial drugs inside the micro-organisms<sup>1</sup>. The various contributing factors that create a suitable environment for the rapid development of resistance are; lack of surveillance of resistance development, poor quality of available antibiotics, clinical misuse in all the domains (over use, under use, under dosing and ease of availability of antibiotics), suboptimal point of care diagnostics, poor hospital-level regulations and infection prevention/control practices, sub optimal preventive medicine/vaccination and where available low intake and excessive antibiotic use in food-producing animals, environmental contamination and travel<sup>2,3</sup>.

Pakistan is not an exception and is actually facing a crisis like situation due to AMR. Excessively registered products are amongst the important root causes. Other serious concerns include: 18% of the advertisements are "unjustified or misleading"; only 15% of promotional brochures meeting WHO criteria; self-medication in 51% of cases; and the presence of more than 600,000 quacks in Pakistan. Moreover, Pakistan has one of the highest numbers of drugs prescribed (>3 drugs/patient) and antibiotics are prescribed to 70% of patients. The magnitude of drug overuse for expensive antibiotics and specifically third generation cephalosporins was found

to be higher in public hospitals as well as among general practitioners (GPs)4-7. Centre for Disease Control, USA in its report "antibiotic resistance threats in the United States 2019" has classified the organisms with AMR into 4 categories i.e.; urgent, serious, concerning threats and watch list. As AMR can spread through people, animals and environment, therefore, AMR is considered as One Health challenge; the health of people being connected to the health of animals and the environment. Progress in health care, life expectancy and food production are adversely affected by threats related to antibiotic resistance. Aggressive measures, in the form of infection prevention, judicial antibiotic use with resultant slowing of the development of resistance and stopping the spread of resistance when it does develop, are required to address this threat. Most of the advances made in the field of medicine like oncology, organ transplants, prosthesis and medical devices placement are at risk due to the phenomenal rise of AMR. These and many other medications will fail if the spread of AMR is not controlled by identifying the gaps and implementation of a strong action plan8.

The World Health Assembly (WHA) recommended a global action plan under One Health concept in 2015 regarding establishment of a well-coordinated, collaborative and sustainable AMR containment system with measurable outcomes. All the member countries are supposed to develop a National Action Plan for AMR containment in line with the strategic priorities outlined by WHA as per the individual country needs. The main objectives of this plan are: 1) utilizing education, training and effective communication to improve awareness and understanding of AMR; 2) undertaking research and surveillance to strengthen the knowledge and evidence base; 3) taking infection control measures, improving hygiene and sanitation to decrease the incidence of infection; 4) optimizing the use of antimicrobials in human and animal health; and 5) economic development for sustainable investment taking care of the needs of all countries as well as increase investment in new medicines, vaccines, diagnostic tools and other interventions9.

One of the integral interventions for the control of AMR in healthcare settings is an antibiotic stewardship program. Only a few hospitals in the country have functioning antibiotic stewardship activities. The major limitations include lack of awareness and shortage of human resources. Similarly, diagnostic stewardship is also the need of the day because unnecessary, untimely and inappropriate investigations are requested or incorrectly interpreted with potential harm to the patients, promotion of wrong practices and AMR. Furthermore, infection control and prevention (IPC) remains one of the key elements in controlling AMR, by limiting the transmission of resistant organisms. In Pakistan, infec-

tion control (IC) practices are not universal and even where present, are suboptimal. Only a limited number of large private and public hospitals have functional infection prevention and control (IPC) programs. Local experiences show health professionals in the country lack basic IC knowledge, there is a shortage of IC expertise at a national level, dedicated IPC programs are not a priority in hospitals with budgetary restraints and healthcare facilities face a shortage of IC supplies and isolation beds. All these can be addressed easily by changing the health care priorities and regulatory models and investment in the HR with proper budgetary allocations.

In case of general public and patients, the hunger for information from those affected will be fed no matter who feeds them and through what ever means, we must communicate with them quickly, frequently and with empathy. Multiple factors are responsible for their behaviors about antimicrobials which include structural components like access to medications and adequate medical services, narratives, social mechanisms, various myths regarding the power of antimicrobials and nature of the available information. Such information may not be appropriately formatted and may have business driven models. Similarly, the information provided to the public may not be used effectively due to lack of the requisite skills.

In summary, the evidence is suggestive of existence of gaps among the public and healthcare providers regarding knowledge and understanding of antimicrobials and AMR. With the global prevalence of apathy and alerts fatigue, messages comprising case studies of affected people may prove more effective especially when delivered through trustable means <sup>10</sup>. All the health care workers and facilities have a moral obligation to collect the data of AMR and share with the regional and national public health authorities for a timely response and not to miss any opportunity to educate our health care related colleagues and the public.

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## ANTIMICROBIAL RESISTANCE: ARE WE READY TO FACE THE CALAMITY?

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