

## Antibiotic Resistance Antimicrobial Resistance (AMR) in post COVID era 'Second Pandemic' Slowly Moving Across the World

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Antimicrobials are the drugs used to prevent and treat infections caused by bacteria, viruses, fungi and parasites in humans, animals and plants. Their use is increasing globally, across the species with desired beneficial effects when used judiciously. On the other hand, their overuse for prolonged period of time in unjustified doses, duration and indication is leading to drug resistance. Consequently, these agents are becoming ineffective rendering the management of infections increasingly difficult or impossible. In a way, drug resistance is largely a man-made problem and it can be tackled with good prescribing practices. Growing trends in the emergence of AMR is considered a major threat to global health and economy. World Health Organisation (WHO) considered it one of the top 10 global health threats.

O'Neill J. et al published an excellent review on antimicrobial resistance in 2016. In this report, they studied the global trends, track the possible result of drug-resistant infections on health and economy globally if issue unaddressed and gave recommendations to tackle this menace.<sup>1</sup> Even at the time of collection of data (2014-16), AMR was directly responsible for death of 700,000 deaths. It was estimated that if the trends went on un-addressed, world may see loss of 10 million lives by 2050, overtaking diabetes, heart disease and cancer as the leading cause of death in human and an approximate cost reaching 100 trillion USD. No country or region is immune but the low and middle-income countries are likely to suffer most.

Although some experts and researcher had doubts about these estimates,<sup>2,3</sup> WHO and most of other authorities agree that the spread of AMR is a real, seriously growing global threat to be addressed by a well-coordinated global action plan.

A recently published systematic analysis confirmed rising trends. Data from 204 countries and territories showed an estimated 1.27 million deaths caused directly by AMR worldwide, and 4.95 million deaths were associated with AMR, in 2019, higher than the mortality of HIV/AIDS and malaria which have been estimated to be 860,000 and 640,000 deaths, respectively, in same year.<sup>4</sup>

After the start of COVID -19, in 2020 hospitals have to cater a different patient population. Higher number of seriously ill, aged patients with comorbidities, who needed intensive care for a prolonged period. Without a clear guideline to deal with the newly emerged infectious outbreak, multiple therapeutic agents were used. These agents included many antibiotics, antiviral and sometimes antifungal agents used empirically. Many new and old drugs were also used on experimental basis. Additionally, all the seriously ill patients received corticosteroids as recommended in guidelines and many of the patients required invasive devices, equipment or catheters etc. for prolong time. All these are risk factors for development of drug resistance. To make the situation worse, due to increased burden of seriously ill patients, many temporary/makeshift ICUs have to be started with inadequately trained staff and compromised preventive measures. Lack of proper personal protective equipment for the health care workers and patients and their carers promoted the spread of infection in hospitals and communities.

Evidence has proved that the single most important risk factor for the development of drug resistant bugs is prolonged use of broad-spectrum antibiotics. Although Viral aetiology of Covid -19 was established right from start of pandemic, but still majority of patients received antibiotics. Langford and colleagues<sup>5</sup> performed a systematic meta-analysis of studies published in English language on this subject from 2019 to April 16, 2020. Out of 1308 studies, 24 qualified for inclusion into this meta-analysis. A total of 3338 patients in the 24 studies were evaluated for acute bacterial infection. Overall, only 6.9% (95%CI 4.3-9.5%) had bacterial infection (either at time of presentation or acquired as secondary infection during course of disease) while 71.9%, (95%CI 56.1 to 87.7%) received antibiotics. This unjustified excessive use of antibiotics in Covid patients with a threat to development of drug resistance has been widely reported in other publications as well.<sup>6,7,8</sup>

Unfortunately, social media also played a negative part. Many drugs including some antibiotics have been promoted as magical cures without any evidence. Many world leaders and even some health professionals also become a tool in spreading incorrect information which led to self-medication.

Relevant authorities failed to counter this false campaign resulting in over the counter sale of such agents without prescription. Azithromycin is one of the many such agents which gained undue reputation as curative and preventive therapy. Demand was so high that many pharmaceuticals (more than 20 companies in Pakistan) started manufacturing and marketing azithromycin. Macrolides are already known to have high level microbial resistance,<sup>9,10</sup> what havoc this excessive usage will play is within everyone's imagination. Remember, this unjustified use is not limited to one antibiotic, all new and old, narrow and broad-spectrum antibiotics have the same fate.

Exact scale of AMR in post Covid era is yet to be seen. It must be noted that this unjustified use is not limited to antibiotics only, same hold true for other antimicrobials like antifungal, antiviral and others. Authorities consider AMR, a 'Second Pandemic' which may speed up the emergence of drug resistance. If corrective measures are not taken, the estimated yearly mortality of 10 million1 due to AMR in 2050 may be seen much earlier. No stone should be left unturned to halt this deadly second pandemic. Authorities must focus on health care workers for judicious use of antimicrobial agents but must not ignore the health education of general public and media. It is important to convey all to learn and comply the principles of healthy life and be a safe patient. Avoiding the development of disease and prevention of its spread to others is responsibility of every member of society. Covid -19 pandemic has proved beyond doubt that only coordinated efforts by all can help tackle such disasters. Let's not be complacent, and continue in same manner we did during pandemic to avoid AMR catastrophe.

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