Misuse of Antibiotics in COVID-19 Era

The emergence of SARS-COV-2 pandemic in late December 2019 has taken the health care community around the world by storm. The race to medical breakthroughs for COVID treatment has shifted focus from other public health concerns that were at the forefront in the pre-COVID era. Among these are the alarming developments in antimicrobial resistance; a crisis in its own right which Larry Kerr, co-chair of the transatlantic task force on antimicrobial resistance describes as 'a multitude of small fires that are much less visible than the single massive firestorm that is the covid-19 pandemic.[1] The first wave of the pandemic marked by diagnostic limitations and uncertainty about the pathophysiological nature of the virus saw a gigantic upsurge in the indiscriminate use of broad-spectrum antibiotics that has not declined even as we approach the end of a year. The scarcity of sufficient data detailing antibiotic prescription to Covid patients during the pandemic masks the probable long-term consequences of this lapse in antibiotic stewardship.

Based on limited data, we know that 70% of hospitalized COVID 19 patients receive antibiotics although only 8% had a bacterial co-infection and only 16% later developed a secondary bacterial infection.[2] The unpredictable course of the disease in addition to the high workloads in hospitals and increased admissions and antimicrobial prescriptions for respiratory tract infections has undoubtedly contributed to exacerbation of difficulties already present in implementation of antibiotic stewardship. Guidelines published by different authorities, especially during the initial period, contain varying recommendations thus creating a degree of uncertainty about best practice. These recommendations also lacked a solid evidence base with the use of antibiotics being recommended in severe disease by European and Italian guidelines and only for critical patients under Chinese guidelines.[3]

In Pakistan, as in other places around the globe, the documentation of the selection and course of antibiotic therapy has been largely ignored. Of more than 900,000 cases thus far confirmed in Pakistan, only 2.1% deaths and a 90% recovery rate showcase a wide mismatch between infectivity and serious disease in the country.[4] Since many patients have mild disease, the majority must have only passed through Pakistan's weak primary care system. With already a pandemic of antibiotic usage in Pakistan, highly broad-spectrum antibiotics are being prophylactically prescribed to all patients with any respiratory tract symptoms in the last 1 year. It must be acknowledged that antibiotic prescription is often also a patient's demand, fuelled by the misinformation on social and mainstream media. Poor regulation of antibiotics and easy access to all kinds of information gives way to self-medication.

A retrospective observational study of COVID-19 patients from March 2020 to April 2020 in New York City shows that 70% of all admitted patients received antibiotics among which were doxycycline, azithromycin, levofloxacin, ciprofloxacin, ceftriaxone, cefepime, intravenous vancomycin, and piperacillin/tazobactam. The use of triple therapy was also very common with 70% of patients receiving >3 classes of antibiotics together (β-lactams, glycopeptides, macrolides, or tetracyclines).The study also shows 100% of patients with MDR strains had previous history of broad spectrum antibiotic use within the same hospital stay. The same institute saw the susceptibility of *Klebsiella pneumoniae* to Cephalosporins, Ciprofloxacin and Meropenem fall by 10% from 2019. The number of *Enterobacteriaceae* isolates resistant to Carbapenems also increased in number compared to previous year.[5] The ramifications of the liberal use of drugs classified as 'critically important antimicrobials' by WHO such as Azithromycin, Vancomycin, Carbapenems, Tigecycline, Ceftriaxone and Linezolid may well be felt during the pandemic. The development of resistance against these drugs reduces the survival of COVID patients with secondary bacterial infections due to prolonged hospital stays and immunosuppressants like Tocilizumab. The long-term implications of exacerbating one crisis while averting another will cost lives and resources, for example Azithromycin use in Covid pneumonia has not shown definite benefits yet but uninterrupted use of the last resort antibiotic for XDR salmonella can cause a major crises in the management of this highly resistant bug in the future.

The United Nations report for urgent action to avert the AMR crises, published before the COVID pandemic hit, declares that AMR could force up to 24 million people into extreme poverty by 2030 and drug-resistant diseases could cause 10 million deaths each year by 2050.[6]

The need for responsible antibiotic prescribing practices is greater now than ever. Strengthening antimicrobial stewardship programmes, especially in the midst of epidemics and pandemics when antibiotic misuse is rife, is extremely important in salvaging the hard work of decades.

Liew et al describe the Antibiotic Stewardship Program which was fully operational at Singapore General Hospital during the COVID pandemic. Daily electronic audits of selected broad-spectrum antibiotic prescriptions (Carbapenems, piperacillin-tazobactam, ciprofloxacin and levofloxacin) were performed to assess suitability in terms of indication, route, duration and choice by the pharmacy services in collaboration with Infectious Diseases team. The result was decreased duration of antibiotic therapy and shorter hospital stays where ASP intervention was accepted. This also alleviated the problem of overcrowded wards.[7]

It is difficult to distinguish severe Covid infection from sepsis due to secondary bacterial infections because the traditional

inflammatory markers and vital signs may already be deranged. In this scenario, empirical antibiotics are entirely justifiable. The need is for constant vigilance and quick de-escalation of therapy, conversion from IV to oral formulations and shortest possible duration of antibiotics. Real time antibiograms developed by institutions to guide empirical antibiotic therapy in their centre would be an added benefit.

It is important for the public health policy makers to reprioritize the fight against AMR. Prospective studies recording antibiotic use and misuse are an essential component required to guide recommendations. Clear, concise and identical guidelines for the management of COVID-19 should be made available at all levels of healthcare. Reinforcing AS programs at the hospital level and combatting disinformation at the community level with awareness campaigns such as Nigeria's 'Take Responsibility Campaign' launched by the Nigerian CDC may well forestall a pandemic of antimicrobial resistance.

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