***Editorial:***

# COVID-19: Questions of Antimicrobial Resistance

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"*It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body* [1]." Sir Alexander Fleming

World Health Organization (WHO) reported that there had been 96,658,420 confirmed cases of COVID-19, including 2,092,062 deaths, till January-23-2021 [2]. Additionally, it has been reported that 17 348 389 and 427 798 confirmed cases and deaths, respectively in the EU/EEA and the UK till the last week of December 2020 [3]. On the other hand, it has speculated that by the end of 2020, microbial infections with antimicrobial resistance (AMR) will claim more than 30,000 and 874 541 European life and DALYs, respectively [4, 5]. It has been estimated by 2050, AMR related death rate may rise upto 10 million annually. [6-8] Although Antimicrobial resistance (AMR) is a natural phenomenon of an evolution process that arises as soon as microorganisms are detected, antimicrobial agents[9,10]. Nevertheless, the development of AMR pathogens and their dispersal throughout the planet are the consequences of several years of constant selection pressure from human, especially health professionals irresponsible use of antimicrobials through imprudent use (underuse, overuse, and misuse) [11-18], poverty [19-21], poor sewage clearance set-up [22-24], profound escalation of international travel [25, 26], and better healthcare access for progressively more marginalized communities without any regulatory control often increases the imprudent use of antibiotics (Figure 1) [13, 27-29]. In this miserable background, the current global pandemic of COVID-19 impacts the antimicrobial consumption and increases the selection pressure of appropriate antimicrobials to curb the additional impending burden of antimicrobial resistance during this pandemic is yet to be determined [27, 30, 31]. However, multiple studies have reported that a high quantity of broad-spectrum antimicrobials are prescribed and consumed among COVID-19 patients [13, 30-35]. Furthermore, in many low and middle countries (LMICs), the antimicrobials are available over the counter [36, 37]. Thereby, ordinary people purchase and consume antimicrobials without prescription for many self-limiting illnesses in LMICs compared to other modern world countries [38-41]. Consequently, it is expected that people around the globe would have consumed a vast quantity of antimicrobials as self-medication due to the fear of COVID-19 [30, 42, 43]. COVID-19 has led to the disruption of global AMR surveillance program [35, 44] with increasing economic

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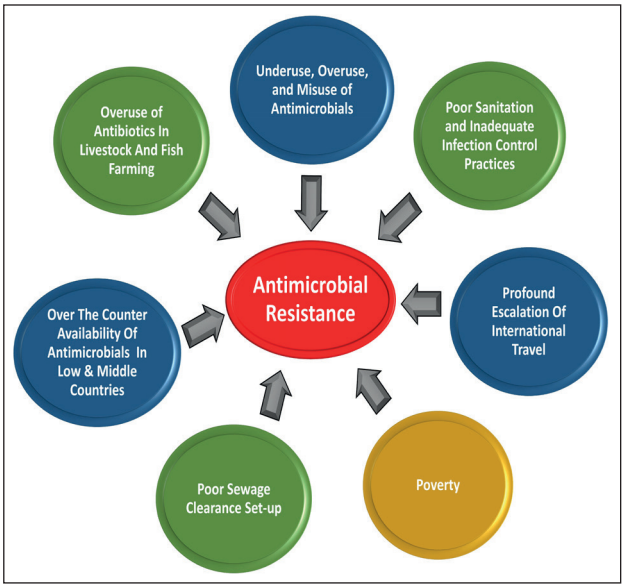


**Figure 1**: Crucial Reasons Responsible for Antimicrobial Resistance.

standstill due to lockdown and other social distancing measures that increase poverty in many countries of our planet [45] and increase the possibility of microbial resistance.

> "*The SARS-CoV-2 pandemic is currently dominating every aspect of health care across the globe, putting other longer-term public health issues—including the steady rise of antimicrobial resistance—in the shade*" [46].

A study conducted in the United States reported that antimicrobials were administered in more than half of the COVID-19 patients as early empiric therapy. However, only 3.5% of patients had documented evidence of community-acquired microbial infection [47]. Another European study similarly revealed that only 1.2% of the COVID-19 patients had confirmed bacterial co-infection, but these patients had primarily received empiric antimicrobial treatment [48]. Additionally, another study concluded that "bacterial and fungal co-infections were rare in COVID-19 patients and were mainly prevalent in critically ill patients" [49]. Similarly, another European study revealed either low or zero bacterial and fungal infection incidence among COVID-19 hospitalized patients [50]. Another study reported that around 8% of the COVID-19 cases were identified with bacterial or fungal respiratory co-infections [51, 52].

Furthermore, in Singapore, empiric use of antimicrobials was low among confirmed and suspected cases of COVID-19. Nonetheless, it has been observed that a significant proportion of antimicrobial was prescribed imprudently where microbial or bacterial infection possibility were improbable [53]. Multivariate analysis revealed that at the hospital's point of admission, pneumonic changes in chest radiograph were suggestive of bacterial co-infection among the COVID-19 patients and demands prudent use of antimicrobials [54]. Similarly, multiple research studies revealed that only those COVID-19 patients with radiologically identified bilateral pulmonary infection required antimicrobials therapy [55-60]. The current US guideline does not recommend the empiric use of antimicrobials in COVID-19 if not supported by documentary evidence of secondary bacterial or fungal infections [55]. Although COVID-19 is a viral origin disease, medical doctors' typical response is to prescribe antimicrobials since cough, fever, and chest X-Ray findings denote bacteriological community-acquired pneumonia [46].

Additionally, this pandemic generates tremendous anxiety and worries as there are no specific medicine or antiviral agents with proven usefulness. Perhaps this issue is an added instigating force to the extensive and unnecessary prescribing, utilization, and prescription of antimicrobials [46, 61-63]. Multiple studies conducted globally have reported that educational antimicrobial stewardship intervention among health professionals have effectively reduced the imprudent consumption of antimicrobial [64-66]. Thereby, it decreases the incidence of hospital-acquired candidemia and the emergence of Multi-Drug Resistant (MDR) Blood Stream Infection (BSI) [64]. Injudicious use of antimicrobials among COVID-19 patients tends to possess as a global public threat [46]. It has been reported that about 43% of severe to critical COVID-19 patients received anti-methicillin-resistant Staphylococcus aureus (MRSA) or anti-pseudomonal antimicrobials [67].

The irrational use of these antimicrobials for pneumonia to treat possibly drug-resistant microbes increases the likelihood of acute renal complication, *Clostridium difficile* infection, and colonization by multidrug-*resistant Pseudomonas aeruginosa* and *Acinetobacter baumannii* [68-70]. Subsequently, multiple studies revealed that antimicrobials should be postponed while waiting for a culture-sensitivity confirmatory microbial superinfection report to minimize such injurious effects. Additionally, severe to critical COVID-19 patients' empirical antimicrobials therapy may need to be started

to prevent the worsening of secondary bacterial infections. Nevertheless, if started, it should be re-appraised according to laboratory findings. Physicians should think twice regarding antimicrobials therapy for COVID-19 cases, as the possibility of microbial coinfection is low; thereby, if necessary, antimicrobials should be stopped immediately or deescalated as and when required [46, 71, 72]. COVID-19 global pandemic possesses challenges in the form of increased imprudent use of antimicrobials and AMR. It has been advocated to minimize such disaster; health professionals must uphold the current struggle of antimicrobial stewardship actions in all health-related sectors globally [72-75].

## Consent for Publication

All authors reviewed and approved the final version and have agreed to be accountable for all aspects of the work, including any issues related to accuracy or integrity.

## Disclosure

The authors declare that they do not have any financial involvement or affiliations with any organization, association, or entity directly or indirectly with the subject matter or materials presented in this article. This also includes honoraria, expert testimony, employment, ownership of stocks or options, patents or grants received or pending, or royalties.

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