Antibiotic resistance: A disregarded concern for misuse of azithromycin in COVID-19 treatment

Dear Editor,

In late November 2019, a new viral infection began to spread from Wuhan, China, resulting in an outbreak that was later declared a pandemic on March 12, 2020. So far, over 125,000,000 confirmed cases and 2,700,000 deaths have resulted from the spread of coronavirus disease-2019 (COVID-19) infection. Concerns about the disease increase when we consider the fact that no definitive cure is currently available. Due to time constraints, many researchers and physicians have begun to use existing drugs that could rationally invade the underlying mechanisms of the disease, hoping to achieve positive results in stopping the progression of the disease or preventing the expected complications.[1] One of the proposed protocols was the use of azithromycin, mostly combined with hydroxychloroquine. At the beginning of the pandemic, azithromycin was thought to be a beneficial agent against COVID-19. However, at present, it is not recommended – either alone or in combination with hydroxychloroquine – since it has shown no antiviral effect, and no positive results have been observed on patients' mortality or the severity of the disease.[2]

The recommenders used to emphasize the fact that the usefulness and efficiency of macrolides have been previously proven in similar viral cases such as rhinovirus infection and influenza.[3] Furthermore, in addition to the antibacterial properties, macrolides have shown immunomodulatory effects, including anti-inflammatory outcomes.Macrolides' ability to suppress the infections lies in their ability to terminate the viral replication, block the internalization of the virus into the host cells, and modify the endosomal and lysosomal pH.[4]

A wide range of usage and fewer side effects, along with the possibility of rapid production, has turned azithromycin into a strategic antimicrobial agent. Despite all potential benefits, it should be noted that considering azithromycin as a treatment for COVID-19 infection can have its consequences. According to the World Health Organization, azithromycin is one of the "highest priority critically important antimicrobials," which should be used prudently to prevent antimicrobial resistance.[5] Therefore, the excessive consumption of azithromycin – among the terrified community, who are looking for ways to prevent the infection, and the clinical wards treating the COVID-19 patients – may result in an undeniable crisis of resistance to this irreplaceable agent. This could also leave short-term complications if the resistance happens in vulnerable COVID-19 patients with immunodeficiency or underlying diseases, such as cancer and metabolic disorders. Hence, misuse and overuse of azithromycin have to be strongly avoided, and it should always be administered with caution in vulnerable patients [Figure 1].

As a global state of emergency, any effort to achieve a reliable treatment or prevention is quite rational and valuable during the pandemics. However, it should be considered that a wrong move may result in an irreversible catastrophe, which can cause life-long trouble for human beings.

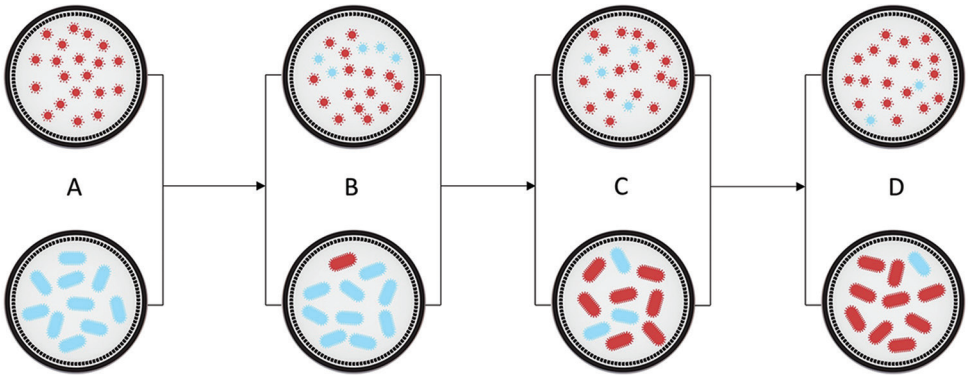

Figure 1: Status of viral (SARS-CoV-2) and bacterial (e.g., Streptococcus pneumoniae) resistance. The blue color indicates susceptibility and the red color indicates resistance. At the beginning, azithromycin is prescribed in combination with some antiviral agents. Azithromycin-resistant bacteria appear and gradually grow in number. Eventually, azithromycin loses its place as an effective antibiotic. By the spread of the resistant bacteria, the infected patients with bacterial pneumonia are now more susceptible to other infections, including viral pneumonia, which results in fatal superinfections

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There are no conflicts of interest.

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