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LETTER TO THE EDITOR

Bacterial and fungal co-infection is a major barrier in COVID-19 patients: A specific management and therapeutic strategy is required

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Abstract

Microbial co-infections are another primary concern in patients with coronavirus disease 2019 (COVID-19), yet it is an untouched area among researchers. Preliminary data and systematic reviews only show the type of pathogens responsible for that, but its pathophysiology is still unknown. Studies show that these microbial co-infections are hospital-acquired/nosocomial infections, and patients admitted to intensive care units with invasive mechanical ventilation are highly susceptible to it. Patients with COVID-19 had elevated inflammatory cytokines and a weakened cell-mediated immune response, with lower $CD4^+$ T and $CD8^+$ T cell counts, indicating vulnerability to various co-infections. Despite this, there are only a few studies that recommend the management of co-infections.

Key Words: COVID-19; Co-infection; Bacterial co-infection; Fungal co-infection

Core Tip: The immune systems of coronavirus disease 2019 patients are already compromised, making them vulnerable to bacterial, fungal, and viral co-infections. These secondary infections, also known as co-infections, are hospital-acquired/nosocomial infections, and mechanically ventilated patients are especially vulnerable. There are no specific guidelines or treatment options for these types of co-infections at the moment, which is contributing to an increase in morbidity and mortality among these patients.

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TO THE EDITOR

The first case of coronavirus disease 2019 (COVID-19) was reported in Wuhan, China, in December 2019, and the World Health Organization declared it a pandemic in March 2019. Approximately one-third of patients experienced severe complications of COVID-19 and required hospitalization[1]. Recently, secondary bacterial/fungal infections or co-infections are another major concern in COVID-19 patients, impacting mortality but lacking attention. Less evidence of bacterial and fungal infection was documented in earlier coronavirus pandemics and epidemics, such as severe acute respiratory syndrome (SARS)-1 and Middle East respiratory syndrome[2]. Recently, we have seen a paper by Saeed *et al*[3] entitled "Bacterial co-infection in patients with SARS-CoV-2 in the Kingdom of Bahrain"[3] in your well-regarded journal *World J Virol*. We appreciate the work done by Saeed *et al*[3] as they reported the microbial infections in patients with COVID-19 in the Kingdom of Bahrain.

The most common bacterial species they reported were *K. pneumonia, P. aeruginosa, A. baumannii, E. coli, S. aureus, E. faecalis,* and *E. faecium*. Among all of these, hospital-acquired (HAI)/nosocomial infection was higher (73.8%) than community-acquired infection. Similar results were reported by Mahmoudi[4] and Sharifipour *et al*[5] in the neighboring country Iran. Both authors reported the same species of bacterial strains, which are the most common. Later on, a descriptive study conducted in the United Arab Emirates found bacterial co-infection in patients with COVID-19 and especially *Klebsiella pneumonia, Escherichia coli, Staphylococcus aureus,* and *Acinetobacter baumannii* were most predominant strains[6]. The recent reviews and meta-analysis also show that *Klebsiella pneumonia, Haemophiles influenzae, Streptococcus pneumoniae,* and *Staphylococcus aureus* are the most frequently identified bacteria among co-infected patients[7,8]. A unique case series from Saudi Arabia reported Middle East respiratory syndrome coronavirus co-infection in 12% of patients already suffering from severe acute respiratory syndrome coronavirus 2[9]. At the same time, another case series from Saudi Arabia by Shabrawishi *et al*[10] reported 7 cases of COVID-19 and tuberculosis co-infection[10]. The interesting results of Hashemi *et al*[11] showed influenza A (H1N1) virus, human metapneumovirus, bocavirus, adenovirus, respiratory syncytial virus (RSV), and parainfluenza viruses in 105 dead patients with COVID-19 in northeastern Iran[11].

Other than bacteria, fungal and viral co-infections are also severe issues with COVID-19 patients. In the present article, the authors reported fungal co-infection in about 10% of total microbial co-infection. The most common isolated fungi were *Candida galabrata, Candida tropicalis, Candida albicans,* and *Aspergillus fumigatus*. They also found that the death rates in patients with fungal co-infection were very high (70.4%)[3]. Studies from other different regions found aspergillosis or invasive candidiasis as the common fungal co-infections[12]. In contrast, influenza type A, type B, and RSV were the most common viral co-infections in patients with COVID-19[7]. These co-infections are associated with an increased probability of death. Most of the articles reported that microbial co-infections were HAI/nosocomial infections, similar to Saeed *et al*[3], who found 71% were HAI.

Further, the authors have described well different microbial co-infections in patients of COVID-19. Furthermore, the study has some limitations, such as the authors not providing any treatment or management options for COVID-19 infected patients. That is the most crucial concern for the patient's benefit. In this context, we would like to draw your attention to the management and recommendations for the infection. Chedid *et al*[13] reviewed the most common antibiotics used by COVID-19 hospitalized patients, primarily in an intensive situation, by analyzing the use of antibiotics in different types of bacterial secondary and co-infection[13].

On the other hand, Sieswerda *et al*[14] gave evidence-based recommendations for antibacterial therapy for secondary microbial and co-infection[14]. Wu *et al*[15] described the management of respiratory co-infection and secondary bacterial pneumonia in patients with COVID-19[15]. For the treatment of fungal co-infections, Song *et al*[16] suggested the regimen, which is currently in an induction phase and includes amphotericin B deoxycholate and flucytosine, followed by (1) Fluconazole; alternative options for fluconazole + flucytosine or amphotericin B deoxycholate +

fluconazole; (2) Consolidation phase for fluconazole; and (3) Maintenance (or secondary prophylaxis) phase for fluconazole[16].

Depending upon disease severity, patients with influenza A or B viral co-infection should be treated with oseltamivir or its substitute[17]. Treatment options for other viral co-infection, such as RSV, are restricted and beneficial only in specific circumstances, such as immunosuppression or hypogammaglobulinemia[18,19].

Patients with COVID-19 had elevated levels of inflammatory cytokines and a debilitated cell-mediated immune response, with lower $CD4^+$ T and $CD8^+$ T cell counts, indicating vulnerability to various co-infections. Furthermore, COVID-19 patients who are immunocompromised, such as those with extended neutropenia, hematopoietic stem cell transplantation, hereditary or acquired immunodeficiencies, or tumor, are more likely to develop co-infection. Co-infection and superinfection of pathogens in COVID-19 patients is a critical issue as it is difficult to distinguish the associated complications. Specific diagnostic tests should be recommended for proper treatment and management of these infections to reduce morbidity and mortality.

FOOTNOTES

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