Comprehending the Significance of Bacterial and Fungal Infections in Context of COVID-19

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Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has imposed an unparalleled burden on healthcare systems. A growing concern is the potential impact of this pandemic on Antimicrobial Resistance (AMR) [1,2]. Early studies indicated relatively low rates of bacterial and fungal infections in hospitalized COVID-19 patients, despite the frequent use of broad-spectrum antimicrobials [3-5]. Clinically differentiating between COVID-19 and concurrent bacterial or fungal infections poses a significant challenge for healthcare providers and antimicrobial stewardship efforts [6]. Unfortunately, there is limited high-quality evidence available to guide decisions regarding the treatment of bacterial and fungal infections in the context of COVID-19. As a result, clinical uncertainty may lead to unnecessary antimicrobial prescriptions for COVID-19 patients during their hospital stay, potentially contributing to the rise of drug-resistant infections [7].

In the latest edition of Clinical Microbiology and Infection, Garcia-Vidal and colleagues present their findings on co-infection and superinfection among COVID-19 patients admitted to a hospital [8]. Among 989 patients with COVID-19 in a Barcelona hospital, 31 out of 989 (3%) had community-acquired co-infections. The majority of these cases were respiratory bacterial infections, specifically *Streptococcus pneumoniae* and *Staphylococcus aureus pneumonia* [8].

Additionally, 43 out of 989 patients (4%) were diagnosed with hospital-acquired infections, with 25 out of 44 (57%) of these cases occurring in critical care settings. The most common hospital-acquired infections were ventilator-associated pneumonia, hospital-acquired pneumonia, and bloodstream infections, primarily caused by typical nosocomial pathogens such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella spp.*, and *Staphylococcus Aureus* [8]. Among the documented bloodstream infections, coagulase-negative staphylococci were the most frequently identified organisms, accounting for 7 out of 16 cases (44%).

Fungal co-infections were less common, observed in 7 out of 989 patients (0.7%). Specifically, three patients were diagnosed with *Aspergillus fumigatus tracheobronchitis*, and four patients had Candida albicans infections, including bloodstream infection (n=2), urinary tract infection (n=1), and intraabdominal infection (n=1) [8].

Garcia-Vidal and colleagues concluded that their study showed a low occurrence of bacterial and fungal co-infection and superinfection among their COVID-19 patients, even though a significant number of patients were receiving immunosuppressive therapy. They found that critical care admission was associated with more than half of the diagnosed hospital-acquired infections [8]. Similar low rates of bacterial and fungal infections in COVID-19 patients have also been reported in other countries, such as the UK. Hughes and colleagues identified bacterial infections in only 6% of 836 COVID-19 patients admitted to two London hospitals. Secondary bacterial infection was rare in this cohort, and out of 60 positive blood cultures, 65% were considered contaminants, with coagulase-negative staphylococci being the most prevalent [9].

Both studies mentioned have some limitations that need to be taken into consideration when interpreting their findings. One of the primary limitations is the variable and sometimes low rates of microbiological sampling performed. In the study by Garcia-Vidal and colleagues, limited microbiological sampling was carried out after the COVID-19 diagnosis. Similarly, in the study by Hughes and colleagues, although blood culture was performed on a higher proportion of patients compared to the other study, there were still patients for whom sampling was not done.

Additionally, respiratory sampling was limited in both studies, with only a small percentage of patients undergoing this type of testing. Moreover, a considerable number of patients received empirical antimicrobial therapy, which could potentially affect the accurate detection of infections in hospitalized COVID-19 patients, leading to underreporting.

The retrospective design of these studies is another important limitation to consider. Such designs can introduce inherent biases that may either overestimate or underestimate the true infection rates among COVID-19 patients. Furthermore, many studies investigating infections in COVID-19 patients often fail to define the severity of the disease or differentiate between those who develop infections in critical care settings versus non-critical care settings. This lack of stratification makes it challenging to evaluate risk factors accurately.

In conclusion, while these studies provide valuable insights into the rates of bacterial and fungal infections in COVID-19 patients, their limitations must be acknowledged, and further research with more comprehensive and standardized sampling protocols is needed to obtain a clearer understanding of the true infection rates in this population.

Indeed, an important gap in our understanding of bacterial and fungal infections in COVID-19 lies in determining whether these infections directly result from SARS-CoV-2 or are consequences of other factors, such as managing a high number of critically ill patients, strained healthcare systems, and prolonged mechanical ventilation or critical care admission. In the case of influenza, lower respiratory tract infections are believed to be associated with certain virulence factors that make the host more susceptible to secondary bacterial infections like Streptococcus pneumoniae [10,11]. However, in the context of COVID-19, the relatively low rates of co-infection and the similarity of identified organisms to those found in community-acquired infections suggest that these occurrences are more coincidental rather than directly attributable to SARS-CoV-2 [12].

It is essential to differentiate between infections caused directly by the virus and those that arise due to various factors related to the patient's condition and the healthcare environment. Understanding the mechanisms behind bacterial and fungal infections in COVID-19 will help healthcare providers develop more effective strategies for prevention, management, and antimicrobial stewardship in this patient population. Further research is needed to elucidate the underlying factors contributing to these infections and their relationship to SARS-CoV-2 infection.

Hospital-acquired infections in COVID-19 patients show a consistent trend of being more predominant in critical care settings [13]. Among these

infections, ventilator-associated pneumonia stands out as a commonly reported hospital-acquired infection in the literature [4,13]. Furthermore, critically ill COVID-19 patients are at increased risk of invasive fungal infections [14]. Another noteworthy observation is the higher rates of contaminants in blood and line cultures, which are commonly reported in this context [9].

The data suggest that critical care admission and the use of mechanical ventilation are contributing factors to the higher incidence of bacterial and fungal infections in hospitalized COVID-19 patients. These findings underscore the importance of vigilant infection prevention and control measures, as well as antimicrobial stewardship, to address the specific challenges posed by COVID-19 patients in critical care settings. Improved understanding of these infections' underlying mechanisms can aid in the development of targeted interventions to reduce their impact on patient outcomes.

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