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Research Article

Bacterial and Fungal Infections Among COVID-19 Patients in Intensive Care Unit

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Abstract

Aim: Secondary infections caused by bacteria or fungi are dangerous because they increase death rates, particularly in patients with COVID-19 who are receiving intensive care. In this study, hospital-associated secondary infections resulting from bacteria and fungi amid COVID-19 patients treated in intensive care units, as well as their distribution according to microbial agents, were investigated.
Material and Method: The study comprised 134 COVID-19 patients who were being treated in the Mersin City Hospital of the Ministry of Health intensive care unit between January 1, 2021, and April 30, 2021. The patients' demographics and clinical records, as well as bacterial and fungal infections in the blood, urine and deep tracheal aspirate samples, were analyzed retrospectively.
Results: The rate of secondary infection was found to be quite high in patients hospitalized in intensive care units for over 72 hours (91.4%). The majority of secondary infections were detected in blood samples (n=103, 15%). Secondary infection was detected in 61 (8.9%) deep tracheal aspirate specimens and 59 (8.5%) urine samples. The most common secondary infectious agents were *Candida spp.* (22.3%), *Acinetobacter baumannii* (16.8%). In addition, it was determined that ≥60 years and ≥3 days of mechanical ventilation independently increased the probability of developing secondary infection.
Conclusion: Our findings are emphasized that the concern of secondary infection due to *Candida spp., Acinetobacter baumanii and Stahylococcus epidermidis* agents. Evaluation of bacterial superinfections during the later waves of the pandemic may be critical, especially given the changes in the management of these patients, such as the routine use of corticosteroids and the raise of the different variants of the SARS-CoV-2.

Keywords: Corticosteroids, COVID-19, intensive care unit, secondary infection

INTRODUCTION

Following the reporting of the patients presenting with respiratory tract infections caused by a previously unidentified microbial agent in Wuhan, China; a new beta-coronavirus, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), is defined as a causative pathogen of the disease in December, 2019 (1,2). The World Health Organization (WHO) later gave the illness the term coronavirus disease 2019 (COVID-19) (2). The virus that enters alveolar epithelial cells and multiplies quickly, in particular, can trigger a potent immune response. Intensive care unit (ICU) treatment is necessary for severe cases, and there are risks including cytokine storm-induced multiple organ failure or acute respiratory distress syndrome (ARDS) (3). To counteract this abnormal immune system activation, immunosuppressive medications, like glucocorticoids, are extensively used (4).

In hospitalized COVID-19 patients, infections from bacteria and fungi are frequent as with other viral pneumonias (5,6).

In COVID-19 patients, bacterial and fungal secondary infections are of great concern as they cause increased mortality rates, especially in ICU. Rapid and accurate identification of local flora or pathogenic bacterial or fungal organisms during COVID-19 should make up a vital component in the effective management of patients (7,8).

This study aimed to identify the distribution and prevalence of the microbes causing hospital-associated secondary infections caused by bacteria and fungi in COVID-19 patients admitted to the ICU.

CITATION
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MATERIAL AND METHOD

Ethical Permissions

The Scientific Research Platform of the General Directorate of Health Services of the Turkish Ministry of Health granted authorization for this research. This research was conducted with the permission of the Mersin University Clinical Research Ethics Committee (Decision No: 2021/480 and Date: 07/14/2021).

134 COVID-19 patients who were hospitalized in the intensive care unit of the Ministry of Health Mersin City Hospital between January 2021 and April 2021 were comprised in the study. Demographics, the clinic of the disease, and secondary infections resulting from bacteria or fungi of the patients followed in the ICU were determined retrospectively. All patients had been treated in the ICU for more than 72 hours and were older than 18 years. Patients who were monitored in the ICU were split up into two groups: those receiving glucocorticoids and those receiving no glucocorticoids. Data on age, gender, antibiotic therapy, time spent in the ICU, comorbidities, mechanical ventilation/intubation status, and treatment result (death/discharge) of these two groups were collected.

SARS-CoV-2 RT-PCR

Samples of the patients' nasal and oropharyngeal swabs were collected using the designated swab and inserted into the tubes containing the viral transport medium (VTM) or viral nucleic acid buffer (vNAT). COVID-19 laboratory diagnosis was performed by the real-time reverse transcription polymerase chain reaction (RT-PCR) assay of SARS-CoV-2 RNA from patient samples, using the Bio-speedy SARS-CoV-2 RT-PCR kits (Bioeksen, Türkiye).

Microbiological Culture

Initially, each patient admitted to the ICU had one urine and two blood culture specimens were taken. When patients in the ICU had fever, an elevated leukocyte count, or other symptoms that would suggest a secondary infection, blood and urine samples of the cultures were got. In addition, deep tracheal aspirate (DTA) specimens were got from patients if they were intubated, and if central venous catheter (CVP) was inserted, blood samples from CVP were collected for culture.

The specimens were collected and delivered immediately to the microbiology laboratory. The samples were cultured on 5% sheep blood agar, "Eosin-Methylene Blue" agar, chocolate agar, and "Sabouraud Dextrose" agar and incubated at 37°C for 24-72 hours for the conventional culture of bacterial and fungal agents. The BacT/Alert system from BioMérieux (France) was used to culture blood samples. Colonies formed on the media after incubation were identified by Gram staining, standard biochemical tests, and Vitek 2 (BioMérieux, France) system. The replicating agents were subjected to normal disk diffusion antimicrobial susceptibility testing under EUCAST criteria.

Statistical Analysis

All data collected in Microsoft Excel for analysis. Comparison of data from ICU inpatients was analyzed using SPSS version 22 (IBM, Chicago, USA). The Kolmogorov-Smirnov test was used to analyze the normality of the continuous variable distribution. The chi-square (χ^2) test was used to compare non-parametric data; Mann-Whitney U test was used for comparisons between non-normally distributed continuous variables and independent samples t-test was used for normally distributed continuous variables. Categorical variables were expressed as frequency or percentage, age and the time spent in the ICU is described as mean±standard deviation, $p \leq 0.05$ was considered significant.

RESULTS

Demographic Data

90 of the 134 COVID-19 patients included in our study were taking corticosteroids during their hospitalization besides the standard treatment specified in the T.C. Ministry of Health COVID-19 Outbreak Management and Study Guide (9). The patient group who did not take steroids comprised 44 people.

Of the patients, 63 were women and 71 were men, with a mean age of 68.3±15 for women and 65.1±12.7 for men. The mean age was 64.5±14.1 years in the group that received steroids, while it was 70.9±12.5 in the group that did not. The patients' average stay in the ICU was 19.9 days. When the distribution of hospitalization periods according to steroid treatment was evaluated, it was determined as 19.8±11.9 days in those who received steroid treatment and 18±12.4 days in those who did not. No difference exists between the patients that received steroid treatment and those who did not, in terms of length of stay. In the study, 106 patients died, 70 of whom received steroid therapy and 36 of those who did not.

Etiology in Secondary Infection

The rate of secondary infection was determined to be considerably high in patients hospitalized in the ICU for over 72 hours, regardless of corticosteroid use (n=115, %92). No significant difference between the patients received steroid treatment (82 individuals, 91.1%) and those who did not (40 people 90.9%) in terms of the presence of secondary infection. When the rate of multiple secondary infections during the hospitalization period in patients receiving steroid therapy was evaluated, it was found that patients with 2 or more secondary infections (46 people 56.1%) were significantly higher than those with a single secondary infection (36 people, 43.9%). The proportion of patients with a single secondary infection (n=20, 50%) and those with two or more secondary infections (n=20, 50%) who did not receive steroid treatment was the same. Bacterial and/or fungal growth was detected in 244 (31.6%) of 771 samples taken for microbiological culture. *Candida species* were determined as the most common secondary infectious agent in COVID-19 patients hospitalized in ICUs included in the study (n=54, 22.1%). *Candida species* were followed in order of prevalence by *Acinetobacter baumanii* (n=41, 16.8%), *Staphylococcus epidermidis* (n=41, 16.8%), *Staphylococcus haemolyticus* (n=23, 9.4%) and *Klebsiella pneumoniae* (n=20, 8.2%) respectively (Table 1).

Table 1. Distribution of secondary infectious agents

Organisms	Blood	Deep tracheal aspirat	Urine	CVP catheter	Total
Candida spp.	12	13	27	2	54
Acinetobacter baumanii	12	21	4	4	41
Stahylococcus epidermidis	35	0	0	6	41
Stahylococcus haemolyticus	21	1	0	1	23
Klebsiella pneumoniae	2	10	6	2	20
Enterococcus spp	9	1	7	1	18
Eschericia coli	0	4	13	0	17
Stenotrophomonas maltophilia	8	3	0	3	14
Pseudomonas aeruginosa	1	7	0	1	9
Other GNBs	2	1	2	0	5
Pseudomonas putida	2	0	0	0	2
Total n/N (%)	104/771 (13.5)	61/771 (7.9)	59/771 (7.6)	20/771 (2.6)	244/771 (31.6)

The majority of secondary infections were detected in blood samples (n=104, 13.5%). The most frequently isolated agent in blood samples was *Staphylococcus epidermidis* (n=35, 33.7%). *Candida species* were followed in order of prevalence by *Staphylococcus haemolyticus* (n=21, 20.2%), *Candida spp*. (n=12, 11.5%), *Acinetobacter baumanii* (n=12, 11.5) (Table 1). Secondary infection was most common in deep tracheal aspirat (DTA)samples after blood samples (n=61, 7.9%). The most commonly isolated agent in DTA samples was *Acinetobacter baumanii* (n=21, 34.4%), followed by *Candida species* (n=13, 21.5%). The most commonly isolated agent in DTA samples was *Acinetobacter baumanii* (n=21, 34.4%), followed respectively by *Candida species* (n=13, 21.5%), The most prevalent pathogens isolated in urine samples (n=59, 7.9%) were *Candida species* (n=27, 45.8%). The most prevalent cause of secondary infections detected in CVC samples (n=20, 2.6%) was *Staphylococcus epidermidis* (n=6, 30%), *Acinetobacter baumanii* (n=4, 20%).

Secondary infection was detected in 14.9% (n=73) of blood samples, 8.3% (n=41) of DTA samples, 7.3% (n=36) of urine samples and 3.1% (n=15) of CVC samples of the patients receiving steroid therapy.

In patients who did not receive steroid treatment, in 10% (n=28) of blood samples, 7.1% (n=20) of DTA samples, 8.2% (n=23) of urine specimens, and 1.8% of central venous catheter (CVC) samples (n=5) bacterial growth was detected. Bacterial or fungal secondary infectious agents were most commonly isolated from blood samples in those receiving steroid therapy (n=73, 14.9%). DTA (n=41, 8.3%), urine (n=36, 7.3%) and CVC (n=15, 3.1%) followed respectively in terms of secondary infection frequency in the samples. When infectious agents were evaluated in patients receiving steroid therapy, the most commonly isolated microorganisms from blood samples were *Staphylococcus epidermidis* (n=25) and *Staphylococcus haemolyticus* (n=16) (Table 2). *Acinetobacter baumanii* (n=14) was the most frequently isolated sample from DTA samples of patients receiving steroid therapy. The most frequently isolated agent in urine samples of the patients who received the corticosteroids during their stay in the ICU was comprised of the *Candida species* (n=19).

The frequency of bacterial and/or fungal secondary infections in patients who did not receive steroid treatment was similar in blood (n=28, 10%), urine (n=23, 8.2%) and DTA (n=20, 7.1%) samples. The most common agents detected in blood samples were *Staphylococcus epidermidis* (n=7), *Acinetobacter baumanii* (n=5), *Candida species* (n=5) and *Staphylococcus haemolyticus* (n=5). The most common agents detected in blood samples were Staphylococcus epidermidis (n=7), *Acinetobacter baumanii* (n=5), *Candida species* (n=5), and *Staphylococcus haemolyticus* (n=5). The most frequently isolated agents in the urine samples of the patients were *Eschericia coli* (n=9) and *Candida species* (n=8) (Table 2).

Table 2. Distribution of secondary infections in patients receiving and not receiving steroid therapy

Organisms	Blood Steroid+	Steroid-	Deep tracheal asp. Steroid+	Steroid-	Urine Steroid+	Steroid-	CVP catheter Steroid+	Steroid-	Total Steroid+	Steroid-
Candida spp.	7	5	9	4	19	8	1	1	36	18
Acinetobacter baumanii	7	5	14	7	4	0	2	2	27	14
Stahylococcus epidermidis	27	7	0	0	0	0	4	2	32	9
Stahylococcus haemolyticus	16	5	1	0	0	0	1	0	18	5
Klebsiella pneumoniae	1	1	7	3	3	3	2	0	13	7
Enterococcus	7	2	1	0	4	3	1	0	13	5
Eschericia coli	0	0	2	2	4	9	0	0	6	11
Stenotrophomonas maltophilia	5	3	3	0	0	0	3	0	11	3
Pseudomonas aeruginosa	1	0	3	4	0	0	1	0	5	4
Other GNBs	0	0	1	0	2	0	0	0	3	0
Pseudomonas putida	1	0	0	0	0	0	0	0	1	0
Total n/N (%)	73/491 (14.9) 28/280 (10)		41/491 (8.3) 20/280 (7.1)		34/491 (7.3) 23/280 (8.2)		15/491 (3.1) 5/280 (1.8)		165/491 (33.6) 76/280 (27.1)	

In the study, it was also determined that mechanical ventilation for over three days and age older than 60 years independently increased the probability of developing a secondary infection. The mortality rate among COVID-19 patients with secondary infection was 79.1% (106/134), 77.8% (70/90) in those that received steroid therapy, and 81.8% (36/44) in those who did not.

Infection was detected in 207 of the samples taken from the cases that resulted in mortality. The most common secondary infections were detected in blood samples at 44.4% (n=92). Secondary infections in the deep tracheal aspirate specimens were in the second rank with 26.1% (n=54), and urine samples were in the third row with 21.3%. The frequency of secondary infection was 8.2% (n=17) in the samples taken from the CVC. Among the patients who lost their lives, *Candida spp* with 21.7% (n=45) were the most frequent cause of secondary infections. *Acinetobacter baumanii* (n=33) was in second place with 15.9%, and *Staphylococcus epidermidis* was in the third row with 14% (n=29). These factors were followed by *Klebsiella pneumoniae* and *Enterococcus spp*, each with 7.7% (n=16).

DISCUSSION

It is well known that COVID-19 patients who get secondary infections have worse health outcomes (6,10). During the first few days after SARS-CoV-2 infection, lung dysbiosis or respiratory tract destruction in patients may develop, which may be converted into a secondary bacterial or fungal infection after a few weeks (11). According to recent studies, in less than 4% of COVID-19 patients, community-acquired bacterial co-infection was stated at admission. While, it has been reported that the prevalence of secondary bacterial infections has been raised to 3.7-21.9% after hospitalization (10,12). However, it has been reported that this rate varies between 7.2% and 58% in ICU patients (12-16). In our study, the rate of secondary infection in patients hospitalized in the ICU for over 72 hours was relatively high, 91.4%. This reasonably high rate is thought to be due to the time in which study samples were included covering the peak of the COVID-19 epidemic.

It has been emphasized that extensive, well-designed clinical trials are needed to determine the incidence, risk factors, and outcome of secondary pulmonary infections in hospitalized COVID-19 patients due to differences in the design of various studies (17).

In our study, it was aimed to reveal the frequency of detection of secondary bacterial and fungal agents and the distribution of the agents in COVID-19 patients who were followed up with steroid therapy in the ICU and were not treated with steroids. The microorganisms most frequently encountered as a secondary infection agent in COVID-19 patients hospitalized in ICUs were determined as *Candida spp*. (n=54, 22.1%), *Acinetobacter baumanii* (n=41, 16,8%), *Staphylococcus epidermidis* (n=41, 16.8%), *Staphylococcus haemolyticus* (n=23, 9.4%), *Klebsiella pneumoniae* (n=20, 8.2%), *Enterococcus spp*. (n=18, 7.4%), *Eschericia coli* (n=17, 7%), respectively. According to the reports of the Infection Control Committee of our hospital, the agents previously isolated from ICUs were reported as *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus saphrophyticus*, *Candida spp.*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Proteus mirabilis*, *Acinetobacter baumanii*. Most of the factors detected in COVID-19 patients followed up in their follow-up period were associated with these bacteria. Most of the factors detected in COVID-19 patients followed up in their follow-up period were associated with these bacteria. In the study, the highest frequency of C. albicans, an opportunistic colonization pathogen, as a cause of secondary infection in critically ill COVID-19 patients, may be explained by the fact that the immune system of the patients were suppressed due to viral sepsis.

In the study of Obata et al., bacterial infection (25% vs. 13.1%, p=0.041) and fungal infection (0.7% vs. 0.7%, p<0.001) in the group receiving steroid treatment compared to the group not receiving steroids have been reported to have a higher incidence (18). In our study, no significant difference was found between the patients who received steroid treatment (82 people, 91.1%) and those who did not (40 people 90.9%) while they were hospitalized in the ICU.

It has been reported that positive culture rates of respiratory tract bacterial pathogens from hospitalized COVID-19 patients ranged from 23% to 86.6% (9,13,19,20). In our study, bacterial secondary infection rate in respiratory tract samples was found to be 7.9%, similar to previous studies.

Streptococcus pneumoniae and *Staphylococcus aureus* have been reported frequently as causative agents in community-acquired co-infections in patients diagnosed with COVID-19 (12). On the other hand, the most frequently identified bacterial agents in respiratory tract cultures were reported as *Psoudomonas aeruginosa*, *Klebsiella spp.*, *Staphylococcus aureus*, *Eschericia coli*, and *Stenotrophomonas maltophilia*. *Aspergillus fumigatus* has been identified as the most common microorganism causing secondary fungal pulmonary infections (17).

In different studies, the most common agents found in respiratory tract samples of COVID-19 patients hospitalized in the ICU were *Acinetobacter baumanii* (21.8-90%) *Stenotrophomonas maltophilia* (9-15.6%), *Pseudomonas spp.* (4.8%-33%), *Klebsiella pneumoniae* (14.4-24.5%), and *Staphylococcus aureus* (10%-21%). These agents were followed by *Burkholderia cepacia* (18.8%), *Haemophilus influenza* (9%), *Enterobacter spp.* (7%), and *Eschericia coli* (7%) (6,8,10,14,19,20). It has been reported that *Aspergillus fumigatus* (9%) (14) and *Candida albicans* were also detected among fungal agents. (6.8%) (6). In a study conducted by Avan Mutlu and Bozok in our country, *Acinetobacter baumanii* (47.8%), *Klebsiella pneumoniae* (13.4%), *Psoudomonas aeruginosa* (12.0%), *Staphylococcus aureus* (4.5%) and *Enterococcus spp.* (2.1%) has been reported to be detected (21). In our study, the most common agents detected in the respiratory tract of critically ill COVID-19 patients hospitalized in ICUs were *Acinetobacter baumanii* (n=21, 34.4%), *Candida species* (n=13, 21.5%), *Klebsiella pneumoniae* (n=10, 16.3% and *Psoudomonas aeruginosa* (n=7, 11.5%). Since these microorganisms are hospital-acquired agents frequently defined in ICUs, it was difficult to distinguish colonization and infection, especially in respiratory tract samples.

In our study, unlike other researches, blood circulation and urinary tract infections were also evaluated besides respiratory tract infections. The rate of hospital-acquired bloodstream infection in COVID-19 patients followed in ICUs has been reported as 31-34% (14-16,22) in other studies. In our study, the most elevated rate of secondary infections was determined in blood samples of 13.5%. It has been concluded that one of the significant reasons underlying the high incidence of infection in blood samples is the use of intravenous catheters in patients treated in the ICU. Similarly, the widespread use of urinary catheters in the ICU is an important factor that can explain the frequency of urinary tract infections. Patients may be exposed to infectious agents due to application errors or deficiencies in antisepsis practice throughout respiratory support with nasal cannula, endotracheal tube, and similar devices during hospitalization (16).

The most common etiologic bacterial pathogens in secondary infections developing in the bloodstream were reported as *coagulase-negative Staphylococci* (34%), *Enterococcus spp.* (22%), *Psoudomonas aeruginosa* (8%), *Klebsiella spp.* (7%) and *Staphylococcus aureus* (7%) (10). In another study, the most common agents were determined as *Enterococcus spp.* (64%), *coagulase-negative staphylococci* (11%), *Psoudomonas aeruginosa* (7%), and *Staphylococcus aureus* (3.5%) (14). In our study, the most frequently isolated agents in the blood were *Staphylococcus epidermidis* (33.7%), *Staphylococcus haemolyticus* (20.2%), *Candida spp.* (11.5%), *Acinetobacter baumanii* (11.5%), *Enterococcus spp.* (8.7%) and *Stenotrophomonas maltophilia* (7.7%). With this aspect, our study reveals new findings on microorganisms that cause secondary infections in COVID-19 patients treated in the ICU.

Graselli et al. reported that the rate of catheter-related bloodstream infection represents 10% while Bardi et al. found the rate 25% (14,15). In our study, secondary infectious agents were determined at a rate of 2.6% in CVC samples. In our study, secondary infectious agents were determined at a rate of 2.6% in CVC samples and the detected pathogens were *Staphylococcus epidermidis* (30%), *Acinetobacter baumanii* (20%), *Stenotrophomonas maltophilia* (15%), *Candida spp.* (10%) and *Klebsiella pneumoniae* (10%). Similarly, in a study, *coagulase-negative staphylococci* (54%) were detected most frequently in CVC samples. The former were followed by *Enterococcus spp.* (25%), *Candida albicans* (17%) and *Staphylococcus aureus* (4%) (14). Since patients with severe COVID-19 and bloodstream infections may have a severe disease course, prolonged hospitalization, and poor clinical outcomes (19), prospective studies in which patients will be evaluated together with risk factors are required for good antimicrobial management of patients (19).

In our study, the secondary infection rate in urine samples was determined as 7.9%. The most common pathogens isolated from urine samples were *Candida species* (n=27, 45.8%), followed by *Eschericia coli* (n=13, 22%), *Enterococcus spp.* (n=7, 11.7%) and *Klebsiella pneumoniae* (n=6, 10.2%), respectively. Our study is compatible with the literature in this aspect. In the study of the Bardi et al., urinary tract infection rate was similarly reported as 8%. The most frequent agents detected in the urine were determined as in this study *Enterococcus spp.* (72%), *Psoudomonas aeruginosa* (14%) and *Acinetobacter baumanii* (14%) (14).

It should be taken into account that the length of stay in the intensive-care unit may be prolonged if the patients are co-infected (19). Studies have shown that the average length of stay in the ICU of critically ill COVID-19 patients who develop secondary infections is 8-40 days (8,22). In our study, the average length of stay of the patients in the ICU was 19.9 days, and it was determined that those who received steroid treatment (21 days) were higher than those who did not (17 days) ($p<0.05$). When compared with other studies, it was observed that the length of stay in the ICUs of the patients was not long.

Secondary infections in hospitalized patients for COVID-19 may cause increased mortality (12,19). In various studies, mortality rates of critical COVID-19 patients during their stay in the ICU have been reported between 30%-95% (8,15,16,23). In our study, the mortality rate was reported to be quite high, as 79.1% in total. However, the mortality rate we found is consistent with the literature.

In the study of Obata et al., it was reported that steroid use did not affect mortality (18). In support of the result obtained in this study, it was revealed in our research that steroid administration during treatment in the ICU did not have an effect on the mortality rate of COVID-19 patients. In our study, the mortality rate was 91.1% in patients who received steroid therapy, while it was 90.9% in patients who did not receive steroid therapy. In addition, the mortality rate in patients aged ≥60 years was significantly higher than in patients aged 18-59 years, regardless of steroid treatment (86.9% vs. 70.5%). It was also determined that mechanical ventilation for ≥3 days independently increased the probability of developing secondary infection (94.3% vs. 64.8%).

One of the shortcomings of our study is that we could not compare our results with the incidence of secondary infections among patients without COVID-19. Another limitation of our study is that we conducted a single-center retrospective study with a relatively small sample size. More prospective multicenter studies are needed to be designed in the future to confirm our findings.

In our study, the incidence of secondary infection was found to be quite high, 91.4%, in patients with COVID-19 and hospitalized in the ICU for over 72 hours. Our findings emphasize the risk of secondary infection due to *Candida spp.*, and *A. Baumanii*. However, we found that there was no difference in the distribution of secondary infection in steroid users compared to non-users. Evaluation of bacterial superinfections during the later waves of the pandemic may be critical, substantially given the changes in the management of these patients, such as the routine use of corticosteroids and the emergence of new SARS-CoV-2 variants. Management of these infections is essential to ensure compliance with hospital infection control measures. In conclusion, it is of vast importance to focus on fungal and bacterial secondary infections and to have information about the distribution of these agents for the appropriate treatment of critical COVID-19 patients in ICUs.

CONCLUSION

In summary, it is of vast importance to focus on fungal and bacterial secondary infections and to have information about the distribution of these agents for the appropriate treatment of critical COVID-19 patients in ICUs.

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