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Original Article

Clinical Evaluation of Candida Infections and their Antifungal Susceptibility Testing in COVID-19 Patients

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ABSTRACT

Background: COVID-19 patients, particularly those with severe disease, are at increased risk of opportunistic fungal infections due to immune dysregulation, lymphopenia, and impaired cell-mediated immunity. Candidiasis is a common complication, especially in patients receiving prolonged antibiotics or steroids or those with underlying comorbidities. In recent years, a shift from *C. albicans* to non-albicans Candida (NAC) species has been observed, with variable antifungal susceptibility patterns posing therapeutic challenges. The present study was conducted to evaluate the prevalence of Candida infections and determine their antifungal susceptibility patterns among COVID-19 patients.

Methods: A prospective observational study was conducted over 6 months (December 2020 to May 2021) at King George Hospital, Visakhapatnam. A total of 126 clinical samples, including oropharyngeal swabs, oronasal swabs, and nasal tissue, were collected from RT-PCR-confirmed COVID-19 patients with suspected fungal infections. Direct microscopy using KOH mount and culture on Sabouraud Dextrose Agar were performed. Species identification and antifungal susceptibility testing were done using VITEK 2 Compact system.

Results: Out of 126 samples, fungal elements were detected in 72 (57.1%) cases. Candida species were isolated in 22 (17.4%) cases, of which *C. albicans* accounted for 12 (54.5%) and non-albicans Candida for 10 (45.5%). Among NAC, *Candida tropicalis* (4), *Candida glabrata* (3), *Candida krusei* (2), and *Candida parapsilosis* (1) were identified. *C. albicans* showed high sensitivity to amphotericin B (100%), voriconazole (91.6%), and fluconazole (83.3%). NAC isolates showed reduced susceptibility to fluconazole (60%) but higher sensitivity to amphotericin B (100%) and voriconazole (80%).

Conclusion: *C. albicans* remains the predominant species; however, the increasing prevalence of NAC species with reduced fluconazole sensitivity highlights the importance of species identification and antifungal susceptibility testing. Early diagnosis and targeted therapy are essential to reduce morbidity in COVID-19 patients.

Key-words: COVID-19, Coronavirus Disease, *C. albicans*, Non-albicans Candida, Antifungal susceptibility

INTRODUCTION

The global outbreak of Coronavirus Disease 2019 (COVID-19), caused by SARS-CoV-2, has significantly altered the landscape of infectious diseases, not only through its direct viral effects but also through its strong association with secondary infections.

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Co-infections and secondary infections in COVID-19 patients complicate treatment and are associated with increased morbidity and mortality [1]. The burden of such infections is particularly high among critically ill patients requiring prolonged hospitalization and intensive care support.

COVID-19 infection leads to immune dysregulation characterized by lymphopenia, cytokine storm, and impaired cell-mediated immunity, thereby predisposing patients to opportunistic infections, especially fungal infections [2]. The widespread use of corticosteroids, immunosuppressive agents, and broad-spectrum antibiotics in the management of severe COVID-19 cases further aggravates this risk [3].

Among fungal pathogens, *Candida* species are one of the most common causes of infections in hospitalized patients worldwide. Although these organisms are normal commensals of human mucosal surfaces, they can become pathogenic under conditions of immunosuppression or disruption of normal microbiota. Several risk factors, including prolonged ICU stay, mechanical ventilation, indwelling catheters, and total parenteral nutrition, significantly contribute to the development of candidiasis in COVID-19 patients [4].

Traditionally, *C. albicans* has been the most frequently isolated species; however, recent epidemiological trends indicate a notable shift towards non-albicans Candida (NAC) species, including *C. tropicalis*, *C. glabrata*, *C. krusei*, and *C. parapsilosis*. These species are clinically important due to differences in virulence and antifungal susceptibility patterns [5]. Non-albicans Candida species are increasingly implicated in invasive infections and often exhibit reduced susceptibility to commonly used antifungal agents, particularly azoles [5].

Another important factor contributing to the increased incidence of candidiasis in COVID-19 patients is the extensive use of empirical antibiotic therapy, which disrupts normal bacterial flora and promotes fungal overgrowth [6]. In addition, endothelial damage and the hyperinflammatory state associated with severe COVID-19 may facilitate fungal invasion into deeper tissues and bloodstream [6].

The clinical significance of Candida infections extends beyond increased morbidity, as invasive candidiasis and candidemia are associated with poor prognosis if not diagnosed and treated promptly. Delayed initiation of antifungal therapy has been shown to increase mortality rates in such patients [7] significantly. Therefore, early recognition, accurate species identification, and antifungal susceptibility testing are crucial for appropriate management.

In this context, the present study aims to evaluate the prevalence of Candida infections in COVID-19 patients and to determine the antifungal susceptibility patterns of the isolated species, thereby aiding clinicians in selecting effective antifungal therapy and improving patient outcomes.

MATERIALS AND METHODS

Study Design and Setting- This prospective observational study was conducted over 6 months, from December 2020 to May 2021, at King George Hospital, Visakhapatnam.

Study Population- A total of 126 clinical samples were collected from laboratory-confirmed COVID-19 patients who were clinically suspected of having fungal infections. Samples included oropharyngeal, oronasal, and nasal tissue, collected aseptically.

Inclusion Criteria

1. Patients with confirmed COVID-19 infection (RT-PCR positive).
2. Patients presenting with clinical features suggestive of fungal infection (such as oral lesions, nasal involvement, and respiratory symptoms).

Exclusion Criteria

1. Patients without confirmed COVID-19 infection.
2. Patients already receiving antifungal therapy before sample collection.
3. Inadequate or improperly collected specimens.

Sample Collection and Processing- Clinical samples were collected under aseptic precautions and transported promptly to the microbiology laboratory for further processing.

Direct Microscopy- All samples were subjected to direct microscopic examination using 10% Potassium Hydroxide (KOH) mount to detect fungal elements such as budding yeast cells and pseudohyphae.

Culture and Isolation- Samples were inoculated on Sabouraud Dextrose Agar (SDA) and incubated at 25°C and 37°C for 24–48 hours. Growth was observed, and colony morphology was suggestive of Candida species.

Identification of Isolates- Preliminary identification of Candida isolates was performed based on colony morphology on SDA, Gram staining, and germ tube test. CHROM agar was used for species differentiation.

Antifungal Susceptibility Testing- Final identification and antifungal susceptibility testing were carried out using the automated VITEK 2 Compact system with AST-YS08 cards, following standard laboratory procedures.

RESULTS

Fig. 1 shows the distribution of fungal elements in clinical specimens (N=126). Out of 126 samples, fungal elements were detected in 72 cases, while 54 samples were negative.

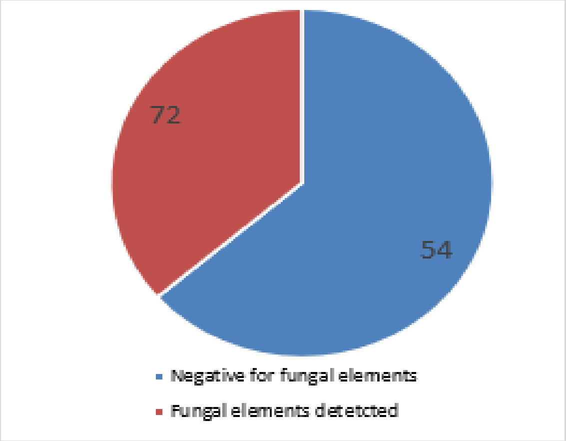

Fig. 1: Distribution of fungal isolates in clinical specimens (n=126)

Fig. 2 shows the distribution of Candida isolates among total fungal isolates (N=72). Candida species were isolated from 22 of 72 fungal-positive samples.

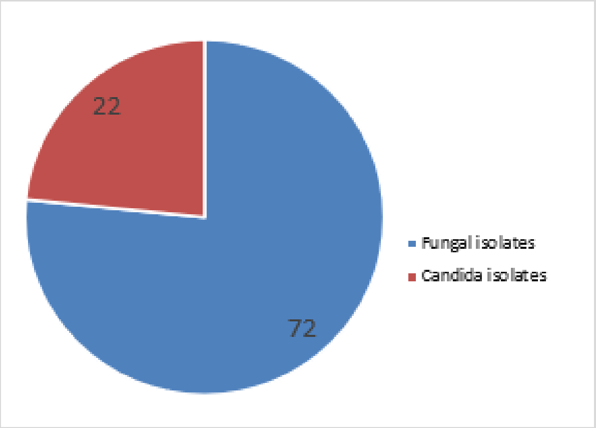

Fig. 2: Distribution of Candida isolates in fungal isolates (n=72)

Fig. 3 shows the distribution of Candida species (N=22). Among the isolates, *C. albicans* constituted 12 cases, while non-albicans Candida accounted for 10 cases.

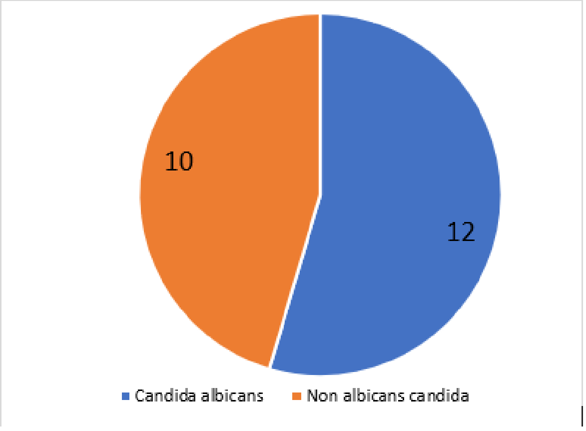

Fig. 3: Distribution of candida isolates (n=22)

Fig. 4 shows the distribution of non-albicans Candida species (N=10). The isolates included *C. tropicalis* (4), *C. glabrata* (3), *C. krusei* (2), and *C. parapsilosis* (1).

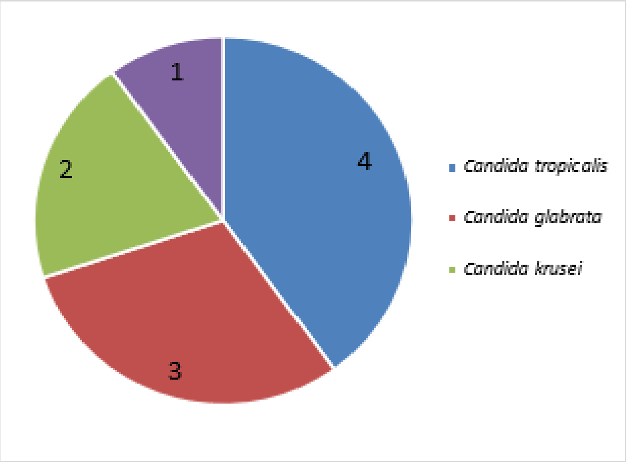

Fig. 4: Distribution of non albicans candida (n=10)

DISCUSSION

The present study highlights the prevalence and antifungal susceptibility patterns of Candida infections among COVID-19 patients, emphasizing the growing significance of fungal co-infections in the pandemic setting. In this study, fungal elements were detected in 57.1% of specimens, with Candida species isolated in 17.4% of cases. These findings are comparable to earlier reports demonstrating a substantial burden of secondary fungal infections among hospitalized COVID-19 patients, particularly those with severe disease and prolonged hospital stays [8,9].

The predominance of *C. albicans* (54.5%) observed in the present study is consistent with traditional epidemiological patterns, where *C. albicans* remains the most commonly isolated species. However, a considerable proportion (45.5%) of isolates were non-albicans Candida (NAC), indicating a shift in epidemiology. Similar trends have been reported globally, where NAC species such as *C. tropicalis*, *Candida glabrata*, *C. krusei*, and *C. parapsilosis* are increasingly implicated in infections, particularly among critically ill and immunocompromised patients [10-12].

The emergence of NAC species is clinically significant due to their variable antifungal susceptibility patterns. In the present study, *C. albicans* isolates showed high susceptibility to amphotericin B (100%), voriconazole (91.6%), and fluconazole (83.3%), suggesting continued effectiveness of commonly used antifungal agents. In contrast, NAC isolates demonstrated reduced susceptibility to fluconazole (60%), which aligns with previous studies reporting decreased azole sensitivity among NAC species [13,14].

Species-specific susceptibility patterns were also observed. *C. tropicalis* showed good sensitivity to amphotericin B and voriconazole, with variable response to fluconazole. *C. glabrata* exhibited dose-dependent susceptibility to fluconazole, while *C. krusei* demonstrated intrinsic resistance to fluconazole. *C. parapsilosis* isolates were largely sensitive to azoles and amphotericin B. These findings are in accordance with earlier studies describing species-specific resistance patterns among Candida isolates [15,16].

The increased incidence of candidiasis in COVID-19 patients can be attributed to multiple factors, including immune dysregulation, lymphopenia, corticosteroid therapy, use of broad-spectrum antibiotics, prolonged ICU stay, and invasive procedures. These factors disrupt host defenses, facilitating fungal colonization and infection. Similar observations have been reported in earlier studies highlighting these risk factors [17,18].

The clinical significance of Candida infections extends beyond increased morbidity, as invasive candidiasis and candidemia are associated with poor prognosis if not diagnosed and treated promptly. Delayed initiation of antifungal therapy has been shown to significantly increase mortality, emphasizing the importance of early diagnosis and timely management [19].

Recent studies have also reported an increased incidence of candidemia in ICU patients with COVID-19, further supporting the growing concern of fungal co-infections in this population [20]. This highlights the need for continuous surveillance and timely intervention in high-risk patients.

Overall, the findings of the present study reinforce the importance of routine fungal surveillance, early detection, species-level identification, and antifungal susceptibility testing in COVID-19 patients. A multidisciplinary approach involving clinicians and microbiologists is essential for effective management and improved patient outcomes.

CONCLUSIONS

The present study demonstrates that *C. albicans* remains the predominant species among COVID-19 patients; however, a significant rise in non-albicans Candida (NAC) species was observed. The increasing prevalence of NAC species is clinically important because of their variable antifungal susceptibility patterns, particularly reduced sensitivity to fluconazole. In contrast, higher susceptibility to amphotericin B and voriconazole was noted across most isolates. These findings highlight the need for routine fungal surveillance and early detection of Candida infections in COVID-19 patients, especially those with risk factors such as prolonged hospitalization, steroid therapy, or broad-spectrum antibiotics. Species-level identification, along with antifungal susceptibility testing, is essential for guiding appropriate and timely therapy. Early diagnosis and targeted antifungal management can significantly reduce morbidity and improve clinical outcomes. A multidisciplinary approach involving clinicians and microbiologists is crucial for effective management of fungal co-infections.

CONTRIBUTION OF AUTHORS

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Data collection- Padmaja Nama, Mounica Pedapalli, Jangam Sushma Rekha
Data analysis and interpretation- B Manjula
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Critical review- B Manjula
Article editing- Padmaja Nama, Mounica Pedapalli
Final approval- B Manjula

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