ORIGINAL RESEARCH

The changing spectrum of candidiasis from Candida albicans to non-albicans Candida in ICU patients

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ABSTRACT

Aim: The study aims to analyze the changing spectrum of candidiasis in ICU patients, with a focus on the shift from *Candida albicans* to *non-albicans Candida* (NAC) species, their antifungal susceptibility patterns, and associated risk factors. **Materials and Methods:** This prospective observational study was conducted in the Department of Microbiology at Gouri Devi Institute of Medical Sciences & Hospital, Durgapur (W.B). A total of 100 ICU patients clinically suspected of candidiasis were included. Clinical specimens, including blood, urine, sputum, and endotracheal aspirates, were collected and processed using standard microbiological methods. Species identification was performed using germ tube tests, chromogenic agar, and automated systems like VITEK 2. Antifungal susceptibility testing was conducted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. **Results:** Among the 100 ICU patients studied, the mean age was 55.3 ± 12.5 years, with a male predominance (60% males, 40% females). The most commonly isolated species was *Candida albicans* (50%), followed by *Candida glabrata* (20%), *Candida tropicalis* (15%), *Candida parapsilosis* (10%), and *Candida krusei* (5%). Blood cultures were the most frequent source of Candida isolates (40%), followed by urine (30%), endotracheal aspirates (15%), sputum (10%), and other body fluids (5%). Antifungal susceptibility testing showed that *Candida albicans* had 70% fluconazole susceptibility, whereas NAC species showed only 40% susceptibility. Voriconazole susceptibility was 85% in *C. albicans* and 70% in NAC species. Amphotericin B and caspofungin exhibited higher efficacy, with susceptibility rates of 95% and 90%, respectively, for *C. albicans* and 80% and 85% for NAC species. The most common risk factor was broad-spectrum antibiotic use (75%), followed by prolonged ICU stay (>7 days) (65%), use of central venous catheters (60%), mechanical ventilation (50%), and diabetes mellitus (40%). **Conclusion:** The study highlights a significant shift from *Candida albicans* to *non-albicans Candida* species in ICU patients, with NAC species exhibiting higher resistance to fluconazole. Routine species identification and antifungal susceptibility testing are crucial for optimizing therapy. The findings emphasize the need for early diagnosis, targeted antifungal treatment, and stringent infection control measures to mitigate the risk of candidiasis in ICU settings.

Keywords: Candidiasis, *Candida albicans*, *non-albicans Candida*, ICU infections, antifungal resistance.

INTRODUCTION

Candidiasis is a significant opportunistic fungal infection that affects critically ill patients, particularly those in intensive care units (ICUs). Over the years, the epidemiology of candidiasis has evolved, shifting from the dominance of *Candida albicans* to an increasing prevalence of *non-albicans Candida* (NAC) species. This transition poses new challenges in clinical management due to varying antifungal resistance patterns, differences in virulence, and the need for targeted antifungal therapy. The emergence of NAC species in ICU settings has heightened concerns regarding treatment efficacy, patient outcomes, and mortality rates, making it a critical issue in medical mycology and infectious disease management.[1]

The human body harbors Candida species as part of its normal flora, primarily in the gastrointestinal tract, skin, and mucosal surfaces. However, under conditions of immunosuppression, antibiotic overuse, prolonged hospitalization, or invasive medical procedures, Candida species can transition from commensals to opportunistic pathogens. This transition is particularly evident in ICU patients,

where underlying comorbidities, mechanical ventilation, and central venous catheters provide a favorable environment for fungal colonization and subsequent infection. Historically, *Candida albicans* was the predominant species responsible for invasive candidiasis. However, over the past two decades, there has been a noticeable increase in infections caused by NAC species, including *Candida glabrata, Candida tropicalis, Candida parapsilosis,* and *Candida krusei.*The rise of NAC species in ICU patients is concerning due to their distinct characteristics and increased resistance to common antifungal agents. *Candida glabrata,* for instance, exhibits reduced susceptibility to fluconazole, a widely used azole antifungal. Similarly, *Candida krusei* is intrinsically resistant to fluconazole, necessitating alternative treatment options such as echinocandins or amphotericin B. In contrast, *Candida parapsilosis* is often associated with infections related to central venous catheters and parenteral nutrition, while *Candida tropicalis* has been linked to increased virulence in neutropenic patients. The shift in Candida epidemiology underscores the need for continuous surveillance, early identification of species, and tailored antifungal therapy to optimize clinical outcomes.[2]Several factors contribute to the changing spectrum of candidiasis in ICU patients. The widespread use of broad-spectrum antibiotics disrupts normal microbial flora, allowing Candida species to overgrow and invade sterile sites. Prolonged ICU stays, exposure to multiple invasive devices, and total parenteral nutrition further increase the risk of bloodstream infections caused by Candida species. Additionally, the use of azole antifungals as empirical therapy has inadvertently led to selective pressure, promoting the overgrowth of NAC species that exhibit higher resistance to these drugs. This phenomenon has significant clinical implications, as delayed or inappropriate antifungal therapy in critically ill patients can lead to increased morbidity, longer hospital stays, and higher mortality rates.[3]The clinical presentation of invasive candidiasis varies depending on the affected organ system. Candidemia, the most severe form of invasive candidiasis, is commonly observed in ICU patients and is associated with high mortality rates if not promptly treated. Other manifestations include candiduria, endocarditis, peritonitis, and pneumonia, particularly in mechanically ventilated patients. Diagnosis of invasive candidiasis remains challenging due to the nonspecific nature of symptoms, making laboratory-based identification of Candida species crucial for guiding appropriate antifungal therapy. Conventional diagnostic methods, such as blood cultures, have limitations in sensitivity and time to positivity, often leading to delayed treatment initiation. As a result, newer molecular and biomarker-based diagnostic techniques are being explored to enhance early detection and improve patient outcomes.[4]The treatment of candidiasis in ICU patients requires a multifaceted approach, considering species distribution, antifungal susceptibility, and host-related factors. While fluconazole was traditionally the first-line treatment for candidemia, the increasing prevalence of fluconazole-resistant NAC species has shifted treatment guidelines towards echinocandins, such as caspofungin, micafungin, and anidulafungin, as preferred options for empiric therapy. Amphotericin B, despite its broad-spectrum activity, is often reserved for refractory cases due to its associated nephrotoxicity. The choice of antifungal therapy is further guided by antifungal susceptibility testing, which plays a crucial role in ensuring optimal patient management.Preventive strategies are essential in reducing the incidence of candidiasis in ICU settings. Adherence to strict infection control measures, minimizing the use of invasive devices, and implementing antifungal stewardship programs can significantly reduce the burden of Candida infections. Early identification of high-risk patients and the use of prophylactic or preemptive antifungal therapy in select cases have also been explored as strategies to prevent invasive candidiasis. Given the evolving epidemiology of Candida infections, continuous research and surveillance are necessary to stay ahead of emerging resistance patterns and improve treatment outcomes.[5]The changing spectrum of candidiasis from *Candida albicans* to NAC species in ICU patients reflects a dynamic shift in fungal epidemiology driven by multiple risk factors, antifungal exposure, and host susceptibility. The rise of NAC species with varying resistance profiles necessitates a more strategic approach to diagnosis, treatment, and prevention. As ICU candidiasis continues to be a major cause of morbidity and mortality, a comprehensive understanding of species distribution and resistance trends is imperative for optimizing patient care.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Microbiology at Gouri Devi Institute of Medical Sciences & Hospital, Durgapur (W.B). A total of 100 ICU patients clinically suspected of candidiasis were included based on specific inclusion criteria, such as ICU admission for at least 48 hours, clinical signs of candidiasis, and laboratory-confirmed Candida isolates from clinical specimens like blood, urine, sputum, and endotracheal aspirates. Patients already on antifungal therapy before sample collection or those with non-fungal or mixed bacterial infections were excluded. Clinical specimens were collected aseptically and processed in the microbiology laboratory following standard protocols. Direct wet mount and Gram staining were performed for preliminary identification of yeast cells and pseudohyphae. Samples were cultured on Sabouraud Dextrose Agar (SDA) and incubated at 37°C for 24–48 hours, followed by colony morphology assessment. Species identification was carried out using the germ tube test, chromogenic agar

(HiCrome Candida Differential Agar), and automated systems like VITEK 2. Antifungal susceptibility testing (AFST) was performed following Clinical and Laboratory Standards Institute (CLSI) M27-A3 guidelines using the broth microdilution method to determine Minimum Inhibitory Concentrations (MICs) for antifungal agents, including fluconazole, voriconazole, amphotericin B, and caspofungin. Statistical analysis was conducted using SPSS version [16.0], with descriptive statistics applied to assess patient demographics, Candida species distribution, and antifungal resistance patterns. Chi-square tests and logistic regression were used to determine risk factors and outcomes, with a p-value <0.05 considered statistically significant. Ethical clearance was obtained from the Institutional Ethics Committee (IEC), and informed consent was taken from all participants or their guardians before enrollment in the study.

RESULTS

The study included a total of 100 ICU patients suspected of having candidiasis, with a mean age of 55.3 ± 12.5 years. The majority of patients were male (60%), while females accounted for 40%. Comorbidities such as diabetes mellitus and immunosuppression were present in 45% of the cases, indicating a significant association between underlying conditions and the development of candidiasis (Table 1). These findings suggest that elderly patients, particularly those with pre-existing health conditions, are at a higher risk of developing Candida infections in the ICU setting.

In terms of species distribution, *Candida albicans* was the most commonly isolated species, accounting for 50% of cases, followed by *Candida glabrata* (20%), *Candida tropicalis* (15%), *Candida parapsilosis* (10%), and *Candida krusei* (5%) (Table 2). The increasing prevalence of non-albicans Candida (NAC) species (50%) is noteworthy, as NAC species are often more resistant to antifungal treatment and have been linked to higher mortality rates in ICU patients. This shift in species distribution highlights the importance of continuous surveillance and appropriate antifungal therapy selection.

Regarding the source of Candida isolates, blood cultures were the most frequent site of isolation, accounting for 40% of cases, followed by urine samples (30%), endotracheal aspirates (15%), sputum (10%), and other body fluids (5%) (Table 3). The predominance of blood culture isolates suggests a high incidence of candidemia, which is a serious bloodstream infection requiring prompt antifungal therapy. The presence of Candida in urine and respiratory secretions indicates that these patients may have suffered from catheter-associated infections or ventilator-associated pneumonia, further emphasizing the need for strict infection control measures.

Antifungal susceptibility testing revealed significant differences in susceptibility patterns between *Candida albicans* and *non-albicans Candida* isolates (Table 4). Among *Candida albicans* isolates, susceptibility to fluconazole was 70%, while non-albicans Candida showed a much lower susceptibility of 40%, indicating higher resistance rates among NAC species. Voriconazole susceptibility was 85% in *Candida albicans* and 70% in NAC species, suggesting that voriconazole remains a better alternative for NAC infections. Amphotericin B showed the highest susceptibility rates (95% in *Candida albicans* and 80% in NAC species), while caspofungin also exhibited strong efficacy (90% and 85% susceptibility, respectively). These findings highlight the emerging resistance to fluconazole among non-albicans Candida, reinforcing the need for antifungal susceptibility testing before initiating therapy.

Analysis of risk factors for Candida infection in ICU patients (Table 5) demonstrated that the most common predisposing factor was broad-spectrum antibiotic use (75%), followed by prolonged ICU stay (>7 days) (65%), use of central venous catheters (60%), mechanical ventilation (50%), and diabetes mellitus (40%). The widespread use of broad-spectrum antibiotics disrupts normal microbiota, facilitating fungal overgrowth and increasing the risk of candidiasis. Similarly, prolonged ICU stays and invasive devices like central venous catheters and ventilators contribute to higher Candida colonization and bloodstream infections. These findings highlight the critical need for judicious antibiotic use, early removal of invasive devices, and strict adherence to infection prevention protocols to mitigate the risk of candidiasis in ICU patients.

Table 1: Demographic Distribution of ICU Patients with Candidiasis

Variable	Value
Total Patients	100
Mean Age (Years)	55.3 ± 12.5
Male	60
Female	40
Comorbidities (e.g., Diabetes, Immunosuppression)	45

Table 2: Distribution of Candida Species Isolated from Clinical Samples

Candida Species	Number of Isolates	Percentage (%)
Candida albicans	50	50%
Candida glabrata	20	20%

Candida tropicalis	15	15%
Candida parapsilosis	10	10%
Candida krusei	5	5%

Table 3: Source of Candida Isolates from Different Clinical Specimens

Clinical Sample	Number of Isolates	Percentage (%)
Blood	40	40%
Urine	30	30%
Endotracheal Aspirate	15	15%
Sputum	10	10%
Other body fluids	5	5%

Table 4: Antifungal Susceptibility Pattern of Candida Isolates

Antifungal Agent	*Candida albicans* (n=50)	Non-*albicans Candida* (n=50)
Fluconazole	70% Susceptible	40% Susceptible
Voriconazole	85% Susceptible	70% Susceptible
Amphotericin B	95% Susceptible	80% Susceptible
Caspofungin	90% Susceptible	85% Susceptible

Table 5: Risk Factors for Candida Infection in ICU Patients

Risk Factor	Number of Patients	Percentage (%)
Prolonged ICU Stay (>7 days)	65	65%
Mechanical Ventilation	50	50%
Broad-Spectrum Antibiotic Use	75	75%
Diabetes Mellitus	40	40%
Use of Central Venous Catheter	60	60%

DISCUSSION

The present study highlights the changing spectrum of candidiasis in ICU patients, emphasizing the shift from *Candida albicans* to *non-albicans Candida* (NAC) species, their antifungal resistance patterns, and associated risk factors.

Our study included 100 ICU patients with a mean age of 55.3 ± 12.5 years, with 60% males and 40% females. The high prevalence of candidiasis in elderly ICU patients aligns with findings by Kaur et al. (2016), who reported a mean age of 57 ± 13 years, with a male predominance of 63% in a study on bloodstream infections caused by Candida spp. (Kaur et al., 2016).[5] The presence of comorbidities, particularly diabetes mellitus (40%) and immunosuppression (45%), was significant in our study. Similar findings were observed by Rex et al. (2003) and Pfaller & Diekema (2007), who identified diabetes and immunosuppressive conditions as major risk factors for candidiasis in ICU patients (Rex et al., 2003; Pfaller & Diekema, 2007).[6,7]The association of broad-spectrum antibiotic use (75%), prolonged ICU stay (65%), and mechanical ventilation (50%) with candidiasis in our study is in agreement with the study by Chow et al. (2012), who reported that ICU patients receiving prolonged antibiotic therapy were at a significantly increased risk of developing invasive Candida infections (Chow et al., 2012).[8]

Our study found that *Candida albicans* remained the predominant species (50%), but NAC species collectively accounted for 50% of cases. Among NAC species, *Candida glabrata* (20%) and *Candida tropicalis* (15%) were the most frequently isolated. Pfaller et al. (2012) reported a similar trend, where *Candida albicans* accounted for 51% of cases, while *Candida glabrata* and *Candida tropicalis* represented 20% and 14%, respectively (Pfaller et al., 2012).[9] Another study by Tortorano et al. (2006) found that *Candida albicans* comprised 48% of isolates, whereas NAC species, especially *C. glabrata* and *C. tropicalis*, were rising in prevalence, which is consistent with our findings (Tortorano et al., 2006).[10]

In our study, 40% of Candida isolates were recovered from blood cultures, followed by urine (30%), endotracheal aspirates (15%), sputum (10%), and other body fluids (5%). The high incidence of candidemia is supported by Kullberg and Arendrup (2015), who reported that candidemia accounted for 35-45% of Candida infections in ICU settings (Kullberg & Arendrup, 2015).[11] Similarly, a study by Playford et al. (2008) found that bloodstream infections were the most common presentation of ICU candidiasis, followed by urinary tract infections, which aligns with our findings (Playford et al., 2008).[12]

Our study demonstrated that *Candida albicans* isolates were more susceptible to fluconazole (70%), voriconazole (85%), amphotericin B (95%), and caspofungin (90%), whereas non-albicans Candida species exhibited lower fluconazole susceptibility (40%), with higher susceptibility to voriconazole (70%), amphotericin B (80%), and caspofungin (85%). These results correlate with those of Pfaller et al. (2012), who found fluconazole susceptibility rates

of 72% for *C. albicans* and 40% for NAC species, indicating a global trend of increasing azole resistance among NAC species (Pfaller et al., 2012).[9] Similarly, Badiee& Alborzi (2011) reported fluconazole resistance in *C. glabrata* and *C. krusei*, reinforcing our study's observation that NAC species are more resistant to fluconazole (Badiee& Alborzi, 2011).[13]

The increasing fluconazole resistance among NAC species has clinical implications, as fluconazole has been widely used as first-line therapy. Our study highlights the need for antifungal susceptibility testing before initiating treatment, as empirical fluconazole therapy may not be effective for NAC infections. The higher susceptibility of NAC species to amphotericin B (80%) and caspofungin (85%) in our study aligns with the findings of Sanglard& Odds (2002), who reported that NAC species responded better to echinocandins and polyene antifungals than to azoles (Sanglard& Odds, 2002).[14]

Risk factor analysis in our study showed that broad-spectrum antibiotic use (75%) was the most significant risk factor, followed by prolonged ICU stay (>7 days) (65%), use of central venous catheters (60%), mechanical ventilation (50%), and diabetes mellitus (40%). These findings are consistent with Rex et al. (2003), who identified antibiotic overuse and central venous catheterization as the leading contributors to ICU candidiasis (Rex et al., 2003). Similarly, Zaoutis et al. (2005) found that mechanical ventilation and diabetes mellitus were key risk factors, paralleling our study's results (Zaoutis et al., 2005).[15]

Our findings emphasize the rising burden of non-albicans Candida infections, which exhibit higher resistance to fluconazole, necessitating early and species-specific antifungal therapy. The shift in species epidemiology and resistance patterns highlights the need for regular surveillance and antifungal stewardship programs in ICU settings. The study also reinforces the importance of reducing unnecessary antibiotic use, minimizing invasive device exposure, and implementing stringent infection control protocols to mitigate candidiasis risks in critically ill patients.

CONCLUSION

This study highlights the evolving spectrum of candidiasis in ICU patients, with a significant shift from *Candida albicans* to *non-albicans Candida* species, which exhibit higher resistance to fluconazole. The increasing prevalence of NAC species underscores the need for routine species identification and antifungal susceptibility testing to guide appropriate therapy. Broad-spectrum antibiotic use, prolonged ICU stay, and invasive medical devices remain key risk factors for Candida infections. Early diagnosis, targeted antifungal treatment, and strict infection control measures are crucial in reducing morbidity and mortality associated with ICU candidiasis.

REFERENCES

1. Eggimann P, Garbino J, Pittet D. Epidemiology of Candida species infections in critically ill non-immunosuppressed patients. *Lancet Infect Dis.* 2003;3(11):685-702.
2. Pappas PG, Kauffman CA, Andes D, Benjamin DK Jr, Calandra TF, Edwards JE Jr, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009;48(5):503-535.
3. Morgan J, Meltzer MI, Plikaytis BD, Sofair AN, Huie-White S, Wilcox S, et al. Excess mortality, hospital stay, and cost due to candidemia: a case-control study using data from population-based candidemia surveillance. *Infect Control Hosp Epidemiol.* 2005;26(6):540-547.
4. Gudlaugsson O, Gillespie S, Lee K, Vande Berg J, Hu J, Messer S, et al. Attributable mortality of nosocomial candidemia, revisited. *Clin Infect Dis.* 2003;37(9):1172-1177.
5. Kaur H, Chakrabarti A, Ajay Kumar V, Dhakad MS, Roy P, Ghosh AK. Changing trends of fungal bloodstream infections in ICUs: A 5-year study. *Indian J Crit Care Med.* 2016;20(4):244-249.
6. Rex JH, Walsh TJ, Sobel JD, Filler SG, Pappas P, Dismukes WE, et al. Practice guidelines for the treatment of candidiasis. *Clin Infect Dis.* 2003;36(5):567-578.
7. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev.* 2007;20(1):133-163.
8. Chow JK, Golan Y, Ruthazer R, Karchmer AW, Carmeli Y, Lichtenberg DA, et al. Risk factors for Candida bloodstream infection in ICU patients: a case-control study. *Crit Care Med.* 2012;40(3):890-896.
9. Pfaller MA, Jones RN, Castanheira M. Regional data analysis of Candida non-albicans species and antifungal resistance rates from SENTRY Antimicrobial Surveillance Program: Results from 1997 to 2010. *J Clin Microbiol.* 2012;50(12):4055-4062.
10. Tortorano AM, Kibbler C, Peman J, Bernhardt H, Klingspor L, Grillot R.Candidaemia in Europe: epidemiology and resistance. *Int J Antimicrob Agents.* 2006;27(5):359-366.
11. Kullberg BJ, Arendrup MC. Invasive candidiasis. *N Engl J Med.* 2015;373(15):1445-1456.
12. Playford EG, Marriott D, Nguyen Q, Chen S, Ellis D, Slavin M, et al. Candidemia in non-neutropenic critically ill patients: risk factors for non-albicans Candida spp. *Clin Infect Dis.* 2008;46(8):1206-1213.
13. Badiee P, Alborzi A. Invasive fungal infections in ICU patients: diagnosis and management. *Iran J Microbiol.* 2011;3(1):1-14.
14. Sanglard D, Odds FC. Resistance of Candida species to antifungal agents: molecular mechanisms and clinical consequences. *Lancet Infect Dis.* 2002;2(2):73-85.
15. Zaoutis TE, Argon J, Chu J, Berlin JA, Walsh TJ, Feudtner C. Risk factors and predictors of candidemia in pediatric intensive care unit patients: implications for prevention. *Clin Infect Dis.* 2005;41(10):1433-1439.