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ICU-Acquired Candidemia: Epidemiological Trends, Risk Factors, Antifungal Resistance, and Clinical Outcomes in a Tertiary Care Centre in India

1 Dr. Abhi Chauhan, 2 Dr. Rashmi Modwal, 3 Dr. Shama Tomar

1 Resident, Department of General Medicine, National Institute of Medical Science & Research, NIMS University, Rajasthan (Jaipur)
2 Professor, Department of General Medicine, National Institute of Medical Science & Research, NIMS University, Rajasthan (Jaipur)
3 Professor, Department of Microbiology, National Institute of Medical Science & Research, NIMS University, Rajasthan (Jaipur)

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ABSTRACT:

Background: Candidemia represents a major nosocomial threat in ICU settings, leading to significant morbidity and mortality. With the rise in non-albicans Candida (NAC) species and antifungal resistance, early diagnosis and targeted management are imperative.

Objective: This study aimed to determine the epidemiological profile, risk factors, antifungal susceptibility patterns, and outcomes of candidemia in ICU patients in a tertiary care hospital in India.

Methods: A prospective observational study was conducted on 66 ICU patients diagnosed with candidemia from May 2023 to October 2024. Data on demographics, clinical parameters, interventions, and laboratory values were collected. Candida species identification and antifungal susceptibility testing were performed. Outcomes were compared based on the timing of antifungal therapy initiation.

Results: Among 438 ICU admissions, 32 patients (7.3%) were confirmed to have candidemia. Candida tropicalis (43.75%) was the most common isolate, followed by C. albicans and C. krusei. Risk factors included broad-spectrum antibiotic use (65.2%), immunosuppression (62.1%), and use of invasive devices. Fluconazole resistance was observed in 50% of isolates. Early antifungal treatment (within 48 hours) significantly reduced mortality (10% vs. 41.7%).

Conclusion: ICU-acquired candidemia is increasingly caused by NAC species with substantial antifungal resistance. Early diagnosis, prompt therapy, and species-level identification are critical to improve outcomes.

Introduction

Candidemia is a life-threatening fungal bloodstream infection caused by Candida species, often associated with intensive care unit (ICU) admissions due to invasive procedures, immunosuppression, and use of broad-spectrum antibiotics. It ranks among the top five causes of nosocomial bloodstream infections globally, with particularly high mortality in critically ill patients【1,2】. Historically, Candida albicans was the predominant pathogen, but recent decades have witnessed an epidemiological shift toward non-albicans Candida (NAC) species, which frequently

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exhibit reduced susceptibility to first-line antifungal agents such as fluconazole【3,4】.

ICU patients are particularly vulnerable to candidemia due to a combination of host-related and iatrogenic factors. The use of central venous catheters, parenteral nutrition, mechanical ventilation, renal replacement therapy, and broad-spectrum antibiotics disrupts the normal microbial flora and facilitates fungal colonization and invasion【5,6】. Furthermore, the immunocompromised state of ICU patients, whether due to underlying illnesses (e.g., diabetes, malignancies) or immunosuppressive therapies (e.g., corticosteroids, chemotherapy), creates a permissive environment for opportunistic fungal infections【7】.

The global burden of candidemia varies widely. Incidence rates range from 2 to 15 per 1,000 ICU admissions globally, with higher rates observed in low- and middle-income countries (LMICs) due to limited infection control practices and delayed antifungal therapy【8,9】. In India, several multicentric studies have demonstrated that candidemia in ICU patients is a growing challenge, with incidence rates significantly higher than those reported in Western countries, primarily due to high prevalence of risk factors such as diabetes, malnutrition, and widespread use of invasive devices【10,11】.

The emergence of multidrug-resistant (MDR) Candida species, particularly Candida auris, has further complicated the clinical landscape. C. auris is often misidentified by conventional methods, is capable of persisting in healthcare environments, and demonstrates resistance to multiple antifungal classes【12,13】. The increasing frequency of NAC infections necessitates routine species-level identification and antifungal susceptibility testing, which are not universally available in resource-limited settings【14】.

Current treatment guidelines recommend echinocandins (e.g., caspofungin, micafungin) as first-line therapy for most cases of candidemia, particularly those caused by NAC species. However, delays in initiating appropriate antifungal treatment have been consistently linked to increased mortality, reinforcing the need for early diagnosis through improved diagnostics such as β-D-glucan assays, PCR-based methods, and rapid blood culture techniques【15,16】.

Despite the increasing awareness of candidemia as a critical nosocomial threat, there remains a paucity of region-specific data in developing countries, especially from tertiary care ICUs. This study seeks to address this knowledge gap by characterizing the epidemiology, risk factors, antifungal resistance, and clinical outcomes of ICU-acquired candidemia in an Indian tertiary care hospital, thereby contributing valuable evidence to inform clinical practice and public health interventions.

Materials and Methods

This prospective observational study was conducted over an 18-month period from May 2023 to October 2024 in the Department of Critical Care Medicine and the Department of Microbiology at a tertiary care hospital affiliated with NIMS University, Rajasthan, India. The study aimed to evaluate the clinical profile, risk factors, microbiological characteristics, antifungal susceptibility, and outcomes of candidemia in ICU patients. Ethical approval was obtained from the Institutional Ethics Committee prior to the commencement of the study, and informed consent was taken from all participants or their legal guardians, in accordance with the Declaration of Helsinki.

The study population comprised adult patients (aged ≥18 years) admitted to the ICU during the study period. Patients were screened for candidemia based on clinical suspicion of sepsis unresponsive to broad-spectrum antibiotics and confirmed through microbiological evidence of Candida species in blood culture. A total of 438 ICU patients were evaluated during the study period, of whom 32 were diagnosed with candidemia and included in the final analysis. The inclusion criteria consisted of patients with clinical signs of sepsis and laboratory-

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confirmed candidemia. Exclusion criteria were patients with incomplete clinical or microbiological data, those transferred from other institutions without full documentation, and patients or family members who declined to provide consent.

Data collection was performed using a predesigned case report form. The demographic data collected included age, sex, residence (urban or rural), and occupation. Clinical history focused on the presence of comorbidities such as diabetes mellitus, chronic kidney disease, malignancy, and immunosuppressive therapy. Detailed records were maintained regarding the reason for ICU admission, baseline vital parameters, and clinical severity assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system at admission. Laboratory investigations included complete blood count (CBC), liver and renal function tests (LFT and RFT), inflammatory markers such as C-reactive protein (CRP) and interleukin-8 (IL-8), and imaging where indicated.

Patients were monitored for potential risk factors associated with candidemia, including the duration and spectrum of antibiotic use, administration of total parenteral nutrition (TPN), requirement for mechanical ventilation, and use of invasive devices such as central venous catheters (CVCs), urinary catheters, and endotracheal tubes. The immunological status of patients was also assessed to determine if they were immunocompromised due to disease or medication. Each patient diagnosed with candidemia was followed prospectively throughout their ICU stay until the time of discharge or death, to evaluate clinical outcomes.

Microbiological confirmation of candidemia was based on at least one positive blood culture for Candida species. Blood samples were collected under aseptic conditions and cultured using standard automated systems. Yeast isolates were identified to the species level using a combination of CHROMagar Candida medium, germ tube tests, and commercial biochemical identification kits. Antifungal susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) M27-A3 guidelines using the disc diffusion method and E-tests where applicable. Antifungal agents tested included fluconazole, amphotericin B, and echinocandins such as caspofungin and micafungin.

Results

During the 18-month study period, a total of 438 patients were admitted to the intensive care unit (ICU) of the tertiary care center and were screened for candidemia based on clinical and microbiological criteria. Among these, 32 patients were confirmed to have candidemia, resulting in an incidence of 7.3%. These 32 patients constituted the final study cohort and were further analyzed for demographic characteristics, risk factors, Candida species distribution, antifungal susceptibility patterns, and clinical outcomes.

The age distribution of patients ranged from 18 to over 80 years, with the majority of cases occurring in the 31–40-year age group (25%), followed by 41–50 years (15.62%) and 51–60 years (15.62%). This suggests that candidemia predominantly affected middle-aged adults, a population often involved in high-risk occupations and with significant exposure to comorbidities and healthcare interventions. Only one patient was above the age of 80 years. The male-to-female ratio in the study was 1.4:1, with 19 (59.38%) males and 13 (40.62%) females affected. This male predominance may reflect a higher burden of predisposing factors such as smoking, alcohol use, or occupational exposures among men in the study population.

In terms of geographical background, the majority of patients (56.25%) came from rural areas, while the remaining 43.75% were from urban regions. This finding highlights the possible role of delayed access to healthcare, poor hygiene conditions, and inadequate awareness regarding early signs of infection in rural populations. Furthermore, patients from rural settings may have presented to healthcare facilities at more advanced stages of sepsis, necessitating ICU admission and increasing the likelihood of nosocomial infections, including candidemia.

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The evaluation of clinical risk factors revealed a significant association with several well-established contributors to candidemia. Broad-spectrum antibiotic use was the most common risk factor, observed in 65.2% of the patients. This was followed by immunosuppressive conditions (62.1%), which included patients with diabetes, malignancies, or those on corticosteroids or other immunosuppressive drugs. More than half of the patients (53.1%) were mechanically ventilated, and a significant proportion (71.8%) had at least one indwelling device, such as central venous catheters or urinary catheters. The use of total parenteral nutrition (TPN) was documented in 43.7% of patients, further supporting its known role in facilitating fungal translocation and bloodstream invasion.

Table 1: Distribution of Cases According to Past Medical History

Past History	No. of Patients	Percentage (%)
Hypertension	8	25.0%
Diabetes	5	15.62%
Malignancy	5	15.62%
Steriod Therapy	6	18.75%
HIV/Immunocomprised	8	25.0%
Total	32	100%

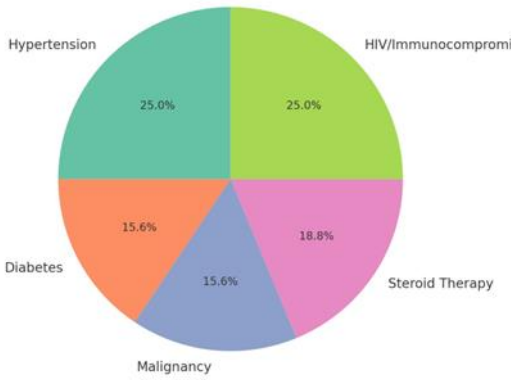

Figure 1:Diagrammatic presentation of Distribution of Cases According to Past Medical History

Laboratory investigations at the time of candidemia diagnosis showed varied levels of inflammatory markers and organ function parameters. Many patients had elevated CRP and IL-8 levels, indicative of systemic inflammation. Thrombocytopenia and leukocytosis were also common, and renal or hepatic dysfunction was noted in several cases. These findings were often nonspecific and overlapped with those seen in bacterial sepsis, emphasizing the difficulty of early clinical diagnosis without microbiological confirmation.

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Microbiological analysis revealed that Candida tropicalis was the most frequently isolated species, accounting for 43.75% of all cases. This was followed by Candida albicans (25%), Candida krusei (21.88%), Candida glabrata (6.25%), and Candida parapsilosis (3.12%). The predominance of non-albicans Candida (NAC) species (75%) represents a significant shift from earlier trends where C. albicans was more common. This trend toward NAC species may be influenced by widespread use of azole antifungals, prolonged ICU stay, and increased use of invasive procedures. The identification was performed using CHROME agar and germ tube tests, confirmed by biochemical methods.

Table 2: Blood Culture Findings

Organism	No. of Patients	Percentage (%)
Candida tropicalis	11	34.375%
Candida parapsilosis	8	25%
Candida albicans	7	21.875%
Candida glabtria	4	12.5%
Candida krusel	2	6.25%
Total	32	100%

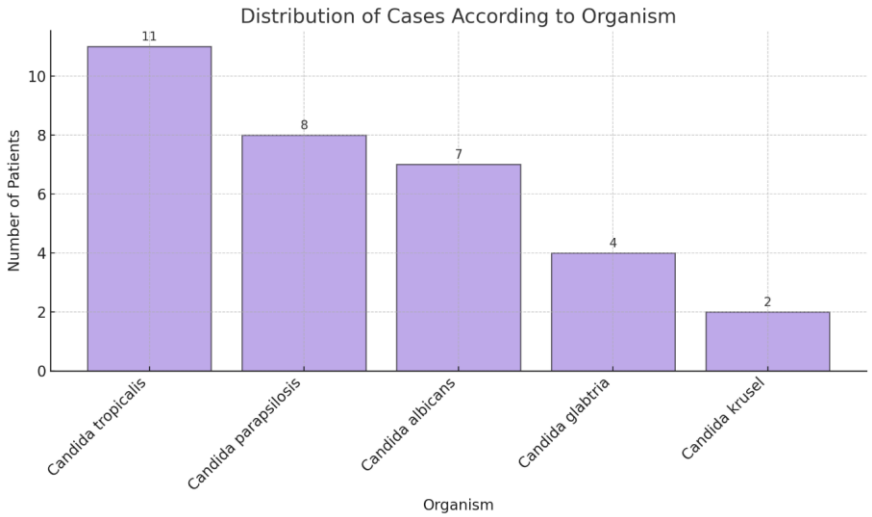

Figure 2: Diagrammatic presentation of Candidia Species Isolated from Blood Culture

Antifungal susceptibility testing revealed alarming resistance patterns, particularly among NAC isolates. Fluconazole resistance was observed in 50% of isolates, especially those of C. glabrata and C. krusei, which are known to exhibit intrinsic or acquired resistance. In contrast, all isolates were susceptible to echinocandins and amphotericin B, suggesting that these agents remain effective treatment options in our setting. However, given the resource constraints in many Indian ICUs, echinocandin use may be limited, which further complicates treatment decisions.

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Table 3: Antifungal Susceptibility

Antifungal	C. albicans	C. tropicalis	C. parapsilosis	C. glabrata	C. krusei
Amphotericin B					
Sensitive	5 (57.14%)	8 (72.7%)	7(87.5%)	2 (50%)	2 (100%)
Resistant	3 (42.85%)	3 (27.2%)	1 (12.5%)	2 (50%)	0 (0%)
Fluconazole					
Sensitive	6 (75%)	10 (90.9%)	6 (75%)	3 (75%)	1 (50%)
Resistant	2 (25%)	1 (9.09%)	2 (25%)	1 (25%)	1 (50%)
Voriconazole					
Sensitive	7 (87.5%)	09 (81.8%)	5 (62.5%)	3 (75%)	0 (0%)
Resistant	1 (12.5%)	2 (18.1%)	3 (37.5%)	1 (25%)	2 (100%)

The clinical outcomes of patients with candidemia were closely linked to the timing of antifungal therapy. Among patients who received early antifungal treatment (within 48 hours of symptom onset or culture suspicion), mortality was significantly lower at 10%, compared to 41.7% among those who received delayed treatment. Early therapy was also associated with shorter ICU stays and more favorable hemodynamic stabilization. Overall, 7 out of the 32 candidemia patients (21.9%) died during their ICU admission, reflecting the serious prognosis associated with this infection, especially in critically ill and immunocompromised patients.

Table 4: Different Species of Candida Isolated on CHROME Agar

Species Identification	No. of Isolates	Percentage (%)
C. albicans	8	25.0%
C. tropicalis	14	43.75%
C. krusei	7	21.88%
C. parapsilosis	1	3.12%
C. glabrata	2	6.25%

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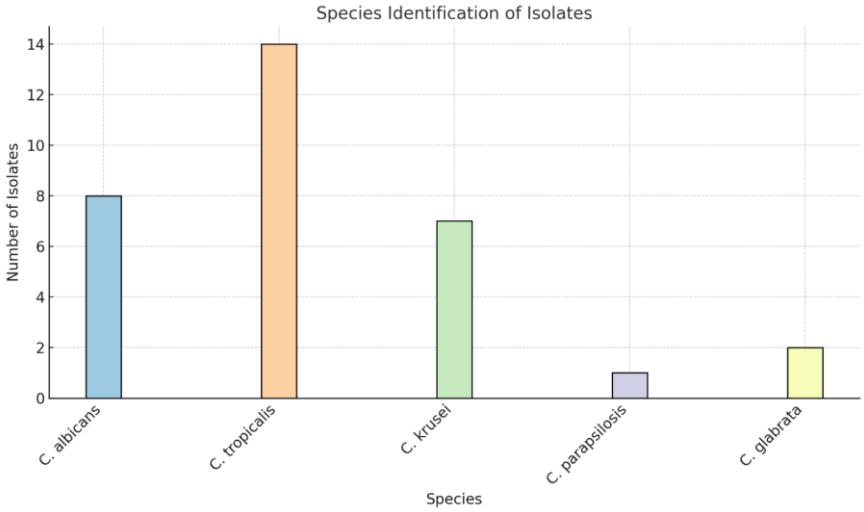

Figure 3:Diagrammatic presentation of Different Species of Candida Isolated on CHROME Agar

In summary, this study highlights that ICU-acquired candidemia is predominantly caused by NAC species, is associated with considerable fluconazole resistance, and has significant morbidity and mortality. Early diagnosis and timely initiation of appropriate antifungal therapy are critical in improving clinical outcomes. The data underline the importance of regular surveillance, antifungal stewardship, and prompt microbiological diagnostics in critically ill patients at risk of fungal bloodstream infections.

Table 5: Outcomes of the subjects.

Parameter	**Early Antifungal Therapy(≤ 48 hours, *n* = 20)**	**Late Antifungal Therapy(> 48 hours, *n* = 12)**	**Total (*N* = 32)**
Number of Cases	20	12	32
Mortality (n)	2	5	7
Mortality (%)	10%	41.7%	21.7%
Average ICU Stay (days)	8–10	10–14	–
Clinical Outcome	Faster recovery, better survival	Delayed recovery, higher complications	–

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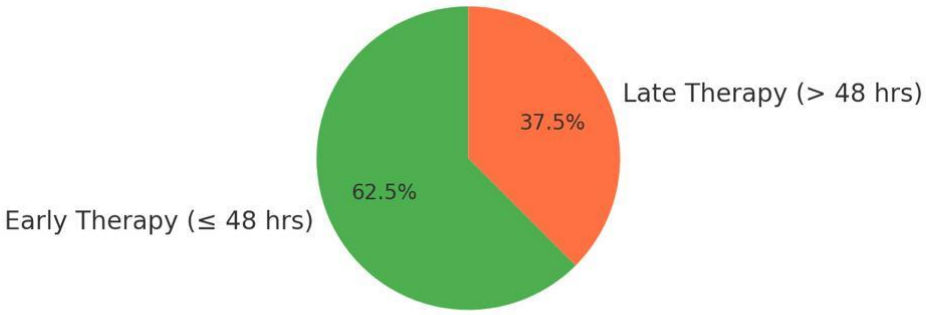

Figure 4:Diagrammatic presentation of Early and Late Antifungal Therapy

Discussion

The findings of this study align with global trends in the epidemiology of candidemia, underscoring an increasing burden in ICU settings and a shift toward non-albicans Candida species as dominant pathogens. Candida tropicalis was the most frequently isolated species in our cohort, consistent with several other Indian studies which report C. tropicalis as the predominant agent in candidemia cases【10,11,17】. This shift may reflect regional differences in antimicrobial usage patterns, environmental exposure, and host susceptibility.

One of the key concerns highlighted by this study is the high level of resistance to fluconazole (50%), particularly among isolates of C. krusei and C. glabrata, which are known for intrinsic or acquired resistance mechanisms【4,12】. This finding reinforces the global trend of declining azole efficacy, necessitating the empirical use of echinocandins, especially in patients with severe illness or those not responding to azole therapy【18】. Resistance to echinocandins and amphotericin B was not observed in our study, indicating that these agents remain viable treatment options in our setting, although emerging resistance globally calls for ongoing surveillance【19,20】.

The role of early antifungal intervention was clearly demonstrated in our study, with significantly lower mortality among patients who received treatment within 48 hours of diagnosis. This corroborates previous findings from both Western and Asian ICUs showing that early initiation of appropriate antifungal therapy substantially reduces mortality, ICU length of stay, and overall healthcare costs【6,15,21】. However, many patients in our cohort were started on antifungals only after culture confirmation, highlighting a critical delay in intervention.

Risk factors for candidemia identified in our study—use of broad-spectrum antibiotics, TPN, mechanical ventilation, and immunosuppression—are well-documented in the literature【5,7,22】. These modifiable risk factors present opportunities for targeted infection control strategies. The implementation of antifungal stewardship programs, coupled with rigorous infection prevention protocols, may help curb the incidence of candidemia in ICU settings【23】.

An important consideration is the diagnostic challenge posed by candidemia. Traditional blood cultures, while still the gold standard, are slow and often insensitive, with a detection rate of only about 50% in some reports【16,24】. Newer technologies like T2Candida and MALDI-TOF MS

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offer faster and more accurate identification, yet are largely inaccessible in many LMICs due to cost and infrastructure limitations. Bridging this diagnostic gap is essential for early, species-directed therapy and optimal patient outcomes【13,25】.

The study also underscores regional differences in Candida species distribution. Whereas C. glabrata and C. parapsilosis are more commonly reported in the US and Europe, Indian ICUs report higher rates of C. tropicalis and C. auris infections【9,10,26】. These species-specific differences have implications for empiric therapy and reinforce the necessity of local epidemiological data to inform antifungal prescribing practices.

Limitations of the current study include its single-center design and relatively small sample size. Nonetheless, it provides a valuable snapshot of the candidemia burden in a typical Indian ICU. Future research should include multicenter studies with larger populations, molecular epidemiology of resistance genes, and cost-effectiveness analyses of diagnostic and therapeutic interventions.

In conclusion, the study highlights that ICU-acquired candidemia in India is primarily driven by non-albicans species, marked by significant antifungal resistance, and associated with high mortality when diagnosis and therapy are delayed. Addressing this challenge will require multifaceted efforts—early diagnostics, antifungal stewardship, improved infection control, and greater access to effective antifungal agents.

Conclusion

This study highlights the growing burden of ICU-acquired candidemia in the Indian healthcare setting, particularly in tertiary care centers that manage critically ill and high-risk patients. With an incidence of 7.3% among ICU admissions in our cohort, candidemia remains a substantial nosocomial threat, especially in patients exposed to multiple invasive interventions and prolonged antimicrobial therapies. The predominance of non-albicans Candida species, particularly Candida tropicalis, and the notable rate of fluconazole resistance emphasize the evolving epidemiological landscape of fungal bloodstream infections in India.

The findings clearly demonstrate that candidemia is not merely an incidental occurrence but a major contributor to morbidity and mortality in ICU patients. Risk factors such as broad-spectrum antibiotic use, immunosuppressive states, mechanical ventilation, central venous catheterization, and total parenteral nutrition were frequently identified in affected patients, many of whom presented with high APACHE II scores. The interplay of these risk factors underscores the need for vigilant screening and timely clinical suspicion in patients with unexplained sepsis or fever unresponsive to antibiotics.

One of the most significant observations from this study was the positive impact of early antifungal therapy on patient outcomes. Patients who received antifungal treatment within 48 hours of suspected candidemia had markedly lower mortality rates and shorter ICU stays compared to those who received delayed therapy. This underscores the crucial importance of prompt diagnosis and immediate therapeutic intervention. Delays in initiating appropriate antifungal treatment continue to be a major obstacle in ICU settings, particularly in resource-limited institutions where advanced diagnostics may not be readily available.

Our study also calls attention to the pressing need for routine fungal surveillance, species-level identification, and antifungal susceptibility testing in critically ill patients. These measures are indispensable in ensuring accurate, species-directed therapy and preventing the overuse of empirical antifungal agents, which can drive resistance. The implementation of antifungal stewardship programs, in parallel with infection control protocols and improved diagnostic infrastructure, is critical to curbing the rise of drug-resistant Candida infections in Indian ICUs and similar settings worldwide.

In conclusion, ICU-acquired candidemia represents a complex, multifactorial, and evolving clinical challenge in tertiary care environments. Its effective management requires a multifaceted strategy

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encompassing early recognition, rapid diagnostics, appropriate empirical therapy, targeted antifungal treatment based on susceptibility patterns, and strong infection prevention measures. Our findings reinforce the need for continued research and policy-level interventions aimed at improving diagnostic capacity, promoting antimicrobial stewardship, and reducing the disease burden of invasive candidiasis in developing countries.

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