

PREVALENCE OF CANDIDA, CANDIDA SPECIES IN BLOOD STREAM AND ITS ANTI-FUNGAL SUSCEPTIBILITY- A RETROSPECTIVE STUDY FROM A TERTIARY CARE SET UP – NORTH KERALA

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ABSTRACT

Invasive candidiasis poses a significant challenge in healthcare settings, particularly among critically ill patients receiving broad-spectrum antibiotics and immunosuppressants. The prevalence of candidemia, caused by various *Candida* species, has been rising, with increasing concern over antifungal resistance and the emergence of multidrug-resistant pathogens such as *Candida auris*. This retrospective study aimed to investigate the prevalence of *Candida* species isolated from bloodstream infections and their antifungal susceptibility profiles in a tertiary care center in North Kerala, India. The study covered patients admitted from April 2021 to April 2023 with positive *Candida* blood cultures. Microbiological identification and sensitivity testing utilized automated and manual methods. Patient data were collected from hospital systems and analyzed descriptively.

Among 514 cases of blood culture-positive, *Candida* species were isolated in 50 instances (9.72%). Predominantly, candidemia affected males (68%) and elderly patients (>60 years) (64%), notably from invasive care units (54%). The most prevalent species was *Candida tropicalis* (26%), followed by *C. parapsilosis* (18%), *C. glabrata*, and *C. auris* (16% each), with *C. albicans* comprising 10%. Antifungal susceptibility testing demonstrated varying sensitivities, with most isolates responsive to amphotericin B (95.65%) and flucytosine (86.95%), but less sensitive to fluconazole (65). Candidemia poses a significant burden on ICU patients, with a notable shift from *Candida albicans* to non-*albicans* species. Antifungal stewardship, prudent use of antibiotics, maintenance of aseptic techniques, and improved hand hygiene practices are imperative to address this escalating public health concern.

Keywords: *Candidemia, Antifungal Susceptibility, Candida albicans, Fungal Infections*

INTRODUCTION

Along with the increasing number of critically ill patients receiving broad spectrum antibiotics, immunosuppressants, and invasive devices, invasive candidiasis has emerged as a significant public health problem.^[1,2]

The incidence of Candidemia in the overall population ranges from 1.7 to 10 episodes per 100,000 inhabitants and *Candida* is one of the ten leading causes of bloodstream infections in developed countries.^[3] Until recent times, *Candida albicans* was considered the most frequently isolated *Candida* species but non-*albicans* *Candida* have now become predominant.^[4] The commonly isolated non-*albicans* *Candida* species are *C. tropicalis*, *C. parapsilosis*, *C. guilliermondii*, *C. dubliniensis*, *C. glabrata*, *C. lusitanae*, *C. kefyr* and *C. krusei*. Some of the non-*albicans* *Candida* are intrinsically resistant to fluconazole (*C. krusei*) and some of them show resistance through enzyme modification to fluconazole (*C. glabrata*).^[5] *Candida auris* is a newly emerging multidrug-resistant yeast pathogen notorious for causing nosocomial outbreaks in many healthcare facilities worldwide. High mortality rates of *C. auris* infection have been reported among critically ill patients.^[6]

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Regular surveys on the distribution of *Candida* species and their antifungal susceptibility profiles are needed to understand the predominant species distribution and their susceptibility to antifungal drugs. Speciation and susceptibility testing of *Candida* is not yet a routine practice in most centers. However, due to significant regional variability, local epidemiological knowledge is crucial for effectively managing invasive Candidiasis. The objective of this study was to determine the prevalence of *Candida* spp in the bloodstream and their susceptibility to antifungal drugs in a tertiary care setting in North Kerala.

MATERIALS AND METHODS

This retrospective study was conducted at a tertiary care center in Kozhikode, Kerala. All patients admitted during the period from April 2021 to April 2023 were included in the study. The aim of this study was to identify *Candida* isolated in blood culture positive cases from all age groups. All blood cultures positive for *Candida* species underwent microbiological identification and sensitivity testing.

All blood cultures are routinely performed in an automated blood culture system (BACT/ALERT 3D). Primary identification of positive culture bottles is done through gram staining, and the result is immediately communicated to the concerned department clinician. The samples are then plated onto solid media such as Hichrome *Candida* Differential Agar (Himedia). Species identification is done manually by reading the media, as well as through the automated VITEK 2 system using the ID (YST card) and sensitivity (YSO8 card) tests. Isolated colonies of yeasts are also subjected to the Germ tube test, which is a screening test used to differentiate *Candida albicans* from other species of *Candida*. The antifungal agents tested include Amphotericin B, Caspofungin, Flucytosine, Micafungin, Voriconazole, and Fluconazole. Data on patient characteristics (age, sex, and ward) and medical records are retrieved from the hospital information system and lab registry. After collecting the data, it is analyzed and presented using graphs and tables.

RESULTS

From April 2021 to April 2023, among 514 blood culture positive the prevalence of *Candida* species was 50 (9.72%). Candidemic patient’s characteristics are described in **Table 1**.

Table 1: Distribution of patients with Candidemia

Category	April 2021 to March 2022	April 2022 to April 2023	Cumulative
SEX			
Male	24	10	34 (68%)
Female	5	11	16 (32%)
AGE			
Infants (0 – 1 yr.)	0	0	
Children (2 – 10 yr.)	0	0	
Adolescent (11 – 19 yr.)	0	0	
Adult (20 - 60)	7	11	18 (36%)
Elderly (>60 yr.)	22	10	32(64%)
WARD			
Non – Intensive Care Unit	13	10	23 (46%)
Intensive Care Unit	16	11	27 (54%)

Over the study period in both years, Candidemia cases were predominant in the male gender group, with a cumulative total of 68%. There were no reported cases of Candidemia in infants, children, and adolescents. However, elderly patients (>60 years) accounted for more cases than the adult group, making up over half of the total Candidemia cases (64%). Additionally, patients in the invasive care unit accounted for a

significant proportion of cases (54%) compared to the non-invasive care units. All isolates exhibited gram-positive budding yeast forms, and the germ tube test effectively differentiated *C. albicans* from non-*albicans* Candida. In Hichrome Candida Differential Agar (Himedia), inoculation showed colonies of different colors depending on the species of Candida (Figure 1).

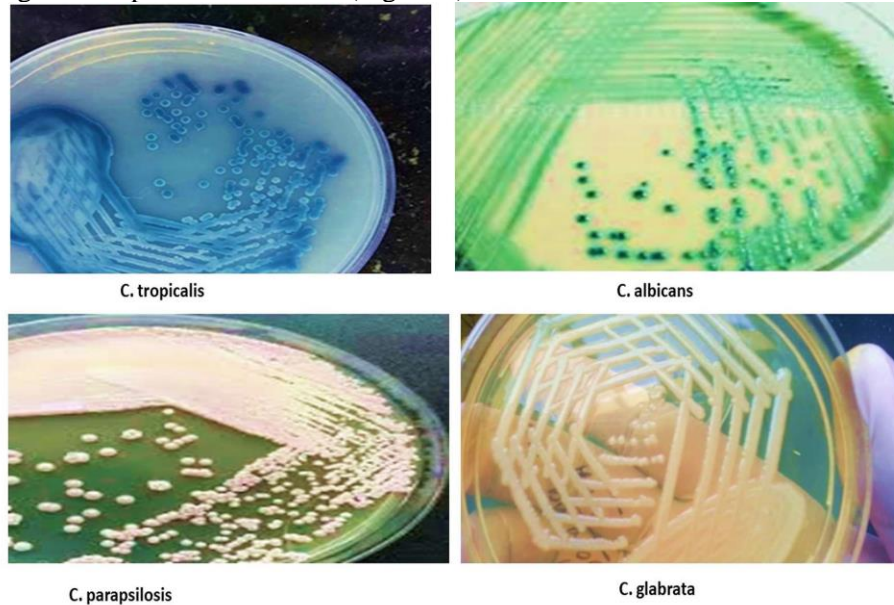


Figure 1: Different species of Candida in Hichrome Candida Differential Agar

Out of 50 isolates, *C. tropicalis* (n=13, 26%) was the most common, followed by *C. parapsilosis* (n=9, 18%), *C. glabrata* (n=8, 16%), *C. auris* (n=8, 16%), and *C. albicans* (n=5, 10%). *C. krusei*, *C. dubliniensis*, *C. lusitaniae*, *C. haemulonil*, and *C. duobushaemulonil* were the other species of Candida, accounting for much smaller proportions (Figure 2). Therefore, the prevalence of non-*albicans* Candida (90%) was higher compared to *C. albicans* (10%).

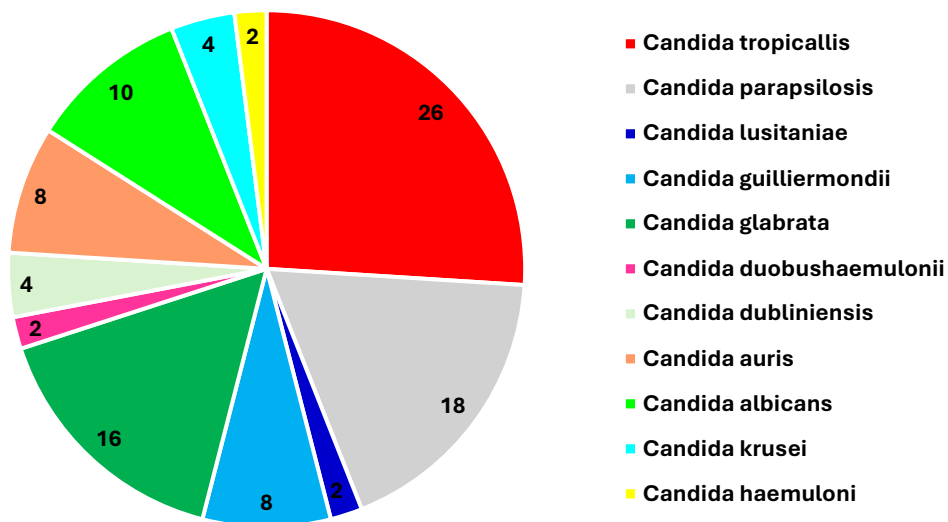


Figure 2: Organisms Frequency and Percentage

The antifungal susceptibility profile of 50 isolated *Candida* is described in Figure 3. The susceptibility profile of all *Candida* isolates showed that 95.65% were sensitive to Amphotericin B, 86.95% to Flucytosine, 84.78% to voriconazole, 80.43% to Micafungin, 73.91% to Caspofungin, and finally only 65.78% were sensitive to fluconazole. Nearly all the isolates of *Candida albicans* showed 80% sensitivity to all the antifungal agents, except for fluconazole (60%).

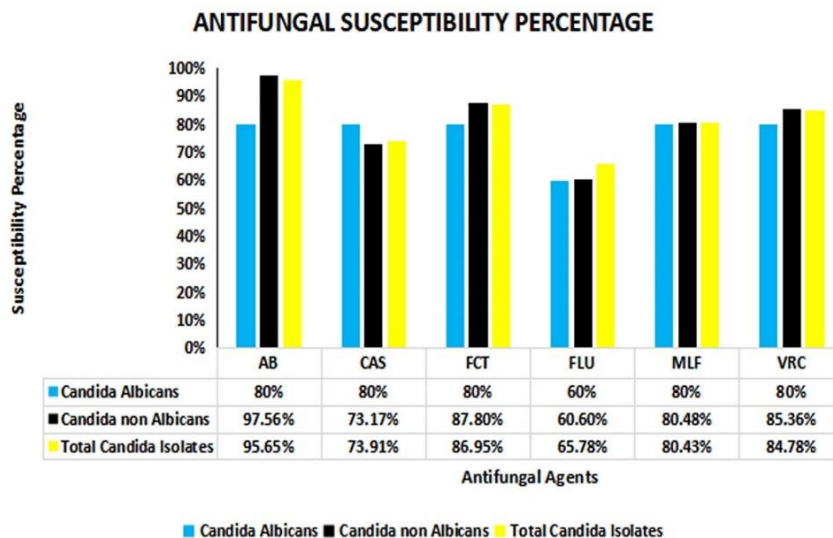


Figure 3: Multiple Bar chart of Antifungal Susceptibility Percentage.

DISCUSSION

In the present study, the total number of *Candida* species isolated was 50 (9.72%) out of 514 blood culture positive samples. The most prevalent species of *Candida* isolated was *C. tropicalis* (26%), followed by *C. parapsilosis* (18%), *C. glabrata* and *C. auris* (16%), and *C. albicans* (10%). Other species of *Candida*, including *C. krusei*, *C. dubliniensis*, *C. lusitaniae*, *C. haemulonil*, and *C. duobushaemulonil*, accounted for smaller proportions.

Unlike our results, an international study^[2] showed that *Candida albicans* was the most common species (50%) isolated from candidemic patients, followed by *C. glabrata* (25%) and *C. krusei* (16.6%). The least common species in their study was *C. tropicalis* (8.3%). Our results were in line with a similar Indian study by Prasanna et al.^[4] and Vibor tak et al.^[3]. In their study, *Candida tropicalis* (39%) was the most common species, followed by *C. parapsilosis* (20%), *C. albicans* (14%), *C. glabrata* (11%), and *C. guilliermondii* (2%).

Over the course of 1.5 years, in a prospective study conducted at Kochi, Kerala they found an overall incidence of 120 cases of candidemia among 1600 positive blood cultures (7.5%). In the same study candidemia ranked fourth in terms of bloodstream isolate infections, behind *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae*.^[7] In a different prospective, multicenter, nationwide observational study, 1400 cases of candidemia were isolated at 27 Indian ICUs between April 2011 and September 2012. According to a 2002 study conducted at SGPGI Lucknow, the eighth most common bloodstream infection was caused by candidemia, with a 1.61% incidence. The incidence was 1.74% at Gangaram Hospital, 8.1% at Rohatk Medical College, 6% at AIIMS, and 6.9% at MAMC New Delhi.^[8]

In our investigation, there were more patients with *Candida non-albicans* than with *Candida albicans*. *Candida tropicalis* accounted for 30.8% of the total species in our investigation. This is in contrast to the developed world, where the prevalence of *Candida albicans* (45.0–74.0%), *Candida tropicalis* (5.6–12.0%) and *Candida glabrata* (16.7–22.6%) is higher International Journal of Medical Research and Review.^[8] In contrast, we have only found *Candida albicans* candidemia in 0.83% of patients. 82% of medical

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professionals had yeast on their hands in a previous study conducted at the coordinating center, with 80% of the yeast being *C. tropicalis*.^[8]

Therefore, there are two main reasons why *C. tropicalis* candidemia is so common in India: horizontal transmission and compromised infection control systems. Other Asian nations have also reported a high prevalence of *C. tropicalis* candidemia.^[8] Adequate hygiene practices are necessary to reduce the frequency of horizontal transmission of candidemia. The majority of candidemia cases (30%) were admitted to the department of general medicine. The co-morbidities of our patients are somewhat consistent with previous data. According to the current study, the population with diabetes had a higher frequency of candidemia (63.3%).

Previous research has demonstrated that they have also documented significant rates of diabetes (10.7–28.0%) in their community with candidemia.^[8] We found that 5% of our patients with candidemia had an underlying hematological malignancy, which was lower than the 24.6–36.1% rate reported in another research.

Contrary to popular belief, *C. krusei* and numerous closely related strains of other rare species, such as *C. inconspicua* and *C. norvegensis*, are inherently resistant to fluconazole. It's possible that around 10% of the *C. glabrata* strains from BSI have a high level of fluconazole resistance.^[9]

When it comes to fluconazole resistance, *C. glabrata* is the most common species of *Candida* isolated from BSI in many nations, including the United States. Similar to how *C. glabrata* is isolated from candidemia cases, the frequency of fluconazole resistance in this species varies geographically. Resistance to fluconazole has been reported to be low (10–13%) in areas such as Asia–Pacific and Latin America, where the isolation of *C. glabrata* is less common. On the other hand, fluconazole resistance rates are significantly higher (18%) in nations like the United States where candidemia is primarily caused by *C. glabrata*.^[9]

CONCLUSION

To conclude, candidemia is a significant cause of morbidity and mortality in the ICU. There has been a noticeable shift in the species causing candidemia, with *Candida albicans* being replaced by *Candida non-albicans*. Specifically, *Candida tropicalis* and *Candida parapsilosis* have emerged as the predominant pathogens, along with the recent emergence of *Candida auris*. It is important to note that resistance to antifungal treatment is gradually increasing. Therefore, there is an urgent need for antifungal stewardship, a decrease in the excessive use of broad-spectrum antibiotics, the maintenance of aseptic techniques, and better hand hygiene practices.

Data availability

All data supporting the findings of this study are available within the paper and its Supplementary Information.

Declarations

Ethical Approval:

“This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Malabar Medical College and Research Centre’s Ethics Committee on December 14th 2023. Institutional Ethical committee reference number: MMCH&RC/IEC/2023/10

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Declaration of informed consent: The author(s) hereby declare that there is no information (names, initials, hospital identification numbers or photographs) in the submitted manuscript that can be used to identify patients.

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Aswathi K P:- Visualisation, Investigation
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Amina Yameena K: Validation
Alwin Prince:- Formal Analysis
Swetha P: Project administration
Soulesh P: Validation