Research Article

Candidiasis Among ICU Patients: Risk factors, Speciation and Antifungal Resistance Pattern: A Retrospective study from a tertiary care hospital in south Gujarat.

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Abstract

Introduction:Candidiasis is a significant cause of morbidity and mortality in immunocompromised patients admitted in intensive care units. Identification of Candida species is essential for effective treatment. However, in absence of proven fungemia, guidelines to initiate therapy are yet to be defined. **Materials and methods** - During the study (18 months: July 2018 to December 2019), samples (urine, sputum, blood, sterile body fluids) were collected from ICU patients and prospectively evaluated. Microscopy, culture, and antifungal susceptibility testing were performed as per standard laboratory protocol. **Results-** One hundred twenty-one non-duplicate samples (from 121 patients) positive on culture were included in the study. Female was significantly associated with the development of Candida infections than males with a ratio of 1.2:1. The most prevalent co-morbid condition among patients with Candida infections was diabetes mellitus (36.36%). Candida species revealed that Candida Albicans (51.24%) was the most frequently isolated species surpassing other non-albicans Candida species. Among non-albicans Candida species Candida glabrata (43.80%) was the most common isolated species followed by Candida tropical (4.13%). Candida species were mostly isolated from urine (70.25%) followed by blood(22.31%) and sterile body fluids(7.4%). Candida albican sensitivity was lowest for fluconazole (69.35%). Candida glabrata and candida tropicalis had shown alarming resistance to flucanazole and clotrimazole.**Conclusion** - The growing resistance to fluconazole necessitates the consideration of voriconazole as a highly effective alternative when initial treatment regimens do not succeed. In summary, the rising resistance of Candida species to ketoconazole emphasizes the vital need for precise species identification and antifungal susceptibility testing prior to the commencement of treatment. As resistance patterns develop, it is essential to maintain continuous surveillance and prudent application of antifungal medications to enhance patient outcomes and address the escalating challenge posed by drug-resistant fungal pathogens. This situation underscores the importance of antifungal susceptibility testing and monitoring to effectively tackle and manage resistance.

Keywords:candidiasis,antifungal,resistance

Introduction

Candidiasis is a critical infection affecting immune-compromised individuals, especially those in intensive care units (ICUs). It significantly contributes to both morbidity and mortality among these patients due to their weakened immune systems and the high likelihood of invasive procedures. Accurate identification of the Candida species involved is crucial for selecting appropriate antifungal therapy and improving patient outcomes. However, clinical guidelines for initiating treatment in cases where fungemia is not confirmed are still not well-established. This lack of clear guidelines can result in delays in treatment and potentially adverse outcomes. To enhance the management of candidiasis, it is important to understand the key risk factors, the distribution of Candida species, and the patterns of antifungal resistance prevalent in ICU settings.

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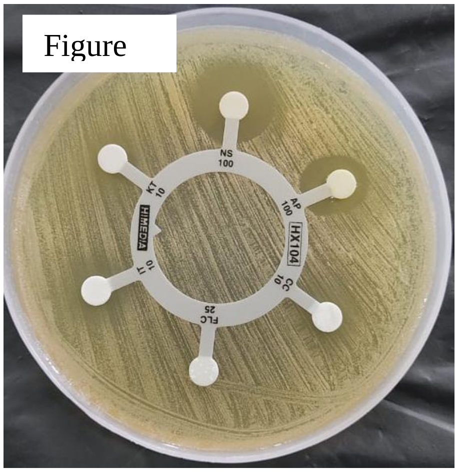
Materials and Methods

Study Duration and Sample Collection: This retrospective study was conducted over a period of 18 months, from July 2018 to December 2019. During this time, a range of clinical specimens—including urine, sputum, blood, tracheal aspirate, and samples from urinary catheters—were collected from patients admitted to the ICU. These samples were collected based on clinical indications of suspected candidiasis.

Laboratory Procedures: Upon collection, all specimens were processed in the laboratory following standard diagnostic protocols. Microscopic examination of samples was conducted using wet mounts and Gram staining to identify the presence of Candida species. For culture-based identification, samples were inoculated onto Sabouraud dextrose agar and incubated at 35-37°C. Cultures were monitored for growth, and yeast colonies were further identified using standard culture techniques including chromogenic medium.Antifungal susceptibility testing was performed to assess the resistance patterns of the Candida isolates. The susceptibility profiles were determined using the disc diffusion method, following the guidelines provided by European Committee for Antimicrobial Susceptibility Testing (EUCAST 10.0), epidemiological cut-off values (ECVs) and Clinical and Laboratory Standards Institute (CLSI M 44A). This testing involved exposing the Candida isolates to a panel of antifungal agents including fluconazole (25mcg), Amphotericin B (100 units), clotrimazole (10mcg), ketoconazole(10mcg), itraconazole(10mcg), nystatin(100 units) procured from HiMedia laboratories, Mumbai.



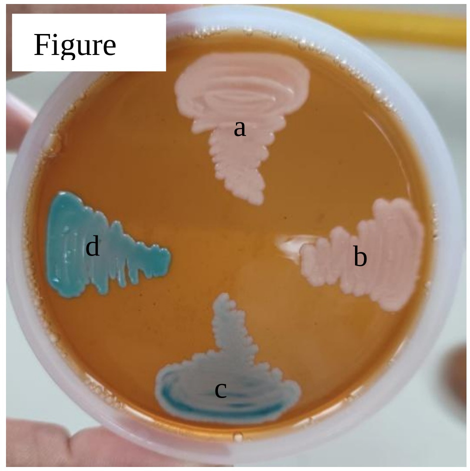


Figure A- Antifungal sensitivity used for this study.

Figure B- Colonies On Chorme Agar (Himedia) -

a. Candida Glabrata. b. Candida Krusei,

c. Candida Albicans, d. Candida Tropicalis

Data collection and analysis

Demographic information and clinical risk factors for each patient were extracted from their medical records. This included data on underlying health conditions, previous antibiotic or antifungal use, and other relevant clinical variables.

Statistical Analysis

Data were analyzed to determine the prevalence of different Candida species, identify risk factors associated with infection, and evaluate patterns of antifungal resistance. Descriptive statistics were used to summarize demographic and clinical characteristics, while chi-square tests and logistic regression analyses were employed to assess the relationships between risk factors and Candida infection outcomes.

Results

A total of 121 non-duplicate samples from 121 patients, all positive for Candida on culture, were included in this study.

Age and gender distribution: Candida infection was more common in females (55.3%) compared to males (44.7%). Female was significantly associated with the development of Candida infections than males with a ratio of 1.2:1. 61 -75 years (42.1%) were the most commonly affected age group followed by 46-60 years (28.9%) and 0-15 years (12%) with a mean age of 52.27 years.

Table 1.Age and gender-wise distribution of Candida infections-

Sr no.	Age (yrs)	Candida species isolated		Total
		Male	Female	
1	0-15	8	4	12(9.9%)
2	16-30	3	4	7(5.7%)

3	31-45	3	7	10(8.2%)
4	46-60	16	19	35(28.9%)
5	61-75	20	31	51(42.1%)
6	76-90	4	2	6(4.9%)
Total:		54 (44.7%)	67 (55.3%)	121(100%)

Co-morbid Conditions

The most prevalent co-morbid condition among patients with Candida infections was diabetes mellitus (36.36%), which was observed in a significant proportion among the study group. This condition was frequently associated with the development of fungemia.

Table 2. Co-morbid condition -wise distribution of Candida infections-

Sr. no.	Co-morbid Conditions	No.of patients (%)
1	Diabetes mellitus(with complications)	44 (36.36%)
2	Tuberculosis (pulmonary/extra pulmonary)	21(17.3%)
3	Acute renal failure(with/without sepsis)	26(21.4%)
4	Multiple infarct/Heart disease	8(6.6%)
5	Alcoholic liver disease/hepatic encephalopathy	6(5.7%)

Risk Factors

The primary risk factor identified for Candida infections in this study was the use of total parenteral nutrition (31.4%). This practice was common among the patients and was strongly correlated with the presence of Candida in the cultures.

Table 3. Risk factors-wise distribution of Candida infections-

Sr. no.	Risk Factors	No.of patients(%)
1	Sepsis or SIRS	26(21.4%)
2	Surgery	10 (8.2%)
3	Total Parenteral nutrition	38(31.4%)
4	Multifocal Candida colonization	9(7.4%)

Candida Species Distribution

The distribution of Candida species revealed that Candida albicans (51.24%)was the most frequently isolated species surpassing other non-albicans Candida species. Among non-albicans Candida species Candida glabrata (43.80%) was the most common isolated species followed by candida tropical (4.13%).

Table 4. Distribution of Albicans and Non-albicans Candida infections-

Candida species	No. of isolates	% of isolates
Candida albicans	62	51.24%
Non-albicans Candida	59	48.76%

Table 5. Distribution of Non-albicans Candida infections-

Candida Species	No. of isolates	% of isolates
Candida albicans	62	51.24%
Candida glabrata	53	43.80%

Candida tropicalis	5	4.13%
Candida krusei	1	0.83%
Total Candida species isolated	121	100%

Clinical Sample wise distribution: Among all the clinical samples that were received, Candida species were mostly isolated from urine (70.25%) followed by blood (22.31%) and sterile body fluids (7.4%).

TABLE 6. Clinical Sample wise distribution of Candida infections.

Candida Distribution With Sample Type	URINE	Sterile body fluids	BLOOD
Candida Albicans	44	6	12
Candida Glabrata	38	3	12
Candida Tropicalis	3	0	2
Candida Krusei	0	0	1
Total	85(70.25%)	9(7.4%)	27(22.31%)

ANTIBIOGRAM FOR (SENSITIVITY %) ICU patients: Among all the antifungal that were tested for Candida albican sensitivity was lowest for fluconazole (69.35%), followed by clotrimazole (74.19%). Similar pattern was also seen amongst isolates of non albicans candida species.In this study, Candida glabrata and candida tropicalis had shown alarming resistance to flucanazole and clotrimazole as shown in the Table below. while no resistance for any antifungals was observed in Candida Krusei.

TABLE 7. ANTIBIOGRAM(SENSITIVITY %) for Candida species infections in ICU patients.

Candida species	No. of isolates	ANTIFUNGAL AGENT					
		Amphotericin-B	Clotrimazole	Fluconazole	Ketoconazole	Itraconazole	Nystatin
Candida albicans	62	80.65%	74.19%	69.35%	80.65%	77.42%	88.71%
Non-albicans Candida	59	86.44%	77.97%	76.27%	86.44%	81.36%	88.14%

TABLE 8. ANTIBIOGRAM(SENSITIVITY %) for Non-albicans Candida species infections in ICU patients.

Non-Albicans Candida Species	No. of isolates	ANTIFUNGAL AGENT					
		Amphotericin-B	Clotrimazole	Fluconazole	Ketoconazole	Itraconazole	Nystatin
Candida Glabrata	53	86.79%	75.47%	75.47%	84.91%	79.25%	88.68%
Candida Tropicalis	5	80.00%	100.00%	80.00%	100.00%	100.00%	80.00%
Candida Krusei	1	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

Discussion

In this study, a total of 121 Candida isolates were obtained over 18 months of period from different clinical specimens.

Sex & Age Distribution: In this study 55.3% of infections occurred in females with a female-to-male ratio of 1.2:1. In this study the highest infection rates in the 61–75 years age group (42.1%) aligns with findings on the vulnerability of older adults.*A study by* Bhattacharjee P. shows that *Candia albicans*; most of the patients were within the age group of 51-60 years, whereas for NAC, most of the patients were aged 31-60 years; it also shows that candidiasis is more prevalent in females than males[4].Another study done in cancer patients at South Indian tertiary care hospital reported 55.8% of the patients were males followed by females at 44.1% (male-to-female ratio 1.26:1) [5].Other Studies in India show that older populations, especially those with underlying health conditions (e.g., diabetes, use of catheters), are more susceptible to systemic infections. The age and gender distribution of our study correlates the observation of other researchers in India [6, 7].

1.1 **Variations in Regional Data:**Though the overall pattern is similar, regional variations do exist. For example, in some urban hospital settings, the proportion of Candida isolates from blood tends to be slightly higher due to the higher prevalence of invasive Candidiasis in ICU patients and those undergoing immunosuppressive treatments.

1.2 **Sample wise Distribution:**Candida species were predominantly isolated from urine samples (70.25%), followed by blood (22.31%) and sterile body fluids (7.4%). This distribution reflects the clinical manifestation of Candida infections, with urinary tract infections (UTIs) being the most common. The high isolation rate in urine samples can be attributed to factors such as catheterization, diabetes, and prolonged antibiotic use, which are common predisposing conditions for Candiduria, especially in hospitalized and immune-compromised patients.

1.3 **Species wise Distribution:**Out Of the 121 Candida isolates, Candida species revealed that Candida albicans (51.24%) was the most frequently isolated species surpassing other non-albicans Candida species. Among non-albicans Candida species Candida glabrata (43.80%) was the most common isolated species followed by Candida tropical (4.13%). Our finding shows similar prevalence scenario of Candida species and susceptibility pattern to the previous data reported by two independent groups from India which showed C. albicans is more prevalent among the Candida isolates [16, 17].

Similar study conducted by Sajjan et al. also reported C. albicans as the major isolate. Among the NAC species, C. glabrata is the most common causative agent for NAC in Lebanon [18]. Study by Khadka, S., Sherchand, J.B., Pokhrel shows C. tropicalis (20%), C. glabrata (14%) and C. krusei (10%) respectively [19]. However, many studies have shown that NAC species have more isolation rate than C. albicans which suggest the emergence of non-albicans Candida species as important pathogens [23, 24].Speciation of Candida species by CHROMagar on the basis of colour differentiation offered a rapid, convenient and reliable method for identification of clinically important Candida species when compared with cumbersome traditional techniques. In developing countries, CHROMagar can be taken as a simple phenotypic test alternative to molecular based assay. CHROMagar has high sensitivity as well as specificity for the identification of Candida species [10, 25].

Antifungal resistance wise distributation: Among all the antifungal that were tested for candida albican sensitivity was lowest for fluconazole (69.35%), followed by clotrimazole (74.19%). Similar pattern was also seen amongst isolates of non albicans candida species. Candida glabrata shows similar sensitivity for fluconazole and clotrimazole that was 75.47% and candida tropicalis shows different sensitivity for flucanazole (80 %) and clotrimazole (100%).

Our finding is very close with the findings of Mondal et al., which also showed 18% Candida spp. and 19.2% C. tropicalis were resistance to fluconazole [17]. The study conducted by Zomorodian et al. showed that fluconazole sensitivity was seen in 96.6% of the Candida isolates [31].

On the contrary, all C. Krusei isolates were sensitive to fluconazole in our study. In a case of C. Krusei, some degree of susceptibility was seen to fluconazole, comparable to other studies by applying same interpretative criteria as introduced by CLSI [15, 29].

It has been noted that there is an intrinsic resistance to fluconazole. Consequently, further investigation is required to address the issue of fluconazole sensitivity. The rising resistance to fluconazole is particularly alarming, given that it is the most frequently utilized azole for both superficial and systemic candidiasis.

This study also reveals the higher rate of ketoconazole resistance was seen in C. albicans (19.35%), C. glabrata (15.09%). Our result hugely differs from the findings by Mondal et al. revealed overall 11.7% resistance to ketoconazole and with Candida krusei (20%) followed by C. glabrata (17.6%), C. tropicalis (15.2%) and least being C. albicans (7.8%) [17]. Furthermore Binesh et al. in which only 2.1% C. albicans isolates were resistant to ketoconazole [30].

The results indicate a swift rise in resistance among Candida species to ketoconazole, highlighting the necessity for accurate speciation and antifungal susceptibility testing prior to the administration of antifungal medications.

Conclusion

C.Albicans is the common isolate; however the incidence of NAC has also been increased considerably. The NAC species has changes in their sensitivity pattern to various antifungal agents used commonly in clinical practice which is a common cause of concern. Hence it is necessary to monitor closely the incidence of various species along with their antifungal susceptibility.

Fluconazole, available in both oral and intravenous forms, is a widely used antifungal medication effective against various Candida species. Its versatility in administration makes it a valuable option for treating candidiasis. However, due to increasing resistance to fluconazole, voriconazole, which is a excellent alternative should be considered when initial treatments fail. In conclusion, the increasing resistance of *Candida* species to ketoconazole underscores the critical importance of accurate species identification and antifungal susceptibility testing before initiating treatment.

As resistance patterns continue to evolve, ongoing surveillance and judicious use of antifungal agents are necessary to optimize patient outcomes and combat the rising threat of drug-resistant fungal pathogens. This trend highlights the need for antifungal susceptibility testing and surveillance to address and manage resistance effectively.

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