

## Candida Infection in Intensive Care Unit Patients at Tertiary Care Hospital

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### Abstract:

**Introduction:** Candidiasis is an opportunistic infection, an important cause of morbidity and mortality among the critically ill Intensive Care Unit (ICU) patients. **Objective:** The main aim of this study is to examine the trend of *Candida* infection in Intensive Care Unit (ICU) patients and to compare it with co-morbidities. All the patients admitted to Intensive Care Unit (ICU) were included in this study. **Method:** A clinical and laboratory study of critically ill patients admitted at adult ICU, Civil hospital, Ahmedabad from August-October 2014 was done. Laboratory findings of cultures including the infecting *Candida* species, resistance to antifungals and clinical profile along with associated risk factors were analyzed. Overall 45 patients with positive blood culture and 116 patients with positive urine culture were included in the study. **Results:** Total 32 cases of candidiasis were identified over the study period which includes 4 cases of candidemia and 28 cases of candiduria. The most common co-morbidities were prolonged ICU stay [for more than 4 days (100%)], multiple antibiotics [more than two (100%)], urinary catheterization (100%), diabetes (25%), mechanical ventilator support (31.25%) and central venous catheterization (9.3%). *C. krusei* was the most common species identified in blood and *C. tropicalis* in urine. The rates of susceptibility to antifungal agents were found as Amphotericin B (100%), Voriconazole (97%), Fluconazole (81%), Itraconazole (75%) and Miconazole (47%). **Conclusions:** Prevalence of candidiasis in ICU is significantly high than general wards ( $p < 0.0001$ ). Most patients had one or more co-morbidities at the time of the diagnosis of candidemia. Prolonged ICU stay, multiple antibiotics, prolonged indwelling devices and diabetes mellitus were the common underlying conditions documented prior to candidemia.

**Keywords:** candidiasis, intensive care unit, risk factors

### Introduction:

During the past two decades, the incidence of candidemia has increased and *Candida* species currently ranks as fourth most common bloodstream pathogen in North American studies.<sup>[1]</sup> Prolonged ICU admission, diabetes, administration of broad spectrum antibiotics, corticoids and widespread use of invasive therapeutic equipment increases the risk of fungal colonization and infection.<sup>[2]</sup> Candidemia is the most common manifestation of invasive candidiasis and requires antifungal treatment. Patients with candiduria are frequently colonized at other body sites, increasing the risk of developing candidemia. Candiduria should be considered as a marker of severity.<sup>[3]</sup> *Candida* colonization of the urinary tract is common in patients who are catheterized for prolonged period. The discovery of pyuria and high *Candida* colony counts along with

clinical symptoms can differentiate infection from colonization.<sup>[4,5]</sup> *C. albicans* is the most common cause of candidemia worldwide. However, in recent years, some studies have reported an increase of candidemia due to non-*albicans Candida* species.<sup>[6-9]</sup> The intrinsic and emerging resistance to azoles represents a major challenge for therapeutic strategies.<sup>[10]</sup>

### Method:

In the present study, a three month analysis (August-October 2014) was conducted to evaluate the frequency, species distribution, associated resistance patterns of *Candida* species for the antifungal agents used and clinical profile with other risk factors of patients admitted at adult ICU [Medicine, Trauma, Neurosurgery, General surgery] at Civil hospital, Ahmedabad. Data such as sex, age, and variables such as possible predisposing factors,

including antibiotics, underlying diseases or comorbid conditions and stay in the hospital, were collected from the patient record files.

**Inclusion Criteria :** All the patients admitted in the ICU  $\geq$ 18 years of age.

**Exclusion Criteria :** Patients who had less than 18 years of age and an ICU stay of less than 4 days were excluded from the study.

An episode of candidemia was defined as an isolation of non-commensal *Candida* species from blood culture in a patient with clinical signs and symptoms, such as fever, leukocytosis etc. and candiduria was defined in patients who had pyuria and at least one positive urine culture by semi-quantitative culture method. Associated risk factors were diabetes mellitus, indwelling central vascular catheter, long duration stay at intensive care unit during hospitalization, mechanical ventilation, urinary catheterization, use of broad spectrum antibiotics, acute renal failure, etc.

**Organism identification :** All blood samples were received in BacT/ALERT aerobic blood culture bottle (Biomerieux) and after being signal positive, were sub cultured. All urine samples were received in sterile universal container and cultured on blood agar (Himedia) by semi-quantitative plating method using the calibrated loop technique (0.001 ml). Isolated colonies were identified considering their macroscopic and microscopic appearance, germ tube test, biochemical properties on CHROM agar (CHROMagar Company, Paris France), carbohydrate fermentation and assimilation, morphology on corn meal agar, etc.

**Anti-fungal susceptibility :** All isolates were tested for antifungal susceptibility by disc diffusion method (recommended by CLSI) on Mueller-Hinton agar + Glucose (2%) and 0.5mg/ml Methylene blue dye by loan culture of 0.5 Mcfarland standards and incubated at 37°C for 24 hours. Sensitivity testing is a standardized agar diffusion method which includes antifungal agents (Hi-Media) as Amphotericin B (100unit), Voriconazole (1µg), Fluconazole (10µg), Itraconazole (30 µg), Miconazole (30 µg). Additional incubation was done for 24hours, if confluent growth was not obtained. Zones of Inhibition were measured and interpreted by referring CLSI M44-A2.

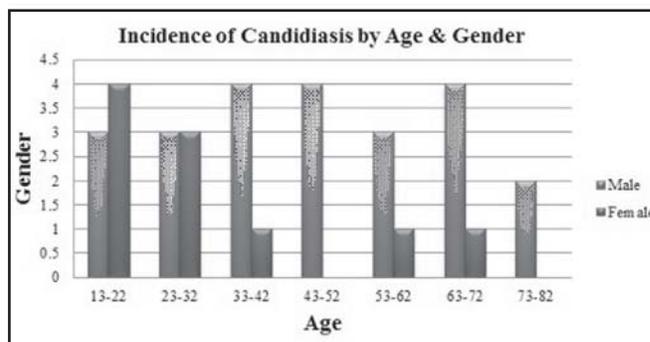
**Statistical Analysis :**

The data is analyzed using Chi-Square test to determine the level of significance. Qualitative data was expressed in terms of frequencies.

**Results :**

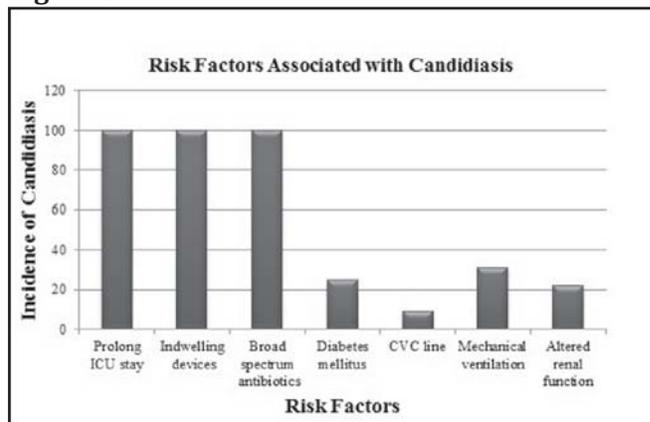
Out of 45 positive blood culture, 4(8.88%) of the isolates were *Candida* species and out of 116 positive urine cultures, 28(24.1%) were positive for *Candida* species. occurrence of *Candida* infection was high in males than females, though not statistically significant, mainly in patients of >35 years of age [Figure 1].

**Figure 1 : Incidence of candidiasis by age and gender**



Most common conditions associated with candidiasis among patients with ICU stay of more than 4 days or 96 hours were broad multiple antibiotic treatment (more than two)(n=32, (100%)) and indwelling urinary catheterization (n=32, (100%)). Whereas, mechanical ventilator support (n=10 (31.25%)), diabetes mellitus (n=8, (25%)), altered renal function (n=7, (21.8%)), central venous catheterization (n=3, (9.3%)) were less common risk factors [Figure 2].

**Figure 2 : Risk factors associated with candidiasis**



**Table 1 : The most common isolates from Blood and Urine Samples**

Isolates from Urine		Isolates from Blood	
Candida Sp.	No (%)	Candida Sp.	No (%)
<i>C. tropicalis</i>	59 (51)	<i>C. krusei</i>	16 (35)
<i>C. albicans</i>	29 (25)	<i>C. albicans</i>	13 (28)
<i>C. krusei</i>	14 (12)	<i>C. glabrata</i>	8 (17)
Others	14 (12)	Others	9 (20)

Table 1 describes the three most commonly occurring *Candida* species. Blood isolated *Candida* species included *C. krusei* (n=16 (35%)) as most occurring followed by *C. albicans* (n=13 (28%)), *C. glabrata* (n=8 (17%)). Other infections (n=9 (20%)) obtained from blood accounted 20% of the total infections. Isolated obtained from urine were *C. tropicalis* (n=59, (51%)), *C. albicans* (n=29 (25%)) and *C. krusei* (n=14 (12%)) in common, whereas the other infecting micro-organisms (n=14 (12%)) accounted only for 12% of the total infection considered in the study. Amphotericin B (100%) had the maximum rate of susceptibility amongst all the antifungal agents, which was found to be 100%. It was followed by Voriconazole with 97% susceptibility. Fluconazole and Itraconazole were 81% and 75% susceptible respectively. Infecting *Candida* species were least vulnerable to Miconazole with only 47% susceptibility.

**Discussion :**

Hospital acquired infections is a frequent complication among patients admitted to tertiary hospitals. Patients with conditions as critically ill or weakened immune systems are at most risk. Infections with fungal pathogens, of which *Candida* species predominate, are an important cause of morbidity and mortality among the critically ill. [2] In particular, the incidence of candidiasis has been increasing during the past years. Our study revealed males encountered more frequent infections than females, but this difference remains statistically insignificant and the main reason for this can be considered small sample size of the study population. In our study, *C. tropicalis* is more prevalent, as compared to other *non albican candida* species. *C. albicans* was found second in line of infecting agents in our study which was also found the

most common infecting agent of hospital acquired infections of different studies around the world. [11] Although prophylactic treatments with fluconazole causes a decrease in the frequency of candidiasis is caused by *C. tropicalis* but it is increasingly showing a moderate level offluconazole resistance. [12] The antifungal susceptibility patterns revealed that Amphotericin B and Voriconazole has excellent in vitro activity overall against *Candida* species with 100 and 97% susceptibility respectively. We observed a significant predominance of *non-albicans Candida* species (75%), with *C. tropicalis* (51%) being the most common isolate in urine and *C. krusei* (35%) in blood. In our study, *C. tropicalis* surpassed other *Candida* species and was most common contributors of infections to ICU admitted patients. The majority of *Candida* isolates were susceptible to azoles, with the exception of those belonging to the intrinsically less susceptible or resistant species, like *C. glabrata* and *C. krusei*. [13] Some studies showed that Voriconazole may be a suitable agent for salvage therapy of invasive candidiasis among all azoles, even with *C. krusei* infection. [14] In our study, Amphotericin B was found to be the best option available to treat hospital acquired infections in general, *Candida* infections which was followed by Voriconazole. This was also demonstrated in other studies too, as shown by Voriconazole activity which was better than other azoles demonstrating poor activity against *C. krusei*, whereas amphotericin showed good activity. [15] *C. krusei* is intrinsically resistant to fluconazole due to an altered cytochrome P450 isoenzyme. [16] Use of higher doses too cannot overcome this resistance. Hence, we would like to suggest improving prevention strategies as simple as infection control which are always better.

**Conclusion :**

Candidiasis is an important risk factor in case of ICU patients in form of hospital acquired infections both in terms of morbidity and mortality. Prolonged ICU stay, multiple antibiotics (>2) and prolonged use of catheterization devices were found the most common co-morbid conditions. One or more co-morbidities were frequently observed at the time of the diagnosis of candidemia in ICU patients. Prevalence of candidiasis in ICU was also significantly

higher than general wards ( $p < 0.0001$ ). Hence, developing and implementation of prevention strategies would provide us better control of *Candida* infections in ICU patients.

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