Research Article

# Prevalence of non-albicans Candida species versus Candida albicans in critical care patients of a tertiary care hospital

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## Abstract

**Introduction**: Candida species are the most common cause of opportune- istic fungal infections. Although *C.albicans* is most common cause of candidiasis, a shift towards non-albicans Candida species is evident in recent years. The transition of Candida spp. from commensal to a potent pathogen is facilitated by a number of virulence factors viz. adherence to host tissues and medical devices, biofilm formation, and secretion of extracellular hydrolytic enzymes. **Objective:** To study the prevalence of *C.albicans* & Non-albicans isolates in critical care settings and determine their virulence factors and antifungal susceptibility profile. **Material & Methods:** The present study was carried out in the Department of Microbiology, SGRIMSAR, Amritsar during the period of July 2014 to June 2016. Candida strains isolated from various clinical samples received from different ICUs of the hospital were included in the study. The isolates were identified upto species level by both conventional and automated methods (vitek 2 compact system) as per CLSI guidelines. Relevant history of all the patients was taken. They were also screened for the production of virulence factors such as biofilm formation, haemolytic activity, and production of extracellular hydrolytic enzymes i.e. coagulase. **Results:** Out of the 115 isolates obtained from various ICUs, most common isolate was *C. tropicalis* 60/115(52.17%) followed by *C. albicans* 45/115(39.13%), *C.utilis* 7/115(6.25%). Isolates of *C. lusitaniae*, *C. parasillosis* & *C. glabrata* were 1/115 (0.86%) each. Among these 95/115(82.6%), 75/115(65.2%), and 83/115(72.17%) isolates showed biofilm formation, coagulase production and haemolytic properties respectively. **Conclusions:** Our study showed a shift among Candida species from albicans (39.13%) to non-albicans (60.86%), thus stressing their presence as major fungal pathogens in critical care settings.

**Key words**: Non-albicans candida, Critical care units, Prevalence, Candida albicans

## Introduction

Candida species are the most common cause of opportunistic fungal infections, resulting in a variety of manifestations ranging from mucocutaneous lesions to life threatening invasive diseases particularly in immunocompromised patients [1]. Although *Candida albicans* is the most common cause of candidiasis, a shift towards non albicans candida species is evident in recent years [2]. The problem of emergence of Non albicans candida has become more acute because different species of the same exhibit varying degrees of resistance either intrinsic or acquired or both, to commonly used antifungal drugs. *C.tropicalis* is one of the most common Non-Candida albicans species isolated from various clinical types of candidiasis [3].

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In India, it is the most common cause of health care associated candidemia [4]. The increased isolation of *C. tropicalis* from various clinical types of candidiasis is of concern because of its ability to develop resistance to fluconazole [5].

The transition of *Candida* spp. from commensal to potent pathogens is facilitated by a number of virulence factors such as adherence to host tissues and medical devices, biofilm formation, and secretion of extracellular hydrolytic enzymes [6].

The present study was therefore conducted in a tertiary care teaching hospital of North India with the aim of knowing the prevalence of *C. albicans* & Non-albicans isolates in critical care settings and determine their virulence factors and antifungal susceptibility profile.

## Material and Methods

Ours was a prospective study, carried out in the Mycology section of Microbiology department of SGRDIMSAR, Amritsar during a period of 2 years from July 2014 to June 2016. Candida species isolated from various clinical specimens from different ICUs of the hospital were included in the study. Patient's information such as duration of hospitalisation, ward, underlying medical conditions, associated risk factors such as presence of urinary catheter, respiratory ventilation, central line insertion, duration of antibiotic therapy, antifungal prophylaxis, exposure to invasive medical procedures, and use of corticosteroids was obtained from clinical records and analysed. The isolates collected were consecutive and were derived from various clinical samples including blood, urine, foley's catheter tip, vaginal discharge etc. Blood culture samples collected in blood culture bottles were incubated in BacT alert 3D (Biomerieux) automated blood culture system and upon getting a positive alarm were subcultured onto Sabouraud's Dextrose Agar & blood agar plates. Samples were processed for microscopy and culture using standard mycological procedures. Candida isolates were characterized by colony morphology, gram staining, germ tube formation, chlamydospore formation on corn meal agar, growth on CHRO Magar candida medium. The isolates were identified upto species level & their antifungal susceptibility was done by automated method (vitek 2 compact). Virulence of all the isolates was assessed by Biofilm production assay, detection of haemolytic activity and the production of extracellular hydrolytic enzymes eg.coagulase [6,7].

## Results

Out of a total of 300 Candida species isolated from clinical samples, 115 were obtained from patients admitted in various ICUs (MICU, MEDICU, SICU, NICU, PICU, BICU etc.). Among the latter the most common isolate was *C.tropicalis* (52.17%), followed by *C.albicans* (39.13%) & *C.utilis* 7/115 as shown in Table 1. The formation of biofilm, coagulase & haemolysin production by various species of Candida is shown in Table 2. Most of the isolates which were virulent showed biofilm formation and coagulase production. Isolates of *C.lusitaniae*, *C.parapsillosis* & *C.glabrata* were 1 (0.86%) each. Antifungal susceptibility testing in our study showed nearly similar resistance to fluconazole by C.albicans (22.22%) & Candida non albicans (28.5%) as shown in Table 2.

**Table-1: Candida spp isolated from various clinical specimens.**

| Candida species | No. of isolates | Urine | Blood | Foley's Catheter tip | Suction tip / Endotracheal tube |
|---|---|---|---|---|---|
| C.tropicalis | 60 (52.17%) | 26 (43.33%) | 1 (1.67%) | 25 (41.67%) | 8 (13.34%) |
| C.albicans | 45 (39.13%) | 19 (42.23) | 0 | 21 (46.67%) | 5 (11.12%) |
| C.glabrata | 1 (0.86%) | 0 | 0 | 1 (100%) | 0 |
| C.utilis | 7 (6.08%) | 0 | 7 (100%) | 0 (0%) | 0 |
| C.lusitaniae | 1 (0.86%) | 0 | 1 (100%) | 0 | 0 |
| C.parasillosis | 1 (0.86%) | 1(100%) | 0 | 0 | 0 |
| **Total** | **115** | **46 (40%)** | **9 (7.82%)** | **47 (40.86%)** | **13 (11.30%)** |

**Table-2: Production of various virulence factors by *Candida* spp**

| Candida species | No. of isolates % | Biofilm formation assay | Coagulase production | Haemolysin production |
|---|---|---|---|---|
| *C.tropicalis* | 60 | 56(93.34%) | 40(66.67%) | 43(71.67%) |
| *C.albicans* | 45 | 40(88.89%) | 32(71.12%) | 39(86.67%) |
| *C.glabrata* | 1 | 1(100%) | 1(100%) | 1(100%) |
| *C.utilis* | 7 | 7(100%) | 0(0%) | 0(0%) |
| *C.lusitaniae* | 1 | 1(100%) | 1(100%) | 0 |
| *C.parapsilosis* | 1 | 1(100%) | 1(100%) | 0 |
| **Total** | **115** | **106(92.17%)** | **75(65.2%)** | **83(72.17%)** |

However resistance to Amphotericin B by *Candida albicans* (11.33%) was almost one third compared to non albicans (33.33%). Further, all isolates of *C.albicans* were susceptible to Caspofungin, reduced susceptibility was observed in only one isolate of *C.lusitaniae*, a non albicans strain. Resistance to Flucytosine was however observed in 5/45 (11.33%) *Candida albicans* & 10/70 (14.28%) Candida non albicans. All the isolates in our study were found to be totally susceptible to Voriconazole and Micafungin.

**Table-3: Antifungal susceptibility pattern.**

| **Antifungal Drugs** | ***C.albicans*** **45/115** **(39.13%)** | **Candida non-albicans** **70/115** **(60.86%)** | **Total** **115** |
|---|---|---|---|
| **Fluconazole** | | | |
| Resistance | 10 (22.22%) | 20(28.5%) | 30(26.08%) |
| Intermediate | 5(11.11%) | 3(4.28%) | 8 (6.95%) |
| Sensitive | 30(66.67%) | 47(67.14%) | 77(69.95%) |
| **Voriconazole** | | | |
| Resistance | 0 | 0 | 0 |
| Intermediate | 0 | 0 | 0 |
| Sensitive | 45(100%) | 70(100%) | 113(98.2%) |
| **Amphotericin B** | | | |
| Resistance | 5(11.11%) | 15(33.33%) | 20(17.39%) |
| Intermediate | 10(22.22%) | 10(14.28%) | 20(17.39%) |
| Sensitive | 30(66.67%) | 45(64.28%) | 75(65.21%) |
| **Flucytosine** | | | |
| Resistance | 5(11.11%) | 10(14.28%) | 15(13.04%) |
| Intermediate | 0 | 0 | 0 |
| Sensitive | 40(88.89%) | 60(85.17%) | 100(86.95%) |
| **Micafungin** | | | |
| Resistance | 0 | 0 | 0 |
| Intermediate | 0 | 0 | 0 |
| Sensitive | 45(100%) | 70(100%) | 115(100%) |
| **Caspofungin** | | | |
| Resistance | 0 | 1(1.42%) | 1(0.86%) |
| Intermediate | 0 | 0 | 0 |
| Sensitive | 45(100%) | 69(98.57%) | 114(99.13%) |

## Discussion

In our study, we observed that isolates of non-albicans Candida had predominance over *C.albicans* similar to various other studies from different parts of the world [8,9]. Also *C.tropicalis* followed by *C.albicans* were the most common species isolated which is in concordance with other studies [3,10]. Non candida albicans were more prevalent in urine, foley's catheter tip & respiratory samples.We also observed 7 cases of *C.utilis* candedemia in neonatal ICU patients within a period of 2 months in 2016. All these pateints were premature, critically ill, had low birth weight, were on ventilator, on multi drug antibiotic therapy and on total parenteral nutrition. One of them was operated for tracheo-esophageal fistula. 2 of them had oral candidiasis. Repeated isolation of *C.utilis* from the blood samples has been shown in other studies as well [11]. Biofilm production assay was positive in all *C.utilis* strains which indicates the potential pathogenicity of this strain. All of them were being treated with Fluconazole which was started empirically even before sending the blood samples for culture. Inspite of the treatment with Fluconazole, candidemia did not resolve. Similar results were observed in a study by Bougnoux et alin 1993 & AmarelaLukic-Grlic et al in 2011[11,12]. One similar case of candidemia with *C.utilis* has been reported in a new born baby by Jayasree Shivadasan et al [13]. Factors like biofilm production, coagulase production & production of extracellular hydrolytic enzymes such as coagulase indicates virulence of Candida species [14]. Biofilm production was seen in 89% of *C.albicans* & 62.2% isolates of non candida albicans in the current study.

Other virulence factors viz. coagulase production and haemolytic activity were also observed respectively in 71.12% and 86.67% of *Candida albicans*. However non candida albicans also showed 57.33% & 53.01% coagulase production and haemolytic properties respectively which again indicates the increasing virulence of non candida albicans species [14,15]. Among all candida isolates *C.tropicalis* showed more (93.34%) ability ofbiofilm formation which has been observed in other studies also [16]. The notable finding was one isolate of *C.glabrata* which showed presence of all the virulence factors.

Antifungal susceptibility pattern observed in our study showed that among all the resistant strains of Candida sp., maximum resistance was observed with Fluconazole and Amphotericin B. In comparison to *C.albicans* isolates, non albicans strains showed more resistance to both Fluconazole and Amphotericin B. Among the latter, *C.tropicalis*, the most common strain in our study, was found to be almost sensitive to all the antifungals.

Only one isolate of *C.lusitania,* which was obtained from the blood of a 5year old child, was found to be resistant to Caspofungin however it was susceptible to Fluconazole.

## Conclusion

So far non albicans-Candida has been considered non pathogenic, however trends are changing with time. Our study showed a shift among Candida species from albicans (39.13%) to non-albicans (60.86%), thus stressing their emergence as major fungal pathogens**.**

Presence of non albicans-Candida in any specimen therefore cannot be ignored now, especially in the critically ill patients of any age, keeping in mind their potential to become resistant to many antifungal drugs routinely used.

**Conflict of Interests-** The authors declare that there is no conflict of interests regarding the publication of this paper.

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