Emergence of non-albicans *Candida species* in critical care patients of a tertiary care hospital

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Abstract

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. 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.

Material & Methods: The present study was carried out in the Mycology section of Microbiology Department, SGRUHS, Amritsar during the period of July 2014 to June 2016. *Candida strains* isolated from various clinical samples (i.e. urine, blood, foley's catheter tip etc.) 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.

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%) and *C.utilis* 7/115 (6.25%). Isolates of *C.lusitaniae*, *C.parasillosis* & *C.glabrata* were 1/115 (0.86%) each.

Conclusions: 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 in critical care settings.

Keywords: Non-albicans candida, Candida albicans, Critical care units, Predominance, Tertiary care hospital

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] 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.

Material and Methods

Ours was a prospective study, carried out in the Mycology section of Microbiology department of SGRUHS, 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, mechanical 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 BacTalert3D (Biomerieux) automated blood culture system and upon getting a positive alarm were sub-cultured onto Sabouraud's Dextrose Agar & blood agar plates. Samples were processed for microscopy and culture using standard mycological procedures. 3 or more repeat samples were processed.[19,20] Candida isolates were characterized by colony morphology, gram staining, germ tube formation, chlamydospore formation on corn meal agar, growth on CHROMagar candida medium. The isolates

were identified upto species level by automated method (vitek 2 compact).

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* 60/115 (52.17%), followed by *C.albicans* 45/115(39.13%) & *C.utilis* 7/115 (6.25%). Isolates of *C.lusitaniae*, *C.parapsillosis* & *C.glabrata* were 1/115 (0.86%) each. (Table 1)

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: Predisposing factors associated with Candida infections

Predisposing factors	No. of patients (115)	%age
More than 2weeks of stay in ICU	110	95.67%
Prior antibiotic therapy for 2weeks	112	97.30%
Presence of urinary catheter	110	95.67%
Presence of central venous catheter	95	82.62%
Antifungal prophylaxis	30	26.08%
Previous surgery	55	47.82%
Presence of diabetes	12	10.43%
Corticosteroids	20	17.30%
Cancer chemotherapy	7	0.06%
Low birth weight	43	37.39%

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.[7,8,13,14,15] Also *C.tropicalis* followed by *C.albicans* were the most common species isolated which is in concordance with other studies.[3,9] Non candida albicans were more prevalent in urine, foley's catheter tip & respiratory samples. We also observed 7 cases of *C.utilis* candidemia in neonatal ICU patients within a period of 2 months in 2016. All these patient's 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.[10] 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 al in 1993 & AmarelaLukic´ -Grlic et al in 2011.[10,11] In India to our best knowledge only one similar case of candidemia with *C.utilis* has been reported in a new born baby by Jayasree Shivadasan et al.[12]

The presence of various risk factors in cases presenting with candida infections during the study period were also compared (Table 2). The most common factors associated were the use of broad spectrum antimicrobial agents 112/115(97.30%). The association between candida infections and

antimicrobial drugs has been shown in some other studies also.[16]

Candida infection was also found to be associated with the increased duration of ICU stay, with most of the patients (95.67%) staying for more than 15 days. The Presence of indwelling catheters were observed to be associated with a significant number of candida infections which includes 95/115 (82.62%) from central venous catheters and 110/115 (95.67%) from urinary catheters.[17] Various other factors associated were recent surgical history, Presence of diabetes, Corticosteroids intake, Cancer chemotherapy, total parenteral nutrition and Low birth weight in case of neonates. In a case-controlled study, it was shown that the risk to develop candiduria was increased by 12-fold after urinary catheterization, six-fold each after the use of broad spectrum antibiotics and urinary tract abnormalities, four-fold following abdominal surgeries, two-fold in the presence of diabetes mellitus, and one-fold in association with corticosteroid administration.[18]

Conclusion

So far *Candida non-albicans* 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 *Candida non-albicans* 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.

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