Candida Albicans versus Non Albicans Candiduria in the ICU Setting: Evaluation of Risk Factors

Abstract

Background: The indiscriminate use of antibiotic is increasing the prevalence of candiduria worldwide, especially in the ICU setting. Limited studies describe the risk factors associated with candiduria depending on their species.

Objective: This study aims to speciate candida isolated from patients with candiduria admitted in the ICU and evaluate the risk factors associated with *albicans* vs non albicans candiduria.

Material and method: The risk factors were evaluated in 60 yeast isolates using Fisher's exact test (two-tailed) and Odd's ratio with 95% confidence interval.

Result: The non- albican *candida* species isolated were *C. tropicalis* (14), *C. glabrata* (11), *C. krusie* (5) and *C. parapsilosis* (10). Although there was no significant difference between risk factors associated with albicans vs non-albicans *candida spp*., the risk of non-albicans candiduria increased by 3 folds with increasing age(>50yrs.) OR (95%CI) 3.3158 (1.045-10.8693) and by 6 folds in patients with history of antibiotic intake in ICU OR (95%CI) 6.3521 (0.3339-120.8452). Non-albicans candiduria was significantly associated with presence of more pus cells (11-30cells/hpf) P= 0.0002; while *C. albicans* candiduria was significantly present in patients with < 10 puscells/hpf, P= 0.0001. *Pseudophyphae* were significantly less in non-albicans candiduria (P= 0.0113). Use of carbapenems, tigecycline and fluoroquinolones were significantly associated with non-albicans candiduria (P= 0.034; 0.0057; 0.003 respectively).

Conclusion: The risk of acquiring non-albicans candiduria is more than albicans despite having same risk factors. Non albicans candiduria has become more prevalent cause of nosocomial candiduria in the ICUs may be due to the frequent use of antibiotics like fluoroquinolones in the ICU patients. Further studies are required to assess risk factors associated with different *candida spp.* to manage candiduria in ICU patients.

Keywords: Candiduria; *Candida spp.;* Immunosuppressive therapy; ICU; Nosocomial UTIs

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Introduction

The prevalence of candiduria has increased worldwide mainly because of the indiscriminate use of antibiotics, increased immunosuppressive therapy and also due to more frequently performed invasive procedures. About 30% of all nosocomial UTIs are due to *candida spp*., mostly in the ICU setting [1,2]. However, in the ICU, candiduria may indicate bladder colonization most of the time due to indwelling catheters [3]. Asymptomatic candiduria is a benign condition requiring no antifungal therapy but if the patient is immunocompromised the risk of mortality and morbidity is high [4]. There are no clear cut definitive criteria to differentiate colonization, contamination and infection making significance of candiduria a common clinical problem. Apart from antibiotic use, other candiduria risk factors include elderly, female gender, diabetes mellitus, urinary tract abnormality, chronic renal failure, malignancy and neutropenia [5,6]. Limited data is available regarding risk factors associated with non-albicans candiduria in comparison to those associated with *C. albicans* candiduria. In this study, we aimed to speciate candida isolated from patients with candiduria admitted in the ICU and evaluate the risk factors associated with albicans vs non *albicans candiduria.*

Material and Methods

This prospective study was carried out during April 2013 to October 2013 in a superspeciality hospital at New delhi, India. Ethical committee approval was not required since no interventions were done on the patients. Urine samples received in the laboratory for routine urine culture were studied. Sixty (60) yeast isolates were included in the study.

Inclusion criteria

Yeasts isolated as a pure growth with colony count > 10^4 cfu/ml of urine sample. These isolates were from urine specimens of patients admitted in the ICU for > 72hrs.

Exclusion criteria

Urine specimens where candiduria was present as a mixed growth were excluded from the analysis. Repeat isolates from the same patient were also excluded. After obtaining informed consent, data collected for each patient included: gender, age, duration of hospitalization, catheter use, antimicrobial therapy, h/o diabetes mellitus, ICU (department), h/o surgery, and

presence of any genitourinary tract abnormality. None of the patients were on antifungal therapy during sampling. However, antibacterial agents were used such as imipenem, meropenem, amikacin, monocef, tazact, fluoroquinolones and tigecycline.

Identification of yeast

The urine samples were cultured on 5%sheep blood agar and McConkey's agar and incubated at 37°C for 24 hrs. aerobically. A direct Gram stained smear was prepared from colonies grown on blood agar to confirm the colony as yeast. Further identification and speciation was done based on colony morphology on CHROMagar candida, germ tube production and mico-morphology on cornmeal agar. All the yeast isolates were subcultured on SDA (Sabouraud's Dextrose Agar).

Statistical analysis

Fisher's exact test (two-tailed) and Odd's ratio with 95% confidence interval of all categorical variables was calculated to evaluate the risk factors.

Results

In the present study, we identified 60 cases of candiduria from the ICU (Table 1). Most of the cases were from general ICU (19) followed by neurology ICU (16). The age-range of the patients was 21-85yrs. After evaluating 60 cases, *C. albicans* was determined in 20 subjects and non- albicans candida in 40 subjects. The non albican *candida species* isolated in our study were *C. tropicalis* (14), *C. glabrata* (11), *C. krusie* (5) and *C. parapsilosis* (10). The comparison of risk factors and direct microscopic examination of urine for albicans vs non-albicans is presented in Table 2 & 3. It was observed that there was no significant difference between risk factors associated with albicans vs non-albicans *candida spp*. However, the risk of non-albicans candiduria increased by 3 folds with increasing age (>50yrs.) OR (95% CI) 3.3158 (1.045-10.8693) and by 6 folds in patients with history of antibiotic intake in ICU OR (95%CI) 6.3521 (0.3339-120.8452). Other risk factors like gender, urinary catheterization, duration of catheter, diabetes mellitus and any surgery were 0.2-0.5 times higher in non-albicans candiduria. When we compared the findings of direct microscopic examination of urine, non-albicans candiduria was significantly associated with presence of more pus cells (11-30cells/hpf) P= 0.0002; while *C. albicans* candiduria was significantly present in patients with < 10 puscells/hpf, P= 0.0001. The presence of budding yeast cells in the wet mount of urine was not significantly associated with *candida species* but *pseudophyphae* were significantly less in non-albicans candiduria (P= 0.0113). Also, the use of carbapenems, tigecycline and fluoroquinolones were significantly associated with non-albicans candiduria (P= 0.034; 0.0057; 0.003 respectively).

Table 1: General profile of the candiduria cases from ICU.

Total Cases	**60**
Age Range	**21-85 Years**
Gender	
Male	23
Female	37
ICU type	
General ICU	19
Neurology ICU	16
Neurosurgery ICU	10
Gastroentrology ICU	8
Liver transplant unit	3
CTVS ICU	4
Type of *Candida species*	
C. albicans	20
Non-albicans candida	40
C. tropicalis	14
C. glabrata	11
C. krusei	5
C. parapsilosis	10

Table 2: Comparison of risk factors for albicans Vs non-albicans candiduria.

Risk Factor	*C. albicans*	Non-Albicans	OR (95%)	P Value
Gender				
Male	5	18	0.4074 (0.1241-1.3371)	0.1662 (NS)
Female	15	22		
Age group				
21-30 yrs	3	7	0.8319 (0.1906-3.6316)	1 (NS)
31-40 yrs	1	5	0.3684 (0.0401-3.3872)	0.65 (NS)
41-50 yrs	1	9	0.1813 (0.0213-1.5462)	0.142 (NS)
>50yrs	15	19	3.3158 (1.0115-10.8693)	0.05 (NS)
Catheter				
Present	20	40	0.5062 (0.0097-26.4422)	1 (NS)
Absent	0	0		
Catheter days				
<15 days	2	11	0.2929 (0.0581-1.4763)	0.185(NS)
>15 days	18	29		
H/O Surgery				
Present	4	15	0.4167 (0.1171-1.4822)	0.241(NS)
Absent	16	25		
H/O Antibiotic intake				
Present	20	35	6.3521 (0.3339-120.8452)	0.158(NS)
Absent	0	5		
Genitourinary tract abnormality	0	0		
H/O Diabetes Mellitus				
Present	1	9	0.1813 (0.0213-1.5462)	0.142(NS)
Absent	19	31		

S: Significant; NS: Not Significant

Table 3: Direct microscopic examination of urine and type of antibiotic intake.

	C. albicans	Non-Albicans	P Value
Presence of pus cells/hpf			
<10	18	10	0.0001(S)
30-Nov	1	22	0.0002(S)
>30	1	8	0.248(NS)
Presence of yeast cells			
+	16	26	0.370(NS)
_	4	14	
Pseudohyphae			
+	12	10	0.0113(S)
_	8	30	
Type of antibiotic intake			
Beta-lactams	15	30	1(NS)
Carbapenems	10	32	0.034(S)
Aminoglycosides	11	30	0.146(NS)
Tigecycline	5	26	0.0057(S)
Fluoroquinolones	4	28	0.0003(S)

Discussion

To the best of our knowledge, very few data is available regarding the differences in risk factors between albicans and non-albicans candiduria. Mostly the studies have been done on albicans vs non-albicans fungaemia. In this study, we assessed risk factors for albicans vs non-albicans candiduria by conducting a prospective study on urine samples received in the microbiology laboratory of G B Pant hospital from ICU patients. The main finding of this study was that there is no statistically significant difference in risk factors between albicans vs non-albicans candiduria. However, the risk of non-albicans candiduria is more with increasing age, antibiotic intake, catheterization and surgery. There are several other risk factors which have been identified particularly for non-albican species like azole prophylaxis, foreign body insertion, neutropenia and bone marrow transplant [7,8]. In our patients, none of them were on antifungal therapy. However, use of antibiotics like carbapenems, tigecycline and fluoroquinolones were significantly associated with non-albicans candiduria and probably that is why it was observed that non-albicans candiduria was more common (40) than albicans candiduria (20), although urinary catheterization was done in all the patients. A strong relationship between candiduria and use of carbapenems was established by Weinberger and colleagues [9]. Quinolone exposure was identified as a specific risk factor for *C. glabrata* candiduria in one study [10]. A specific association between quinolone treatment and non-albicans candiduria has not been noted in many studies. Maybe more similar studies are required to confirm this finding. When compared with albicans candiduria, we found that the risk of non-albicans candiduria was increased by 6 folds in patients with antibiotic intake.

Out of the 60 cases, 37 were females. Development of urinary infection is more common in females because of the anatomical and functional reasons and therefore it is obvious that incidence of candiduria is higher among females. But we did not observe any significant difference between albicans and non-albicans candiduria in terms of gender. Advanced age is another known risk factor for developing candiduria [8]. Most of the cases in our study were >50yrs. Old. Urinary catheter was administered in all our patients and the risk of non-albicans candiduria was slightly more 0.5 times with catheterization.

In the microscopic examination of urine, pyuria helps in the diagnosis of candida UTI but in patients with indwelling catheters, it loses both specificity and sensitivity because most catheterized patients have WBCs in the urine as nonspecific finding [11]. In our study, pyuria with <10 cells/hpf was significantly associated with *C albicans* candiduria while upto 30cells/hpf were associated with non-albicans candiduria (P= 0.0001). The presence of yeast cells in the urine was not statistically significant with the type of *candida species*. Yeasts visualized by microscopy in the urine specimen maybe the first clue of fungal infection. Both albicans and non-albicans candiduria appear as budding yeasts, 4-10um in diameter, that often show formation of hyphal elements. Smaller yeast cells, 2-4um in diameter, without hyphal structures are likely to be *C glabrata*. In our study, presence of *pseudohyphae* was significantly associated with albicans candiduria (P= 0.0113).

To summarize, the risk factors for candiduria are already known and remain the same, however, the risk of acquiring non-albicans candiduria is more than albicans and therefore it has become more prevalent cause of nosocomial candiduria in the ICUs. This may also be due to the frequent use of antibiotics like fluoroquinolones in the ICU patients. The limitation of our study was the small number of cases (60) that could probably compromise the statistical power of this study. More studies with a larger number of isolates should be done for meaningful analysis of possible association between risk factors and type of *candida species* in order to guide the proper management of candiduria in ICU patients.

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