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Candida species in catheter associated urinary tract infection in ICU patients at a tertiary care hospital in North India: An observational study

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Abstract

Introduction: Catheter associated urinary tract infection (CAUTI) is most common nosocomial infection which constitutes ~80% of nosocomial urinary tract infections (UTIs). *Candida albicans* has been most commonly isolated in past but in recent years non-albicans candida has emerged as the more common agent causing UTI in ICU settings. The study aimed to assess the burden of various candida species in symptomatic CAUTI in ICU patients and to test their susceptibility pattern for various antifungal agents.

Materials and methods: Study was performed at a 1050 bed tertiary care hospital of northern India. Over a period of 1 year, total 147 urine samples from symptomatic CAUTI patients admitted in ICU were collected. Gram's staining and culture on CLED agar was done. All yeast isolates were tested for speciation of Candida & antifungal susceptibility by an automated commercial system - VITEK 2.

Results: Among 147 urine samples, 34 (23.12%) were positive for various *Candida* species. 61.76% positive patients were female and 38.23% were male. Maximum numbers of *Candida* isolates were found in above 60 years age group. 27 (79.41%) were due to *non-albicans Candida spp.* and 7 (20.58%) were due to *Candida albicans.* All *Candida* species were found to be sensitive to voriconazole, amphotericin B, caspofungin and micafungin. Few isolates of certain species like *C.albicans* and *C.non-albicans* showed resistance to fluconazole and/or flucytosine.

Conclusion: Changing pattern of *Candida* species causing UTIs around the world points towards continuous need for surveillance, thus helping us in providing appropriate therapy.

Keywords: *Candida albicans; Candida non-albicans;* urinary tract infections

Introduction

Urinary tract infections (UTIs) are among the most commonly diagnosed infections in both hospital & community settings [1-3]. They are classified into upper and lower urinary tract infections. These can either be asymptomatic or symptomatic [4, 5]. Nosocomial infections are ones which develop in hospitalized patients, were neither present nor in incubation at the time of patient's admission & approximately 40% of such infections are preventable [6].

Most common nosocomial infection is Catheter associated urinary tract infection (CAUTI) which constitutes about

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80% of nosocomial urinary tract infections (UTIs) [7]. Among all the bacterial & fungal agents causative of UTI, incidence of fungal UTIs have been increasing in recent years [1, 8, 9] and more so in the ICU settings [10]. Predisposing factors being instrumentation of urinary tract, prolonged broad-spectrum antibiotic usage, diabetes mellitus, immunosuppressive drugs, extremes of age, AIDS, surgeries, and female gender [4, 5, 11, 12]. Indwelling devices/ catheters are of significance because in hospitalized patients they are very commonly associated with biofilm formation which is inherently resistant to antifungals like amphotericin B and fluconazole [13]. A catheterised patient having candiduria presenting along with symptoms & signs of UTI is considered as symptomatic CAUTI [11]. 10^3 Colony Forming Units per millilitre (CFU/mL) to 10^5 CFU/mL is the acceptable count of bacteriuria/ candiduria in ICU patients to consider CAUTI [11].

Candida albicans has been most commonly isolated opportunistic pathogenic fungi from cases of UTI in the past [1, 14, 15]. In recent years non-albicans candida has emerged as more common agent causing UTI in ICU settings [16, 17]. *Candida* species constitute almost 10-15% of nosocomial UTIs [18, 19]. As far as the choice of antifungals is considered, it is difficult to decide because many antifungals attain a low urinary concentration and some of the candida species show inherent resistance to certain antifungals [20, 21]. This calls for antifungal susceptibility testing and species identification of candida. Hence an aggressive approach in the diagnosis & management of such patients can help in preventing disseminated candidiasis [22].

This study aimed to assess the significance of various candida species in symptomatic CAUTI in ICU patients and test their susceptibility to various antifungal agents.

Materials and methods

Study was performed in a 1050 bed at Rajshree Medical Research Institute, Bareilly, Uttar Pradesh after taking ethical committee approval. This was a prospective observational study conducted over a period of 1 year (January 2022 to December 2022). During this period 147 urine samples were collected from cases of symptomatic CAUTI in ICU patients.

Male and female patients of age ≥18 years were considered for this study. Those who had UTI after 48 hours of hospitalization & were put on Foley's catheter were included in the study. Only those yeast isolates which showed pure growth with significant colony count were included in the study.

Patients who were catheterised before being admitted in ICU, whose Foley's catheter was removed or who were discharged before 48 hours of being catheterised were not included in this study. Urine samples where Candida species was isolated without any pyuria, colony count was $<10^3$ CFU/ml and growth were polymicrobial were also excluded from the study [11].

Urine samples were collected from Foley's catheter using aseptic technique, and a minimum of 3ml of urine was taken in a screw capped, sterile, leak proof container. They were transported within 1 hour to microbiology laboratory. Sample was taken on 1st day to rule out any prior UTI. Then sample collection was done on 3rd, 5th, 7th, 10th, 14th day and then weekly till catheter was removed, or patient developed candiduria, or was discharged/ died [7, 12].

Gram staining of uncentrifuged urine was done to look for the presence of candida. Then sample was centrifuged at 3000 rpm for 3-5 minutes and wet mount of sediment was made. Pus cells/ HPF were counted under 40x objective lens. If >5 WBCs/HPF were found it was considered as significant for diagnosing CAUTI [7, 23]. Each sample was inoculated on Cysteine Lactose Electrolyte Deficient (CLED) agar by semi-quantitative method using calibrated wire loop technique according to standard protocol. This delivered 0.001ml of urine sample to the culture plate. These plates were incubated at 37°C for 24 hours aerobically and then were checked for any growth [7, 24, 25]. If any pure growth was found then Gram's staining was done to look for Gram positive budding yeast cells and pseudohyphae.

All yeast isolates were stored for further speciation of *Candida* spp. & antifungal susceptibility testing by an automated commercial system (VITEK 2, bioMe'rieux, Marcy d'Etoile, France) were reported for fluconazole, voriconazole, caspofungin, micafungin, amphotericin B and flucytosine.

Patients were diagnosed as symptomatic CAUTI as per Centre for Disease Control (CDC) guidelines January, 2014. This included UTI caused by *Candida* spp., with a culture of $\geq 10^3$ CFU/ml for a specimen collected at least 48 hrs after hospital admission and a previous negative urine culture for *Candida* spp. [11].

Statistical analysis

Statistical analyses were performed with SPSS software version 24 (IBM SPSS Statistics for Windows 24.0, Armonk, NY, IBM Corp.). Categorical variables were expressed as frequencies and percentages. Pearson's Chi-square test was done for comparison of categorical variables. Value of $p \leq 0.05$ were considered statistically

significant along with the 95% confidence interval for the test statistic was computed.

Results

In this study total 147 ICU patients developed symptomatic CAUTI, of them 81 were male and 66 were female. Out of these 34 (23.12%) were caused by various *Candida* species. Majority 27 (79.41%) were due to *non-albicans Candida spp.* and 7 (20.58%) were due to *Candida albicans.* The prevalence of *non- albicans Candida spp.* was 18.37% which one was much higher than the *Candida albicans spp.* (4.76%) with p value of 0.000265 (Table 1). Species of non-albicans *Candida* isolated were *Candida tropicalis, Candida krusei*, *Candida kefyr, Candida parapsilosis, Candida glabrata, Candida intermedia* and *Candida guilliermondii. Candida* species were isolated more commonly from female patients (61.76%) as compared to male patients (38.23%) (Table 2).

Table 1: Prevalence of Candida albicans and Candida non-albicans associated urinary tract infection in ICU patient.

Candida species	*Prevalence*	*p value*
Candida albicans spp.	4.76%	
Candida non-albicans spp.	18.36%	0.000265
Total	23.12%	

Table 2: Gender wise distribution of different *Candida* species in urine samples.

Candida species	*Males*	*Females*	*Total no. of isolates (%)*
C. albicans	3	4	7 (20.58%)
C. tropicalis	2	4	6 (17.64%)
C. krusei	2	3	5 (14.70%)
C. kefyr	1	2	3 (8.82%)
C. parapsilosis	1	1	2 (5.88%)
C. glabrata	0	2	2 (5.88%)
C. intermedia	2	3	5 (14.70%)
C. guilliermondii	2	2	4 (11.76%)
Total	13 (38.23%)	21 (61.76%)	34 (100%)

The total prevalence of CAUTI in this study was 23.12%, of which prevalence among female patients was significantly higher (31.12%) as compared to males (16.05%) with *p* value of 0.0247 (Table 3). Maximum number of *Candida* isolates were found in above 60 years age group (Table 4).

Table 3: Prevalence of *Candida* associated urinary tract infection in ICU patient.

	Prevalence	*p value*
Male	16.05%	0.0247
Female	31.81%	
Total	23.12%	

Table 4: *Candida* isolates age-wise distribution in urine samples.

Age groups (years)	*Males*	*Females*
18-30	4	7
31-45	2	3
46-60	2	2
>60	5	9
Total	13	21

Observation of the susceptibility pattern of various species of *Candida* for different antifungals revealed that all *Candida* species were found to be sensitive to voriconazole, amphotericin B, caspofungin and micafungin. Few isolates of certain species like *C.albicans* and non-albicans *Candida (C.tropicalis, C.krusei, C.intermedia and C.glabrata)* showed resistance to fluconazole and/or flucytosine (Table 5).

Table 5: Antifungal susceptibility pattern for all the *Candida* isolates in this study.

Candida spp.	*Fluconazole*	*Voriconazole*	*Caspofungin*	*Micafungin*	*Amphotericin-B*	*Flucytocine*
C.albicans	S	S	S	S	S	S
C.albicans	R	S	S	S	S	S
C.albicans	S	S	S	S	S	S
C.albicans	S	S	S	S	S	S
C.albicans	S	S	S	S	S	S
C.albicans	R	S	S	S	S	S
C.albicans	S	S	S	S	S	S
C.tropicalis	S	S	S	S	S	S
C.tropicalis	R	S	S	S	S	S
C.tropicalis	S	S	S	S	S	S
C.tropicalis	S	S	S	S	S	S
C.tropicalis	S	S	S	S	S	S
C.tropicalis	S	S	S	S	S	S
C.krusei	R	S	S	S	S	R
C.krusei	R	S	S	S	S	R

C.krusei	R	S	S	S	S	S
C.krusei	R	S	S	S	S	S
C.krusei	R	S	S	S	S	S
C.kefyr	S	S	S	S	S	S
C.kefyr	S	S	S	S	S	S
C.kefyr	S	S	S	S	S	S
C.parapsilosis	S	S	S	S	S	S
C.parapsilosis	S	S	S	S	S	S
C.intermedia	S	S	S	S	S	R
C.intermedia	S	S	S	S	S	S
C.intermedia	S	S	S	S	S	S
C.intermedia	S	S	S	S	S	S
C.intermedia	S	S	S	S	S	S
C.guillermondii	S	S	S	S	S	S
C.guillermondii	S	S	S	S	S	S
C.guillermondii	S	S	S	S	S	S
C.guillermondii	S	S	S	S	S	S
C.glabrata	R	S	S	S	S	S
C.glabrata	R	S	S	S	S	S

*S= sensitive, R=resistant

Discussion

Catheter associated UTI is considered to be the most common UTI worldwide, accounting for up to 40% of nosocomial infections [26]. Presence of a urinary catheter is single most important risk factor for developing UTI. This is because of the lateral urethral pressure exerted by catheter which causes decreased mucosal blood flow, urothelial mucosal disruption & impaired mucin secretion. Also, in catheterised patients bladder is often incompletely emptied which serves as a nidus for infection. All these factors predispose to infection [26].

In this study female patients were found to be more commonly infected as compared to male patients with male to female ratio being 1:1.6, which is in accordance with the study conducted by Lundstrom et al. and Bukhary et al. [18, 20].This may be due to ascending infection from *Candida* colonising vulvovaginal area as a commensal. As far as different age groups are concerned, we found that highest incidence was among the patients of age group >60 years which is similar to the findings of various studies conducted by Yashavanth et al. and Jain et al. [10, 27-29]. This might be due to weaker immune system at an old age and hence lowered defences against infection. Results from this study thus indicate that female gender & older age (>60 years) are risk factors for developing CAUTI.

Isolation of *Candida* in CAUTI is a common finding [19, 30-32] and more so in ICUs. In this study prevalence of *Candida* causing CAUTI in ICU patients was found to be 23.12%. In other studies, prevalences were observed in between 18-26% which was almost similar to our study [33-36]. In the past few years, a shift of etiopathogenesis has been seen from *Candida albicans* to non-albicans *Candida* species [37]. In this study we also found that out of 34 positive cases 27(79.41%) were due to Non-albicans *Candida* and only 7(20.58%) were due to *Candida albicans.* In another study conducted by Jain et al. non-albicans *Candida* spp. (71.4%) was the predominant pathogen causing CAUTI [10]. Similar results were obtained in studies conducted by other authors like Yashavanth et al. and Iman et al. [28, 38]. Identification of *Candida* species is important as non albicans *Candida* are more resistant to azoles compared to that of *C.albicans*.

Antifungal susceptibility pattern depends largely on the infecting species of *Candida.* Fluconazole is an antifungal drug of choice for candiduira except for *C.krusei* because *C.krusei* is intrinsically resistant to fluconazole. All C.krusei isolates were thus found to be resistant to fluconazole in the current study also. Amphotericin B, with or without flucytosine, is recommended for treating symptomatic candiduria caused by fluconazole resistant *Candida* species [20, 39-41]. All *Candida* species were found to be sensitive to voriconazole, amphotericin B, caspofungin and micafungin in this study.

Limitations: Sample size in this study was small and such study with a large sample size will help in understanding the current trends of CAUTI better. Other risk factors for developing UTI like diabetes mellitus, other comorbidities, type of catheter material used and duration of catheterization were not assessed in the current study. Thus, further studies are required to asses role of such factors and address some unanswered questions.

Conclusion

The increasing burden of *Candida* associated CAUTI is causing large burden to both the healthcare system and patients. Though there are numerous antifungals available against *Candida*, species of *Candida* and risk factors in patient are determinant of the antifungal to be administered to the patient. Also changing pattern of *Candida* species causing UTIs around the world points towards continuous need for surveillance, thus helping us in providing appropriate therapy.

Conflicts of interest

Authors declare no conflicts of interest.

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