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SPECIATION AND ANTIFUNGAL SUSCEPTIBILITY PROFILE OF CANDIDURIA CASES AT A TERTIARY CARE HOSPITAL

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Abstract: Objective: Urinary tract infections (UTIs) as a result of *Candida* species are becoming common in hospitalised patients. Often the line between Candida colonization and infection is blurred. The species identification of Candida is important, as non albicans *Candida* species are increasing in number and more resistant to antifungal drugs. The aim of the study was to analyze the various risk factors associated with candiduria in hospitalized patients and to determine various *Candida* species causing UTIs, and their antifungal susceptibility patter. **Materials and Methods:** During six months study period suspected patients of UTI were enrolled and their urine samples were analysed. Identification and antifungal susceptibility testing of yeasts was done using VITEK-2 compact system. **Results:** A total of 43(8.54%) showed significant candiduria. Among the yeast isolates non albicans *Candida* species were predominant (62.8%) compared to *Candida albicans* (30.2%). *C. albicans* showed 100% susceptibility to voriconazole, caspofungin and flucytosine whereas *C. tropicalis* was 80%, 86.6% and 86.6% susceptible respectively to these drugs. **Conclusion:** The present study reiterates the prevalence of *Candida* species among UTIs in hospitalised patients and their antifungal susceptibility pattern. Prevalence of non albicans *Candida* was more than *Candida albicans*. Non-albicans *Candida* spp. are replacing *Candida albicans* as the predominant pathogen for nosocomial UTI and are more resistant to antifungal drugs compared to *C. albicans*. Therefore surveillance for nosocomial candiduria should be carried out in hospitalized patients.

Keywords: Candiduria, ICU patients, Non albicans *Candida*, Antifungal susceptibility testing

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INTRODUCTION

Candiduria is rarely present in healthy individuals. In contrast, it is a common finding in hospitalized patients, especially those in intensive care units (ICUs) who often have multiple predisposing factors, including diabetes mellitus, indwelling urinary catheters, and exposure to antimicrobials.[1]

Candida species account for almost 10-15% nosocomial UTIs.[2,3] . Candiduria not properly diagnosed and treated has been source of morbidity and mortality.[4]The clinicians always face a diagnostic dilemma as to whether the presence of candiduria in a patient represents contamination, colonization or true infection.[2,5,6,7] All *Candida* species are capable of causing UTIs, in many centers worldwide non albicans *Candida* species have replaced *Candida albicans* as the predominant pathogen. The species identification of Candida is important, as non albicans *Candida* species are increasing in number and more resistant to antifungal drugs and many non-albicans *Candida* spp. are inherently resistant to treatment with fluconazole.[8,9,10]

In this context the present study was carried out to analyse the various risk factors associated with candiduria in hospitalized patients, to determine various Candida species causing UTIs, and their antifungal susceptibility pattern in a tertiary care hospital.

MATERIALS AND METHODS

Urine samples were received from clinically suspected patients of UTI admitted in Intensive Care Units of Dayanand Medical College and Hospital, Ludhiana from June to November 2014. Patient's demographic details such as age, sex, duration of hospital stay and other clinical details were recorded. Presence of other associated risk factors like diabetes mellitus, history of antibiotic use, any urinary tract instrumentation, mean ICU stay were also recorded.

The urine samples obtained were immediately processed in the microbiology laboratory by semi-quantitative method as per the standard protocols. Samples showing significant growth of yeasts on culture, i.e. $\geq 10^4$ colony forming units/ml of urine sample on repeat culture were included in the study.[2,6,11] Identification, characterisation and antifungal susceptibility of yeasts was done by the VITEK 2 Compact system (Bio Merieux, Mumbai, India) as per CLSI guidelines.[12]

Fischer's exact test was used for comparing the antifungal susceptibilities between *Candida albicans* and non albicans *Candida* isolates. p value of 0.05 was considered as statistically significant. The study protocol was approved by the Institute Ethics Committee.

RESULTS

Out of total number of 504 cases enrolled, 43 (8.54%) cases had significant candiduria.

More than 70% of the patients belonged to age group 60-70 years of age, 60.5% patients were males. Mean ICU stay in these patients was 27.88 ± 22.52 days. Other associated risk factors of the study group are as shown in [Figure 1].

The risk of developing candiduria was high in patients with urinary catheterization. Out of 43 UTI patients, 39 had urinary catheter insertion with a mean duration of catheter days being 9.79 ± 4.94 days. History of antibiotic was a universal risk factor seen in almost all the patients and 25 (58.1%) patients had diabetes.

Non-albicans *Candida* spp. emerged as the predominant pathogen and was responsible for 62.8% of fungal UTI. *Candida tropicalis* accounted for 34.8% of the cases, whereas *C. albicans* accounted in 30.2% of the cases. Species distribution of yeast isolates is shown in Figure 2. *Candida albicans* showed 100% susceptibility to voriconazole, caspofungin and flucytosine. Among non albicans *Candida*, *C. guilliermondii, C. lusitianae* and *C. rugosa* were 100% susceptible to all antifungals while *C. kefyr, C. tropicalis* and *C. krusei* showed maximum susceptibility to caspofungin [Table1]. Non-albicans *Candida* spp. showed lower susceptibility to antifungal drugs as compared to *C. albicans* and it was statistically not significant.[Table 2].

DISCUSSION

Candiduria is rare in healthy people but relatively frequent in hospitalized patients.[13,14]

In the present study, we observed that UTI due to *Candida* spp. was more common old age. This could be due to lowered host defenses at extremes of age. This finding is supported by many other researchers also.[7,15]

Previous history of antibiotic use was a universal risk factor in our patients. Antibiotics increase the risk of colonization of *Candida* spp. by suppressing endogenous flora and the risk of candiduria increases with prolonged antibiotic use.[16]Correlation between candiduria and previous antibiotic usage was also observed by Weinberger *et al.*[14]

Urinary catheters serve as a portal of entry and most catheters become colonized if left for longer duration.[17]In our study urinary catheters were present in 90.7% of cases. In a similar study done by Kauffman *et al* long-term indwelling urethral catheters or other urinary drainage devices were present in 83% of patients.[3]

From case reports and retrospective reviews, it appears that patients having diabetes mellitus are at higher risk for the complications that can arise from UTIs due to *Candida* species.[18,19]

Recent studies highlight the changing epidemiology of candiduria in hospitalized patients.[20,21] Of concern is the finding in our study that the Candida spp. causing UTI might be shifting to non-albicans *Candida* spp. (62.8%). In our study *C. tropicalis* accounted for 34.8% isolates. Kobayashi *et al* reported a high incidence of candiduria caused by species other than *C. albicans*. *C. tropicalis*(22.2%) was the most common isolate in their study.[22] De Oliviera *et al* recovered *C. tropicalis* from 53% of their 101 candiduria patients.[23] Three (6.9%) isolates of *Trichosporon asahii* were also isolated from urine specimens which is scarcely reported in literature in funguria cases.[24]. Trichosporon spp. was reported in a study done at Chandigarh by Singla *et al.*[25] The susceptibility of *Candida* species to frequently used antifungal drugs has various degrees. It has been reported that non-albicans species have had higher resistance rates against fluconazole than *C. albicans*.[26,27] In our study similar results were observed.

CONCLUSION

The non-albicans species of Candida were the major agents of candiduria and are emergent pathogens of the urinary tract in critically ill patients. This shift towards NAC species as a causative agent has generated a concern in clinical practise as NAC species are more resistant to antifungal drugs as compared to *C. albicans*. Therefore species identification of Candida isolates along with their antifungal susceptibility pattern can help the clinician in better treatment of ill patients.

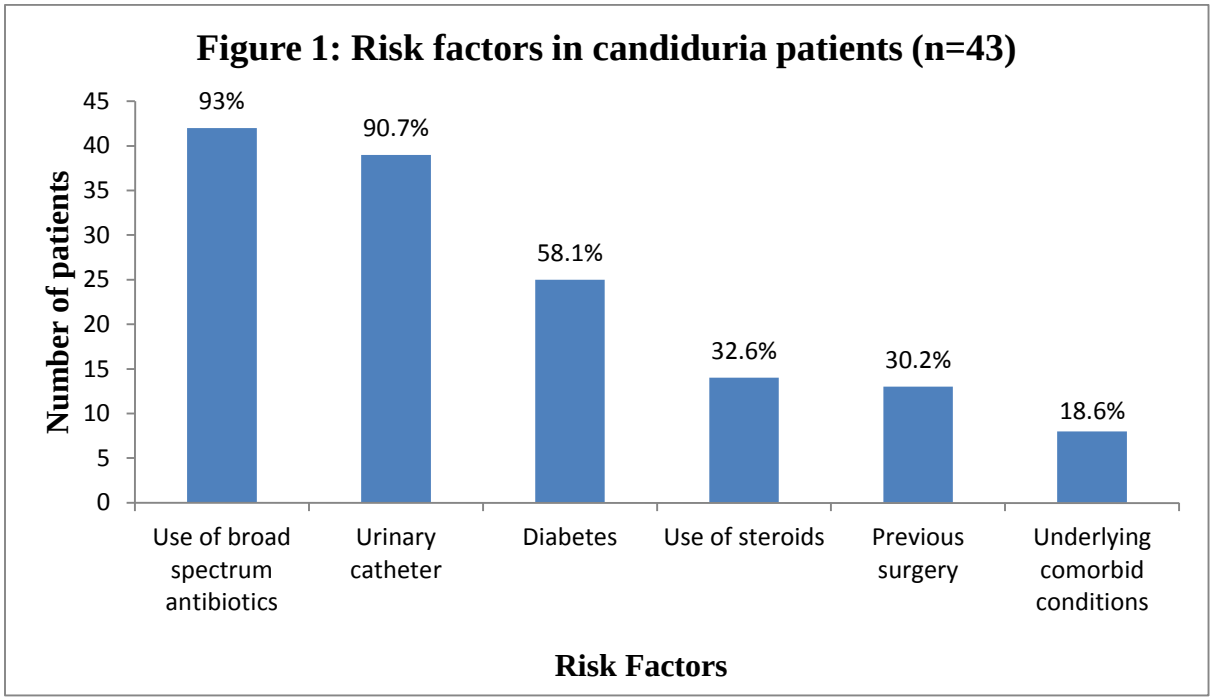
Figure 1: Risk factors in candiduria patients (n=43)
Number of patients
45
40
35
30
25
20
15
10
5
0
93%
90.7%
58.1%
32.6%
30.2%
18.6%
Use of broad spectrum antibiotics
Urinary catheter
Diabetes
Use of steroids
Previous surgery
Underlying comorbid conditions
Risk Factors

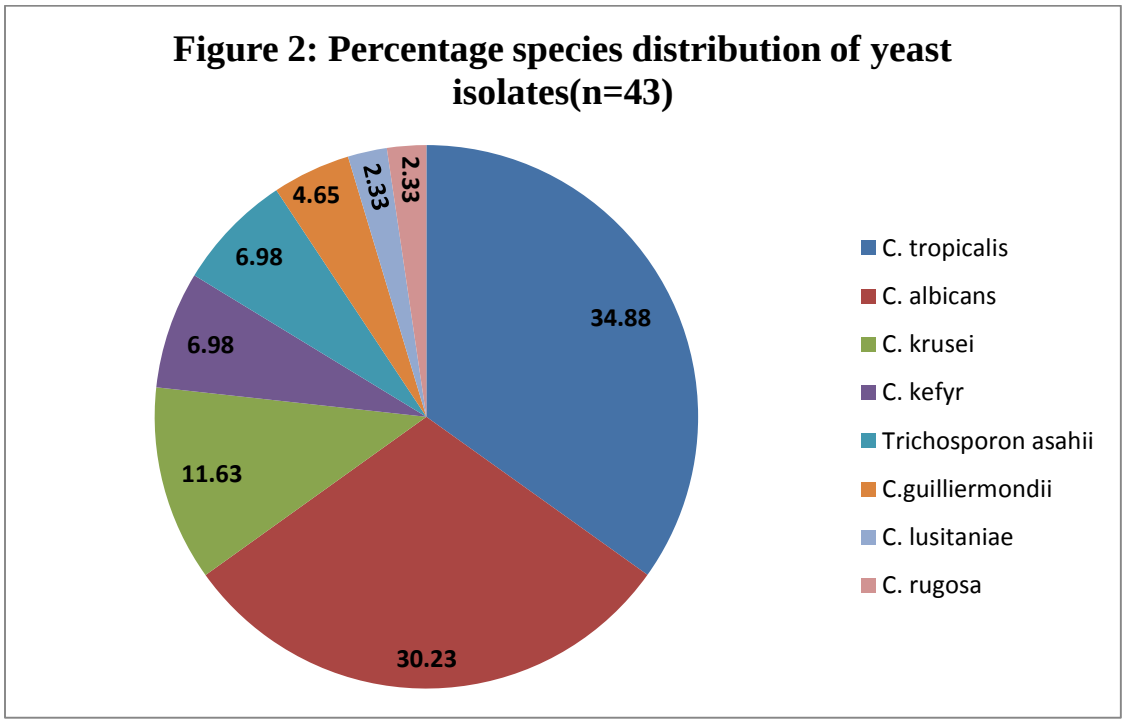
Figure 2: Percentage species distribution of yeast isolates(n=43)
34.88
30.23
11.63
6.98
6.98
4.65
2.33
2.33
C. tropicalis
C. albicans
C. krusei
C. kefyr
Trichosporon asahii
C.guilliermondii
C. lusitaniae
C. rugosa

Table 1: Percentage antifungal susceptibility of yeast isolates (n=43)

Yeast isolates(43)	Fluconazole	Voriconazole	Caspofungin	Amphotericin B	Flucytosine
***C. albicans*(13)**	92.3	100	100	92.3	100
***C. tropicalis*(15)**	80	80	86.6	80	86.6
***C. krusei*(5)**	-	40	100	100	40
***C. kefyr*(3)**	66.6	66.6	66.6	66.6	66.6
***C. guilliermondii*(2)**	100	100	100	100	100
***C. lusitannae*(1)**	100	100	100	100	100
***C. rugosa(*1)**	100	100	100	100	100
***Trichosporon asahii*(3)**	33.3	66.6	33.3	66.6	66.6

Table 2: Comparison of antifungal susceptibility of *C. albicans* & non-albicans *Candida* species.

	C albicans (13)	Non-albicans *Candida* (27)	p value
Fluconazole	92.31	66.67	0.13
Voriconazole	100	74.07	0.095
Caspofungin	100	88.89	0.592
Amphotericin B	92.31	85.19	0.939
Flucytosine	100	77.78	0.154

Significant if p value < 0.05 level of significance

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