

Nosocomial Candiduria - A One Year Prospective Study in Intensive Care Unit.

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Abstract :

Background and Objectives: Urinary tract infections as a result as *Candida* species is becoming increasingly common in hospitalized settings particularly in Intensive Care Units (ICU).

Objectives : To isolate and identify the *Candida* species from urine samples of nosocomial urinary tract infection in intensive care units and their antifungal susceptibility.

Materials and Methods : A prospective study was conducted on urine samples collected from the clinically suspected patients with nosocomial urinary tract infections from Intensive Care Units. *Candida* isolates were identified and speciated by germ tube test, chlamydospore formation in cornmeal agar, sugar assimilation and sugar fermentation using standard protocols. All isolates were tested for Antifungal Susceptibility testing. Results: A total of 91 isolates of *Candida* species were recovered from 305 samples. *C.tropicalis* (67.03%) was the most common isolated followed by *C. albicans* (26.37), *C. krusei* (4.39%) and *C. glabrata* (2.19). Amphotericin B (91%) showed highest sensitivity followed by ketoconazole (85.51), fluconazole (65.88%) and voriconazole(42.8%).

Conclusion : Nonalbicans *Candida* has emerged as an important cause of nosocomial urinary tract infection. Amphotericin B is the drug of choice for systemic candidiasis. Our study equally emphasized the role of ketoconazole for localised and less severe candidiasis. Elderly patients on antibiotics administration, prolonged period of catheterization and having diabetes mellitus admitted to ICU are more susceptible.

Key words : Nosocomial candiduria, *C. tropicalis*, antifungal sensitivity.

Introduction

Candida species are the most common cause of fungal infections leading to a range of life threatening invasive to non-invasive diseases.¹ Urinary tract infections as a result as *Candida* species is becoming increasingly common in hospitalized settings particularly in Intensive Care Units (ICU).² *Candida* species accounts for almost 9-40% of nosocomial urinary tract infections and 80% are acquired by urinary catheter.^{1,3,4}

The predisposing factors causing candiduria are urinary tract instrumentation, Diabetes mellitus, prior antibiotic use, prolonged hospital stay, extremes of ages, female sex, immunosuppressive therapy and immunocompromised conditions.⁵

It is important to know the *Candida* species causing urinary tract infection and its susceptibility pattern before initiating the treatment, as nonalbicans *Candida* species are on the rise and possibility of innate and

acquired resistance to several antimycotic drugs.^{6,7} The present study is undertaken to envisage the various *Candida* species of nosocomial urinary tract infections of Intensive Care Units (ICU) S.S. Institute of Medical Sciences and Research Centre and their antifungal susceptibility tests.

Aim and Objectives

To isolate and identify the *Candida* species from urine samples of nosocomial urinary tract infection patients in intensive care units and its antifungal susceptibility.

Materials and Methods

A one year prospective study was conducted on urine samples collected from the clinically suspected patients with nosocomial urinary tract infections from Intensive Care Units. 305 urine samples were collected with aseptic precaution as per standard techniques from urinary tract infection suspected patient from ICU. Urine sample was collected from both catheterized and non-catheterized patients. Two samples were collected at different occasions from the patients after 72 hours of admission. In non-catheterized patients sample were collected with 24 hours apart. From catheterized patients, first sample will be collected from indwelling catheter and second sample collected after removal of the

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catheter, or else changed the catheter and collected the sample after 30 minutes.⁸

The urine samples obtained will be subjected for routine microscopy. Later were inoculated over Blood agar, MacConkey's and SDA medium. Speciation is done by germ tube test, chlamyospore production on corn meal agar, sugar assimilation and sugar fermentation. Antifungal susceptibility test was done by disk diffusion method following NCCLS M44-A guidelines.

Inclusion criteria: 1. Patients admitted in the ICU for more than 72 hrs with complaints of nosocomial UTI. 2. Colony count of >10³ cfu/ml was considered as significant candiduria.⁸

Exclusion criteria: Patient who had received antifungal treatment prior to admission.⁸

Observation and Results

Among 305 cases 91 were culture positive for *Candida* species. These 91 cases were further evaluated for characterization and antifungal susceptibility. The highest incidence was seen in the age group of above 61 years, comprising 25.2% of cases, followed by age group between 41 to 50 years with 18 % of cases. The least incidence was seen in the age group 11 to 20 years with 6.5%.

Out of 91 isolates, *C. tropicalis* was predominant species accounting for 67.03% of the isolates, followed by *C. albicans* 26.37%, *C. krusei* 4.39% & *C. glabrata* 2.19%.

Table 1: Culture positive for *Candida* in clinically suspected nosocomial urinary tract infection Patients

Culture report	Clinical cases	
	No. of Cases	Percentage (%)
Positive	91	29.84
Negative	214	70.16
Total	305	100

Antibiotic administration was seen in all the patients (100%) which is the highest risk factor followed by catheterization (96.7%) and Diabetes mellitus (13.1%). Out of 91 culture positive patients admitted to Intensive Care Units, 88 were catheterized, showing 96.7% percentage.

Table 2: Different species of candidal isolates from nosocomial candiduria patients

Candidal species	Total number of isolates	Percentage(%)
<i>C. tropicalis</i>	61	67.03
<i>C. albicans</i>	24	26.37
<i>C. krusei</i>	04	4.39
<i>C. glabrata</i>	02	2.19
Total	91	100

CCU sector of ICU had got the maximum number of patients with nosocomial candiduria accounting for 46.1% of cases followed by MICU with 21.9%, SICU with 19.7%. NICU and ICCU has got least candiduria patients showing percentage of 2.1% and 3.2% respectively.

Among the 85 isolates fluconazole was sensitive in 56 isolates accounting for 63.88%. Ketoconazole was sensitive for 85.39% of isolates. Amphotericin B was showing sensitivity 91.01% sensitive among the isolates. Intermediate zones were not appreciated.

DISCUSSION

The present study showed incidence of 29%. Studies from several centres have shown different incidence rates. In the study done by N. Febré et al and Ghiasian SA et al was 18.6% and 32%.^{9, 10} The age group above 61 years showed high incidence and least was found with the age group of < 1 year. The reason for the highest incidence in age above 61 years could be due to lowered host defences at extremes of age.²

Usually female sex are more prone to urinary tract infections because of candidal colonization of vulvo vestibular area.¹¹ But in the present study male predominance is observed, which may be because of increased admission of male population to ICU in our institute. Studies done by Alvarez-lerma F et al showed male predominance which supports findings of our study.¹²

Antibiotic administration suppress the commensals of gastrointestinal tract and lower genital tracts, where by

Table 3 : Showing antifungal susceptibility pattern of candidal isolates

<i>Candida</i> Species	Fluconazole (25 mcg)			Voriconazole (1 mcg)			Ketoconazole (10 mcg)		Amphotericin- B (100 Units)	
	S ≥19	S-DD 15-18	R ≤14	S ≥17	S-DD 14-16	R ≤13	S	R	S	R
<i>C. tropicalis</i> (61)	46	0	15				56	5	57	4
<i>C. albicans</i> (24)	8	2	14	8	0	16	16	8	20	4
<i>C. krusei</i> (4)	-	0	0	4	0	0	4	0	4	0

commensal organisms gains ready access to urinary tract in the presence of indwelling catheter.¹¹ Antibiotic administration was done to all patients, which was the most common risk factor. Diabetes Mellitus patients with glycosuria have impaired phagocytic activity, which causes reduced host defence mechanisms against *Candida* and also causes stasis of urine in neurogenic bladder.^{5,11} Diabetes was important risk factor accounting for about 13% of the total cases.

In the study done by Jain M et al. mean duration of catheterization was 11.1 ± 6 days.² In the present study catheterization was seen with 96.7% and the mean catheter days was 8.9 days. There is a strong relation between days of catheterization and risk of developing candiduria. The mean number of days of catheterization observed in various studies is 6, 7, 12 and 14 days.^{2,12,13}

Studies from different places have shown different distribution of *Candida* species. *C. albicans* (60%) was observed as predominant species followed by *C. glabrata* (14%) in study by Ghiasian SA et al.¹⁰ *C. tropicalis* (40.7%) was predominant isolate followed by *C. albicans* (30.83%) in the study by Kaur R et al.¹⁴ In the above mentioned studies *C. krusei* and *C. glabrata* were in least number. Our study has shown nonalbicans *Candida* group as predominant isolate. Many Indian studies have also shown nonalbicans *Candida*, especially *C. tropicalis* as the predominant isolate. Many studies all over the world have also observed *C. tropicalis* to be predominant *Candida* species causing nosocomial urinary tract infection.¹⁵

In the present study *Candida* isolates were observed highest from Critical Care Unit (46%) patients. Patients who required ventilator, critically ill and debilitated patients are admitted in Critical Care Unit. This could be the possible reason for the highest isolation of *Candida* species among the Critical Care Unit patients in the present study. Much data was not available to compare the nosocomial candiduria among different sectors of Intensive Care Units.

For *C. tropicalis* susceptibility testing is not predictable by disc diffusion method for voriconazole as NCCLS association has observed inter laboratory differences in measuring zone size.¹⁶ Inherent resistance for fluconazole is observed in *C. krusei* is attributed to decreased affinity of ERG11p to the drug.¹⁷ CgCDR1 and PDH1 are the genes detected with azole resistance with *C. glabrata*. For *C. glabrata* antifungal susceptibility could not be done by disc diffusion method.¹⁷ Chaudhary U et al in her work has concluded amphotericin B to be most effective antifungal drug followed by itraconazole,

ketoconazole.¹³ De Freitas AR et al also showed amphotericin B to be best antifungal drug in their study.¹⁸ Fluconazole resistance was observed with *C. albicans* (67.5%) and even with *C. tropicalis* (57.14%) in work done by Ayseynali et al.¹⁹ Fluconazole resistance observed with *C. albicans* are due to up regulation of CDR1, CDR2 and MDR1 genes.¹⁷ Kauffman CA et al in his study showed voriconazole to have greater intrinsic activity and sensitivity than other azole drugs against *C. glabrata* and *C. krusei*.²⁰ In the present study amphotericin B (91.01%) and ketoconazole (85.39%) showed higher sensitivity which can be mimicked in the several studies. Fluconazole resistance was seen in 29 cases (34.11%) in the present study.

Conclusions

Most of the Indian studies have shown the rise of nonalbicans *Candida* particularly *C. tropicalis*. Present study also reiterates the same. Elderly patients on antibiotic administration, with prolonged period of catheterization and Diabetes mellitus admitted to ICU are more susceptible for nosocomial candiduria.

Amphotericin B is the drug of choice for systemic candidiasis. Our study equally emphasized the role of ketoconazole for localised and less severe candidiasis. Advantage of using ketoconazole over amphotericin B is its availability in oral/ topical formulations and has got fewer side effects, thereby making it a better drug in the present study.

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