

Prevalence of *Albicans* and *Non-Albicans* Candiduria in a Tertiary Care Hospital of Jaipur, India

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ABSTRACT

Introduction: An increase in the incidence of Urinary tract infections due to *Candida species* has been observed. The higher rate of Candiduria due to Non albicans *Candida* is now being reported than due to *Candida albicans*. The emergence of drug resistance in *Candida species* has complicated the patient management.

Aim: to observe the prevalence of *Candida species* in UTIs and their antifungal susceptibility pattern in a tertiary care hospital.

Materials and Methods: An observational study was conducted for a period of three months in NIMS, Jaipur. Symptomatic patients belonging to all age groups were included in the study. Catheterized or clean catch midstream urine were centrifuged and the sediment was plated on Sabouraud's Dextrose Agar slants with and without Chloramphenicol. A wet mount preparation was also made and looked for the presence of pus cells, yeast cells, pseudohyphae, etc. Yeast was identified by using germ tube, Chromogenic agar, chlamydospore formation and carbohydrate assimilation tests. Antifungal susceptibility testing was performed on Muller Hinton Methylene Blue Agar.

Result: The *Candida species* were isolated in only 24 (4.8%) samples. Only 8 cases yielded *Candida albicans* (33.33%). The highest cases were found to be of *Candida tropicalis* (n=14) while remaining two cases has growth of *Candida krusei* (n=1) and *Candida glabrata* (n=1).

Keywords: *Albicans*, *Non-Albicans Candiduria*, *Candida species*, UTIs, *Candida albicans*

INTRODUCTION

An increase in the frequency of *Candida* infections among hospitalized patients for past three decades has been observed. Several studies have reported that the incidence of Urinary tract infections (UTIs) due to *Candida* has rose. [1-4] Important risk factors for *Candiduria* includes prolonged hospitalization, Intensive care unit (ICU) patients, urinary tract abnormalities, diabetes mellitus, indwelling urinary catheters, immunocompromised patients, long term antibiotic therapy & immunosuppressive therapy. [4-6] The patient management has become intricate with the emergence of drug resistance in *Candida species*. [7-8]

Though the rate of morbidity due to *Candida species* is high, the mortality rate remains low. *Candiduria* can be caused by *Candida albicans* as well as other *Candida species*. [4] *Candida albicans*, once known as the leading causative yeast of UTI, is now being replaced by Non albicans *Candida species*, as the predominant pathogen. [9] Non albicans *Candida species* are more resistant to antifungal drugs in comparison to *Candida albicans*. [9,10] The present study was conducted to observe the prevalence of *Candida species* in UTIs and their antifungal susceptibility pattern in a tertiary care hospital.

MATERIALS & METHODS

An observational study was conducted in the Department of Microbiology, NIMS, Jaipur for a period of

three months from February 2014 to May 2014.

Inclusion criteria: Symptomatic patients of all age group from both the genders.

Exclusion criteria: Urine sample without pyuria, Candida colony count <1000 CFU/ml.

Permission to conduct the study was taken from Institutional Ethical Committee. A total of 500 catheterized or clean catch midstream urine specimens were collected in sterile, screw capped leak proof containers, after obtaining a written informed consent from patients.

Method: Urine samples were immediately transported to Microbiology laboratory and processed. In case of delay urine samples were stored in 4-8°C. Urine samples were plated semi-quantitatively on 5% sheep blood agar and MacConkey agar. After incubating aerobically at 37°C for 24 hours, any bacterial growth was processed as per Standard Operating Procedure (SOP) of the laboratory using standard Microbiological techniques. Further the urine samples were transferred into a clean, dry and sterile test tube and centrifuged at 3000 rpm for five minutes. After centrifugation, the supernatant was decanted and little fluid remaining was used to reconstitute the sediment within the tube. Sabouraud Dextrose Agar slants with and without Chloramphenicol were inoculated with the sediment and incubated at 37°C for 24 hours to a maximum of 72 hours. A wet mount preparation was also made and looked for the presence of pus cells, yeast cells, pseudohyphae, etc.

The growth on SDA slants were subjected to Gram stain and looked for the morphology of budding yeast cells. Colonies with yeast cell morphology in Gram stain were further tested for identification by Germ tube formation test. Further, the yeast growth was inoculated onto Chromogenic media (HiCrome Candida Agar) and incubated for 24-48 hours at 30°C.

The colonies were identified based on the color of the colonies (chromogenic

reaction) produced by the Candida species on the CHROM Agar. Light green colonies *Candida albicans*, blue colonies with pink halo- *Candida tropicalis*, cream to white colonies- *Candida glabrata*, purple fussy colonies- *Candida krusei*.

Candida species were further confirmed by chlamydospore formation on cornmeal agar and carbon source (carbohydrate) assimilation test.

Antifungal Susceptibility Testing: All the identified *Candida species* were subjected to antifungal susceptibility testing on Muller Hinton Methylene Blue Agar (MHMB) with 2% glucose and 0.5% µg/ml of methylene blue using Disc diffusion method. Antifungals tested were Fluconazole (25µg/ml), Voriconazole (1µg/ml), Nystatin (50µg/ml) and Amphotericin B (100µg/ml). The yeast suspension was adjusted to contain 1 to 5 × 10⁶ cells/ml, which corresponds to 0.5 tube in McFarland turbidity scale. A lawn culture was made from the yeast suspension on MHMB agar and antifungal discs were placed over the agar. The plates were incubated at 35°C for 24 to 48 hours. The reading was performed according to the antifungal discs manufacture's recommendations. Results were expressed as susceptible, intermediate, and resistant.

RESULT

A total of 500 urine samples (305 females and 195 males) were collected during this study period out of which 429 were from inpatients (IPD) and 71 from outpatients (OPD). The Candida species were isolated in only 24 (4.8%) samples (females=19; males=05) while remaining 476 were either sterile or yielded bacterial and other fungal pathogens. Among the 71 OPD cases, only 2 cases had the growth of Candida species. Candida non albicans species (66.66%) outnumbered *Candida albicans* (33.33%). Only 8 cases yielded *Candida albicans* (33.33%). The highest cases were found to be of *Candida tropicalis* (n=14) while remaining two cases

has growth of *Candida krusei* (n=1) and *Candida glabrata* (n=1).

Young adult patients with age ranging from 21-40 years were associated with highest number of *Candida* cases

(Table 1.). *Candida tropicalis* were observed having higher attack rates as the age increases while other *Candida species* were isolated from patients with sexually active age.

Table 1. Age distribution of patients with Candida species isolated from their urine specimens.

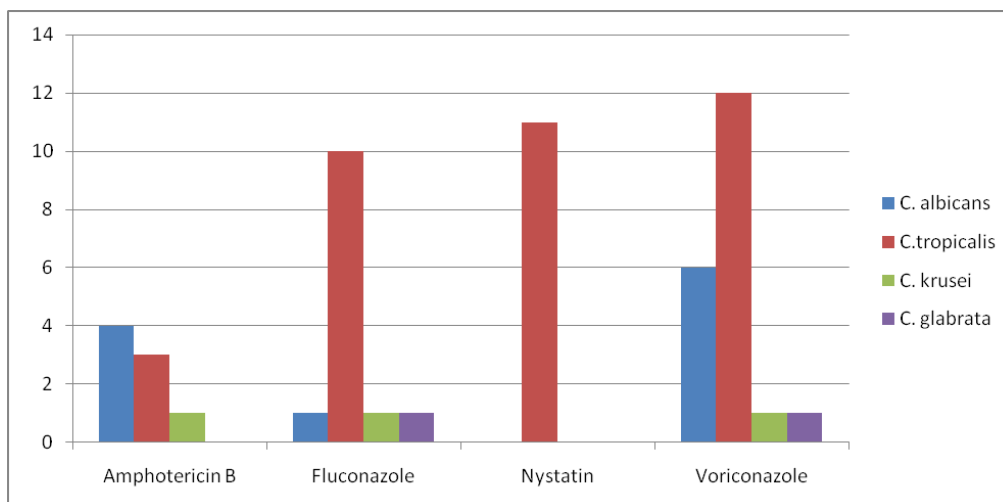
Sr No	Age	C. albicans	C. tropicalis	C.krusei	C.glabrata	Sterile/other pathogens	Total
1	1-20 years	02	-	-	-	167	169
2	21-40 years	06	04	01	01	192	204
3	41-60 years	-	05	-	-	85	90
4	>60 Years	-	05	-	-	32	37
5	Total	08	14	01	01	476	500

Table 2. Different predisposing risk factors and Candida species isolated from their urine.

Risk Factors	Diabetes mellitus	Broad Spectrum antibiotics	On catheters	Pregnancy	No identifiable risk factors
C. albicans	1	1	4	1	1
C. tropicalis	4	1	8	1	0
C. glabrata	1	0	0	0	0
C. krusei	1	0	0	0	0
Total	7	2	12	2	1

The patients with candiduria had certain predisposing risk factors such as diabetes mellitus (n=07), prolonged antibiotic treatment (n=02), catheterization (n=12) and pregnancy (n=02)(Table 2). One patient without any predisposing risk factor had candiduria due to *Candida albicans*.

The *Candida species* isolated in present study had shown low susceptibility towards the common antifungals used for treating fungal infections (Graph 1). *C. tropicalis* was seen to have high resistance against Amphotericin B while *C. albicans* were found to be least susceptible towards Fluconazole and Nystatin. *C. krusei* and *C. glabrata* were not susceptible towards Nystatin while Voriconazole had most promising results against all the *Candida species*.



Graph 1. Antifungal susceptibility pattern of Candida species isolated from urine specimens.

DISCUSSION

The candiduria in present study is high and the rate of *Candida non albicans* is reported higher than that of *C. albicans*. This change in the aetiopathogenesis of candiduria is a matter of concern as

Candida non albicans often found to have intrinsic or/and acquired resistances to commonly used antifungal drugs. [11] Candiduria is facilitated by certain factors such as immunocompromised status, use of immunosuppressive therapy, longer duration

of hospital stay, prolonged antibiotic treatment, catheterization, etc. [12-14] The emergence of antifungal resistance in *Candida* has increased due to indiscriminate use of antifungals specially the azole group. [15]

Presence of *Candida* in urine acts as a marker for haematogenous seeding to the kidneys. Candiduria reflects either colonization or infection of the lower urinary tract or the kidneys. [16] *Candida species* ranks the fifth most common nosocomial urinary pathogen in India. [17]

In present study the highest rate of candiduria was observed in elderly patients i.e. patients above 60 years of age. Similar results were reported by other authors too where *C. tropicalis* was found to be causative agent. People at their extreme of ages usually have decreased immunity which can be reason for the higher attack rate of *Candida species*. [14,18,19] In present study the candiduria was reported commonly in females (79.17%) as compared to males (20.83%). Females are in higher risk of developing candiduria as *Candida species* frequently colonizes vulvovestibular area and from where they can ascend upwards and cause urinary tract infection. [20]

High degree of antifungal resistance was recorded in present study especially in *C.albicans*. *C. tropicalis* was found to be quite sensitive species against all the antifungals except Amphotericin B. Fluconazole has been extensively used as treatment of fungal infection for last 15 years as it was safe and orally administrable. [21] Increase in fluconazole resistance has been reported in many patients especially in HIV- infected patients with oral candidiasis. [22-23] There are various mechanisms which lead to antifungal resistance, namely (i) reduced drug intracellular accumulation, (ii) decreased target affinity/processivity for the drug, and (iii) counteraction of the drug effect. [24]

CONCLUSION

Clinicians are facing challenge to treat the candida infection due to emergence of antifungal resistance. The identification and antifungal susceptibility testing of candida species isolated from clinical sample must be tested as the antifungal susceptibility varies from species to species. Many new antifungals which are under development may have more advantage in terms of overcoming antifungal resistance and safety than current drugs are the need of hour.

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