

# Prevalence of *Candida* species in Urinary Tract Infections from a Tertiary Care Hospital at Lucknow, Uttar Pradesh, India: A Retrospective Study

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## ABSTRACT

**Introduction:** The presence of *Candida* in urine, called Candiduria. Immunocompromised individuals are more susceptible to this infection and it can cause life-threatening complications. *Candida albicans* is most common isolate in Urinary Tract Infections (UTI) but in recent years this is shifting to non-*albicans* groups. Researchers found that azole is the drug of choice against *Candida* infections but due to excess use of these drugs resistance is developing more frequently for azole group drugs and drug resistant isolates are increasing gradually. A unique virulence factor i.e biofilm production, similarly like bacterial species is a crucial factor which contributes to the resistance against antifungal drugs.

**Aim:** To assess the prevalence of *Candida* spp. in UTI retrospectively.

**Materials and Methods:** The present retrospective study was conducted in Department of Microbiology, T.S Misra Medical College, Lucknow, Uttar-Pradesh, India from January 2018 to February 2020. A total of 1576 urine samples were collected from different wards of hospitals and Intensive Care Unit (ICU) with age group 0-80 years. Out of 1576 urine samples received, 786 had fungal growth, from

which 176 *Candida* spp. were isolated. Candiduria and *Candida* UTIs data were collected from Institute's microbiology records retrospectively. The obtained results were statistically analysed in numbers and percentages using MS Excel 2013 version.

**Result:** The prevalence of *Candida* species was 11.2%. The age group between 21-30 years was more prevalent. Diabetes mellitus was the main co-morbidity factor in Candiduria patients. The incidence rate was high in ICU patients 161 (91.5%) than non ICU patients (8.5%). Most the samples were isolated from general medicine (45.3%) and Obstetrics and Gynaecology department (34.8%) followed by general surgery (15.5%) and pediatric department (4.4%).

**Conclusion:** Present study found the high prevalence of candiduria and the isolates were biofilm producers with increasing resistance against most common drugs fluconazole which is a major concern for the treatment and management aspects. In immunocompromised patients, it is important to identify the species of *Candida* isolates as well as their antifungal susceptibility pattern to assist the clinicians in treating the patients with candiduria.

**Keywords:** Antifungal drugs, Candiduria, Prevalence

## INTRODUCTION

Globally, among other *Candida* species, *Candida albicans* is mainly responsible for systemic candidiasis and fungal nosocomial UTIs. *Candida albicans* is a dimorphic fungus which has a unique virulence property so it can switch between yeast and filamentous forms. There are several other attributes pertaining to *C. albicans* that have absolutely been considered as pathogenic markers including adhesion, tissue invasion, secreting hydrolytic enzymes, stereotropism and biofilm production [1-3].

It is possible to isolate *Candida* species from healthy urine samples, but the count can be very low and not significant. The percentage of positive urine cultures in a primary care setting is 5%, while it reaches 10% or more in tertiary care hospitals [4]. A common clinical finding in hospitalised patients is *Candida* species in their urine (candiduria). *Candida* species in urine may be asymptomatic (in healthy people or patients) or symptomatic. There are many clinical conditions in which patients are more prone to candiduria which includes interstitial cystitis, Epididymo-orchitis, prostatitis, pyelonephritis, and renal candidiasis. Asymptomatic candiduria is though mostly benign and is not considered as a disease. More than 200 species of *Candida albicans* are consistently reported to cause candiduria (20% of nosocomial infections). Most of available literature support showed that *Candida* is the most likely *Candida* species to cause candidiasis [5]. The immune status of ICU patients is always on the weaker side which is beneficial for the *Candida*

species to cause infections in these patients resulting in the high mortality rate and the prevalence is also very high [6,7]. There are many factors which includes gender (female), age, prolonged antibiotic intake, sex activities, genetic inheritance, diabetes, immunosuppression, Acquired Immunodeficiency Syndrome (AIDS), pregnancy, cancer patients, multiple clinical procedures, hypertension, hospitalisation, indwelling catheter or prosthetics, malnutrition, social behaviour, these are the predisposing factors leading to UTI candidiasis in patients [8,9]. In general, inpatients are more likely to experience symptomatic candiduria, whereas outpatients and healthy adults are more likely to experience asymptomatic candiduria. Indwelling catheters are the important reservoir for these pathogens and with the help of these procedures (Catheterisation) pathogens easily reach the anatomical site and cause infections. Data is available claiming that non-*albicans Candida* (NAC) species cause significant increases in UTIs and candiduria [10]. While there are non-*albicans* species infections, UTIs and candidiasis caused by *C. albicans* are more prevalent [10]. In case of candiduria, the infection finally reaches to blood stream resulting into severe disseminated bloodstream infections (Candidaemia). The bloodstream infections is responsible for 30-40% mortality rate [11,12]. As the case of candidiasis is increasing gradually resulting into the development of drug resistance which is major health concern worldwide. So to control this stage monitoring at regular intervals is a very necessary and crucial

point. In the clinical case of candidal balanitis and vulvovaginal candidiasis it is very crucial to diagnose this infection in one sexual partner and should be prevented up to this level [13].

Even though the disease i.e. candidal balanitis is well known Sexually Transmitted Disease (STD), but the significant studies are not available [14]. A common fungal infection affecting 75% of women worldwide, vulvovaginal candidiasis is very easy to treat.

Among the *Candida* species causing infections in young and adult individual's three most common species include, *C. albicans*, *C. glabrata*, and *C. tropicalis*. Although *C. parapsilosis* causes candiduria more frequently in neonates [3]. Candiduria and UTIs by *Candida* spp have different prevalence rates depending on geographical location, therefore, regional data is essential for evaluating the shift and to determine the scenario at national level. Hence, this study was done retrospectively to assess the *Candida* prevalence in UTI.

## MATERIAL AND METHODS

The present retrospective study was conducted in Department of Microbiology, T.S Misra Medical College, Lucknow, Uttar-Pradesh, India from January 2018 to February 2020 after permission from Institutional Ethics Committee (IEC) (Reference No: TSMC &H/STC/936/2019). Data was analysed after sample collection, processing and data entry i.e. in March 2022.

**Inclusion criteria:** Microbiology fungal culture records which were related to only urine samples from all wards and ICU were included in the study retrospectively. Pure growth of yeast isolates having significant colony count  $>10^3$  CFU/mL.

**Exclusion criteria:** The study excluded other clinical samples from all wards and ICU. A colony count less than  $10^3$  CFU/mL was excluded from the study.

**Data collection:** The study was conducted on 1576 urine samples received from different clinical departments, Among 1576 samples, 786 were culture positive, out of 786 culture positive samples 176 *Candida* species were reported. Candiduria and Candida UTIs data were collected from Institute's microbiology records retrospectively. Only urine samples received from inpatient and outpatient during the given period were included in this data screening. The collection of patient data, which contained only demographic information and the indication for the submission of samples, was also conducted. The term candiduria in clinical microbiology is described as the isolation of *Candida* species from urine samples on at least one occasion with  $>10^3$  CFU/mL. *Candida* isolate is considered to be separate if it occurred more than 30 days apart or if it contained different species of *Candida*.

**Isolate identification:** A total of 10  $\mu$ L of each uncentrifuged and homogenised urine sample was cultured with a calibrated loop on Cysteine Lactose Electrolyte Deficient (CLED) agar, (Himedia, Mumbai, India) incubated overnight at 37°C for 18 hours, aerobically. If the colony count was  $10^5$  or more CFU/ml and upon suspicion of *Candida* spp. a wet mount of an isolated colony was prepared and examined during microscopy and after confirmation of the *Candida* spp. the isolates were further processed as per standard protocol [7]. Fungal colony morphology was confirmed by using Sabouraud Chloramphenicol Agar (Himedia, Mumbai, India), germ tube production, and micro morphology on Potato Dextrose Agar (PDA) (Himedia, Mumbai, India) and HiCrome Candida Differential Agar (Himedia, Mumbai, India). All clinical samples were processed according to standard microbiology protocol [7] with standard ATCC 25923 control strains.

## STATISTICAL ANALYSIS

The data included demographic information i.e., age; sex, OPD and IPD history. The obtained results were statistically analysed in numbers and percentages using MS Excel 2013 version.

## RESULTS

Out of 176 *Candida* isolates 15 were reported from OPD clinics and 161 were from IPD wards. Out of 1576 total clinical (Urine) samples, 176 isolates were *Candida* species showing prevalence of 11.2%. The incidence rate was high 105 (59.7%) in patients between the age group of 21-30 years and the least incidence rate 4 (2.3%) was found in 71-80 year age group patients as shown in [Table/Fig-1].

Age group (years)	No. of cases	Male (50)	Female (126)
0-10	6 (3.4)	02 (33.3)	04 (66.7)
11-20	6 (3.4)	03 (50)	03 (50)
21-30	105 (59.7)	28 (26.7)	77 (73.3)
31-40	31 (17.6)	09 (29)	22 (71)
41-50	5 (2.8)	02 (40)	03 (60)
51-60	10 (5.7)	03 (30)	07 (70)
61-70	9 (5.1)	02 (22.2)	07 (77.8)
71-80	4 (2.3)	01 (25)	03 (75)
Total	176	50 (28.4)	126 (71.6)

[Table/Fig-1]: Age wise distribution of clinical cases.

The leading cause of these infections, apart from other co-morbidities, was diabetes, as 162 (92.0%) of cases occurred in diabetic patients shown in [Table/Fig-2].

Co-morbidity	No. of cases(n)	Percentage (%)
Diabetic	162	92.0
Non-Diabetic	14	8.0
Total	176	100

[Table/Fig-2]: Distribution of cases according to co-morbidity.

As shown in the [Table/Fig-3] that the majority of cases were found from ICU patients 161 (91.5%) and the incidence rate was very less (8.5%) for non ICU patients.

ICU/Non ICU	No. of cases (n)	Percentage (%)
ICU	161	91.5
Non ICU	15	8.5
Total	176	100

[Table/Fig-3]: Distribution of cases according to samples received from ICU and non-ICU cases.

Most of the samples were isolated from general medicine 73 (45.3%) and Obstetrics and Gynaecology department 56 (34.8%) as shown in [Table/Fig-4].

Department	No. of cases (n)	Percentage (%)
General Medicine	73	45.3
General surgery	25	15.5
Pediatrics	7	4.4
Obstetrics and Gynaecology	56	34.8
Total	161	100

[Table/Fig-4]: Distribution of cases according to sample received from different departments.

Of the total 176 fungal isolates, 50 (28.4%) and 126 (71.6%) were reported from male and female patients respectively. *Candida albicans* (61.9%) were more prevalent as compared to other species [Table/Fig-5].

<i>Candida</i> species	No. of cases (n)	Percentage (%)
<i>Candida albicans</i>	109	61.9
Other <i>Candida</i> spp. ( <i>C. glabrata</i> , <i>C. tropicalis</i> )	67	38.1
Total	176	100

[Table/Fig-5]: Prevalence of *Candida* spp.

## DISCUSSION

This retrospective study was conducted in the Department of Microbiology at T.S, Misra Medical College and Hospital from January 2018 to January 2020. The sample size of the present study was 1576 among them 786 was culture positive, out of 786 culture positive isolates 176 *Candida* strains were isolated. When candiduria is found in a patient, especially if they have no symptoms, it should not be dismissed nor treated lightly, but requires careful evaluation. Female patients with candiduria are more likely to be diagnosed than female patients [15]. The candiduria in present study was high and the rate of NAC was reported lower (38.1%) than that of *C. albicans* (61.9%). Many healthy people shows microbial normal flora of *Candida albicans* and NAC in different anatomical sites like vagina, oral cavity, and alimentary canal. Additionally, in premenopausal and healthy females, *Candida* can colonise the external side of the urethral opening. It can be an opportunistic pathogen leading to fungal UTIs in the host [16-19]. Fungal Urinary Tract Infections (UTIs) are relatively uncommon compared to bacterial UTIs.

The study observed female to male ratio of 1:2.5 in accordance with study by *Nayman Alpat S et al.*, [20]. In the present study the candiduria was reported commonly in females (71.6%) as compared to males (28.4%). Females are at higher risk of developing candiduria as *Candida* species frequently colonised vulvovestibular area and from where they can ascend upwards and cause urinary tract infection [21]. In this study candiduria were more prevalent in the age group 21-30 years (59.7%) followed by age 31-40 years (17.6%) and patients with age range of 51-60 years (5.6%). *Kashid RA et al.*, [22] reported that the prevalence of candiduria in patient's increases gradually as long term stay of Hospital and ICU increases. Moreover, candiduria in ICU patients is the marker of increased mortality [23]. A total of 91.5% of candiduria cases were observed in the ICU, which indicates a higher mortality rate. In critically ill patients, the occurrence of candiduria should be regarded as a marker of invasive candidiasis. Presence of *Candida* in urine acts as a marker for haematogenous seeding to the kidneys. Candiduria reflects either colonisation or infection of the lower urinary tract or the kidneys [24]. *Candida* species ranks the fifth most common nosocomial urinary pathogen in India [25]. In accordance with available data, the most persistent nosocomial fungal infection is urinary tract candidiasis. There has been a rapid shift in the distribution of *Candida* species, which is primarily responsible for nosocomial fungal UTI. Infectious Diseases Society of America (IDSA) suggests that use of indwelling catheters may be eliminated in asymptomatic candiduria patients with no risk factors and for the patients with high risk factor group oral fluconazole should be prescribed for the prevention of severe candidiasis [26]. There are certain factors that facilitate *Candida* infection, including immunocompromised status, immunosuppressive therapy, prolonged antibiotic treatment, catheterization, etc [27-29]. Prevalence of *Candida* species including *Candida albicans* and NAC from candiduria cases documented in the last 10 years from India is shown in [Table/Fig-6] [10,29-38].

The emergence of antifungal resistance in *Candida* has risen due to the liberal use of antifungal, especially those from the azole group [30]. In present study, Diabetes mellitus was a more prevalent co-morbidity factor account for (92.0%). *Candida albicans* was are the most common culprit causing candiduria in present study, but the rise in other *Candida* species is also of significant concern to clinicians [31-35]. NAC species is on the rise along with *Candida albicans* as a cause of candiduria according to present study. *Candida albicans* are gradually being displaced by NAC (*C. glabrata* and *C. tropicalis*) as the scenario shifts progressively [36-38].

### Limitation(s)

The study focused on patients admitted to one hospital only. Hence, the findings may not be applicable to other locations. The study also relied exclusively on retrospective data.

Study	Year of publication	Place	Prevalence		
			<i>Candida</i> spp.	<i>C. albicans</i>	Non- <i>albicans</i>
Awari A, [10]	2011	Bhopal	--	36.6%	63.3%
Yashavanth R. et al., [29]	2013	Mangalore	2.27%	30.3%	69.7%
Prakash V et al., [30]	2015	Bareilly	18.6%	60.25%	39.74%
Goyal RK et al., [31]	2016	Bareilly	2.36%	66.7%	33.33%
Dinoop KP et al., [32]	2017	Tamil Nadu	3.52%	52.4%	17.8%
Datta P et al., [33]	2018	Chandigarh	--	58.7%	24%
Abishek VC et al., [34]	2019	Chennai	2%	38%	62%
Rishi S et al., [35]	2020	Jaipur	4.8%	33.3%	66.6%
Mendem S et al., [36]	2020	Telangana	7.8%	7.84%	--
Jain S et al., [37]	2011	Delhi	--	56%	44%
Pramodhini S et al., [38]	2021	Kolkata	6.7%	17.1%	82.9%
Present study	2022	Lucknow	11.1%	61.9%	38.1%

[Table/Fig-6]: Prevalence of *Candida* species including *Candida albicans* and Non *albicans* from candiduria cases documented in the last 10 years from India.

## CONCLUSION(S)

NAC has caused more UTIs, but *C. albicans* remains the most common fungal cause of UTIs. Clinicians are facing challenges to treat the *Candida* infection due to emergence of resistant strains. As a result of drug resistance, clinicians face challenges in treating *Candida* infections. Many new antifungal agents are under development which may have more advantages over current drugs when it comes to overcoming antifungal resistance and ensuring safety. *Candida* species isolated from clinical samples should be identified and tested for antifungal susceptibility since susceptibility differs between species.

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