Medico Research Chronicles

ISSN No. 2394-3971

Research Article

CANDIDURIA IN IMMUNOCOMPROMISED INDIVIDUALS IN A TERTIARY CARE CENTER IN NORTHERN INDIA

Ved Prakash[1], Prem Prakash[*2], Dakshina Bisht[3], Shashikant V[4], H. K Premi[5], D. Tripathi[6]

1. Associate Professor, Dept of Microbiology, RMCH, Bareilly, U.P

**2. Assistant Professor, Dept of Microbiology, RMCH, Bareilly, U.P*

3. Professor, Dept of Microbiology, Santosh Medical College, Ghaziabad, U.P

4. Professor, Dept of Physiology, RMCH, Bareilly, U.P

5. Professor, Dept of Obst & Gynae, RMCH, Bareilly, U.P

6. Assistant Professor, Dept of Medicine, RMCH, Bareilly, U.P

Submitted on: March 2015
Accepted on: March 2015
For Correspondence
Email ID:
prem6284@gmail.com

Abstract

Fungal infections of the urinary tract, caused by *Candida species*, are becoming prevalent worldwide. The aim of our study was to determine the prevalence of candiduria in immunocompromised patients in our hospital.

During a period of 1 year, a total of 418 urine samples were collected and transported to Department of Microbiology. After direct microscopic examination the samples were inoculated onto Sabaraud's Dextrose agar with antibiotics. The *Candida albicans* and non albicans were identified by colony morphology, Germ tube test and Chlamydospore formation test on Corn Meal agar. The antifungal sensitivity testing was done by Disc diffusion method.

Out of 418 samples {174(41.62%) males and 244 (58.37%) females} Candida species has been isolated from 78 (18.66%) cases. Out of the 78 (100 %) isolates, 47 (60.25%) were *Candida albicans* and 31 (39.74%) were non albicans species. The age ranged from sixteen months to 86 years. Various risk factors observed among the patients were long duration of hospitalization, catheter use, antimicrobial therapy/chemotherapy, diabetes mellitus, HIV etc. Amphotericin B and Itraconazole were the most sensitive antifungal agents. However more resistance was seen in case of *non albicans Candida* species against the same antibiotics.

In conclusion, candiduria is relatively common in immunocompromised patients both by *Candida albicans* as well as non albicans species. In addition, there is a strong correlation between the incidence of candiduria in immunocompromised patients and broad-factors impairing immunity of patients. There is rise in resistance against the antifungal agents for both *Candida albicans* and non albicans species.

Keywords: *Candida*, immunocompromised, antifungal, invasive procedures.

Introduction:

The urinary tract infections are one of the common infections amongst the immunocompromised individuals and candiduria is one of the finding. The Candida is the constituent of normal flora of the skin. The Candida species are detected in the urine due to various risk factors like

Diabetes mellitus, increased age, female sex, antibiotic use, use of urinary drainage devices for example catheter, prior surgical procedure, chronic renal failure, malignancy and neutropenia. [1,2,3]

The vast majority of the patients with candiduria are asymptomatic. However disease in immunocompromised patients has a high risk of morbidity and mortality. [4] Although the majority of the candiduria are caused by *Candida albicans*, non albicans such as *Candida glabrata* and *Candida tropicalis* are emerging as pathogens for U.T.I. *C. albicans* is the most commonly isolated fungus from urine, accounting for 50%–70% of isolates in various studies. [5,6,7] Investigations regarding pyuria and quantitative cultures of urine have proved to be of little use in separating infection from colonization. It had been thought that the presence of pseudohyphae could distinguish yeasts causing infection from those merely colonizing the bladder, but this has been shown to be invalid. [8] The aim of this study is to investigate the incidence of various risk factors associated with candiduria in immunocompromised individuals, their species differentiation and antifungal susceptibility testing.

Material & Methods:

Study Design: This cross sectional study was conducted in the Department of Microbiology in Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh over a period of one year extending from November 2013 to October 2014, after due clearance from the Ethical committee of the institute.

Data collection: Data collected for each patient included; gender, age, duration of hospitalization, catheter use, antimicrobial therapy, diabetes mellitus, HIV etc and hospital ward were collected.

Inclusion criteria: All the inpatients (immunocompromised) with signs and symptoms and of Urinary tract infection were included in the study.

Exclusion Criteria: (1) The patients who were not immunocompromised (2) The patients on antifungal therapy during or from last one month.

Collection of Specimen: The clean catch midstream urine specimen, indwelling catheter specimen, and by suprapubic aspiration were collected under aseptic precautions.

Wet mount examination: The urine specimen was examined microscopically at low and high power to detect pus cells, epithelial cells, casts, crystals, bacteria and yeast like cells.

Mycological Culture: Urine specimens were inoculated on Sabouraud Dextrose Agar (SDA) with chloramphenicol and chlorohexidine. They are than incubated at 37 C and 25 C for 48–72 hours. The colony characteristics were identified as 0.5 to 1 mm in diameter, White, smooth, creamy, sometimes wrinkled.

Germ Tube Test: This test was performed by taking 2ml of serum in a test tube and mixed with 2–3 colonies of Candida and then incubated at 37 °C for 2 hours aerobically. After incubation small amount of suspension were taken on slide and observed under microscope for germ tube formation for *C. albicans*.

Chlamydospore formation test: Identification of *C. albicans* on Corn meal agar was done by taking few colonies from Sabouraud dextrose agar and streaked on corn meal agar then incubated aerobically for 48–72 hours at room temperature. After incubation, chlamydospore was observed under microscope to identify *C. albicans.*

Antifungal susceptibility testing: According to National Committee for Clinical Laboratory Standards (NCCLS) antifungal susceptibility testing were done by using disc diffusion methods. [9] Five antifungal drugs Fluconazole (10 mcg),

Ketoconazole (10 mcg), Clotrimazole (10 mcg), Amphotericin B (20 mcg), Itraconazole (10 mcg) [HIMEDIA, MUMBAI] were used. Mueller Hinton agar containing 2% glucose and 0.5 µg/ml methylene blue were streaked with *Candida*, disc were placed on it and incubated for 48–72 hours at room temperature then checked the zones for susceptibility and inhibition.

Results:

In this study, a total of 418 {174(41.62%) males and 244 (58.37%) females} hospitalized patients with indications of immunocompromised state were sampled. Out of 418 samples Candida species has been isolated from 78 cases (showing more > 10^5 c.f.u/ ml) [30 (38.46%) males and 48 (61.53%) females]. In this study, the age ranged from sixteen months to 86 years.

Table 1 shows the age distribution of culture positive patients.

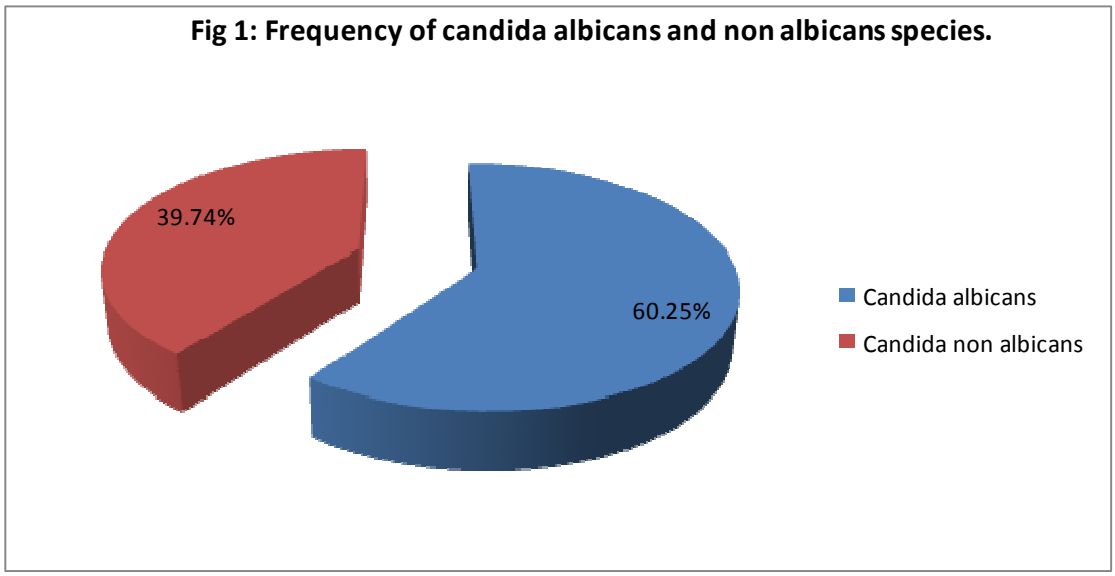
AGE GROUP	MALE	FEMALE
< 10 years	01	01
11-20 years	02	04
21-30 years	06	14
31-40 years	09	12
>40 years	12	17
Total	**30**	**48**

Based on the data of the clinical history, the various observed risk factors among the patients were duration of hospitalization, catheter use, antimicrobial therapy/chemotherapy, diabetes mellitus; HIV etc are documented in **Table 2.**

TABLE 2: The various risk factors in the admitted patients that may be associated with Candiduria are:

S.no	RISK FACTORS	Number of patients
1	Antibacterial therapy/ Chemotherapy	48
2	Indwelling catheters for more than a week	39
3	Diabetes mellitus	29
4	Renal disorders/ Organ Transplantation	11
5	HIV positive patients	04
6	Tuberculosis	03
Note: Some patients had multiple risk factors		

Out of the 78 (100 %) isolates of Candida, 47 (60.25%) were *Candida albicans* and 31 (39.74%) were non albicans *Candida* species as shown in **Figure 1**.

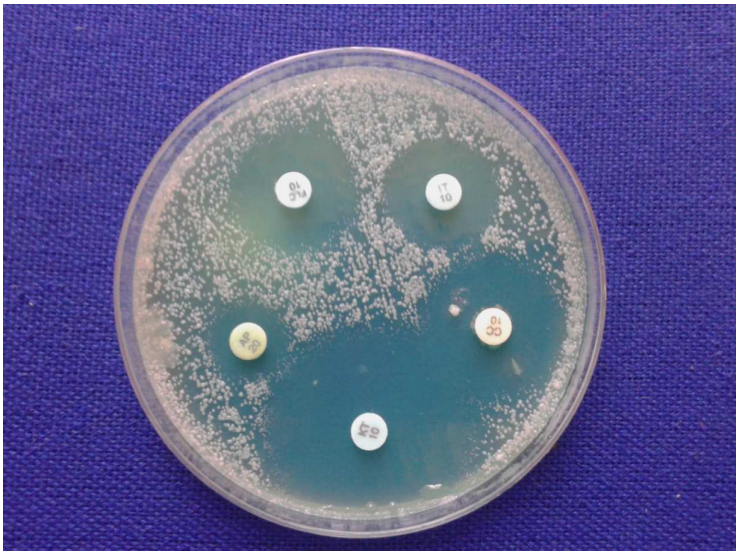


The sensitivity test against 5 antifungal agents has been depicted in **Table 3 and Figure 2.**

Table 3: The sensitivity of *Candida albicans* and *Candida non albicans* species against different antifungal agents.

Antifungal agent	*Candida albicans*	*Candida non albicans species*
Fluconazole (10 mcg)	37 (78.72%)	23 (74.19%)
Ketoconazole (10 mcg)	34 (72.34%)	21 (67.74%)
Clotrimazole (10 mcg)	33 (70.22%)	23 (74.19%)
Amphotericin B (20 mcg)	39 (82.97%)	24 (77.41%)
Itraconazole (10 mcg)	39 (82.97%)	23 (74.19%)

Figure 2: The photo showing antifungal sensitivity test.



Discussion:

Our study shows that Candiduria accounted for 18.66% of the total UTIs in immunocompromised individual. The previous studies had already stated that upto 10% of the total UTI's are caused by *Candida* species. [10,11] This study has reported a slightly higher rate which may be attributed due to increased use of new invasive instruments, blind use of antibiotics, surgery and transplantation, HIV infection, and the most important is the formation of biofilm by *Candida* species which makes the condition more serious especially in immunocompromised individuals.

We observed that the females [244 (58.37%)] are more affected than males [174(41.62%)]. It is in line with several reports in the past which had reported the higher incidence of candiduria in women than in men. [12,13] In our study candiduria were more prevalent in patients aging >40 years (37.18%) followed by age 31-40 years (26.92%) and patients with age range of 21-30 (25.64%). Our study shows a number of risk factors responsible for impairment of immune system of individuals leading to candiduria like indwelling catheters for more than a week, antibacterial therapy, diabetes mellitus, renal disorders (altered Kidney function tests), HIV positive patients and tuberculosis etc. Remarkably several types of studies showed similar risk factors: increased age, female sex, antibiotic use, urinary drainage devices, prior surgical procedures, and diabetes mellitus etc. [14,15,16]

This study shows that the *Candida albicans* [47(60.25%)] are the main culprit causing candiduria in immunocompromised patients, but the rise in non albicans species of *Candida* species [31(39.74%)] is also a major concern for the clinician. The past studies showed that *C. albicans* is the most commonly isolated yeast from urine, accounting for >50% and the incidence of candiduria by non albicans species is also in rise. [14,17] Antifungal test results of the present study indicate that the *C.albicans* were susceptible to Fluconazole 37 (78.72%), Ketoconazole 34 (72.34%), Clotrimazole 33 (70.22%), Amphotericin B 39 (82.97%), Itraconazole 39 (82.97%) which is slightly lower as compared to a five year study from Iran which showed *Candida albicans*, the most species isolated, were sensitive to amphotericin B, ketoconazole, and fluconazole with 93%, 90.6%, and 89.5%, respectively. [18] Susceptibility of *C. albicans* to fluconazole comparable with the susceptibility rates reported in other studies (80.9%, 87%, 79% and 87.5%) [19,20] The non albicans species showed the following sensitivity pattern Fluconazole 23 (74.19%), Ketoconazole 21 (67.74%), Clotrimazole 23 (74.19%), Amphotericin B 24 (77.41%), and Itraconazole 23 (74.19%). The non albicans species of *Candida* showed greater resistance to the antifungal agents as compared to the *C. albicans*. This is in line with a previous study. [18]

In conclusion, candiduria is relatively common in immunocompromised patients. Our study shows that, non albicans species *Candida* is on the rise along with *Candida albicans* causing candiduria. There are various risk factors like invasive procedures; further the diseases causing depressed immunity make the situation more challenging. There are many antifungal agents to manage candiduria, but their appropriate use is important. Educational efforts directed toward treating physicians and other health care professionals are warranted. Curtailing unnecessary antimicrobial use will decrease the risk of adverse effects in patients and potentially decrease antimicrobial resistance.

Acknowledgment: I would like to express my special thanks of gratitude to one of my student who inspired me to involve for the

betterment of mankind. Secondly, I would also like to thank Mr. Abdul Quayum and other technicians who helped me to carry out my work smoothly.

Conflict of interest: None

References:

1. Bukhary ZA. Candiduria: a review of clinical significance and management. *Saudi J Kidney Dis Transpl* 2008; 19:350-360.
2. Achkar JM, Fries BC. *Candida* Infections of the Genitourinary Tract. *Clin Microbiol Rev* 2010; 23: 253-273.
3. Sellami A, Sellami H, Makni F, Bahloul M, Cheikh-Rouhou F, Bouaziz M, Ayadi A. Candiduria in intensive care unit: significance and value of yeast numeration in urine. *Ann Fr Anesth Reanim* 2006; 25: 584-588.
4. Yang YL, Cheng MF, Chang YW, Young TG, Chi H, Lee SC, *et al.* Host factors do not influence the colonization or infection by fluconazole resistant *Candida* species in hospitalized patients. *J Negative Results in BioMed* 2008; 7: 12.
5. Kauffman CA, Vazquez JA, Sobel JD, et al. Prospective multicenter surveillance study of funguria in hospitalized patients. Clin Infect Dis 2000; 30:14–8.
6. Ayeni O, Riederer KM, Wilson FM, Khatib R. Clinicians' reaction to positive urine culture for *Candida* organisms. Mycoses 1999; 42:285–9.
7. Storfer SP, Medoff G, Fraser VJ, Powderly WG, Dunagan WC. Candiduria: retrospective review in hospitalized patients. Infect Dis Clin Pract 1994; 3:23–9.
8. Schoenbeck J. Studies on Candida infection of the urinary tract and on the antimycotic drug 5-fluorocytosine. Scand J Urol Nephrol Suppl 1972; 11:7–48.
9. Rex JH, Pfaller MA, Walsh TJ, Chaturvedi V, Espinel-Ingroff A, Ghannoum MA, et al. Antifungal Susceptibility Testing: Practical Aspects and Current Challenges. Clin Microbiol Rev 2001; 14:643–58.
10. Nayman Alpat S, Özguneş I, Ertem 1. OT, Erben N, Doyuk Kartal E, Tözun M, et al. Evaluation of risk factors in patients with candiduria. Mikrobiyol Bul 2011; 45: 318-324.
11. Jain N, Kohli R, Cook E, Gialanella P, Chang T, Fries BC. Biofilm formation by and antifungal susceptibility of Candida isolates from urine. Appl Environ Microbiol 2007; 73: 1697-1703.
12. Achkar JM, Fries BC. Candida Infections of the Genitourinary Tract. Clin Microbiol Rev 2010; 23: 253-273.
13. Zarei-Mahmoudabadi A, Zarrin M, Ghanatir F, Vazirianzadeh B. Iran. J. Microbiol 2012; 4: 198-203.
14. Kauffman CA, Vazquez JA, Sobel JD, et al. Prospective multicenter surveillance study of funguria in hospitalized patients. Clin Infect Dis 2000; 30:14–8.
15. Ayeni O, Riederer KM, Wilson FM, Khatib R. Clinicians' reaction to positive urine culture for Candida organisms. Mycoses 1999; 42:285–9.
16. Harris AD, Castro J, Sheppard DC, Carmeli Y, Samore MH. Risk factors for nosocomial candiduria due to Candida glabrata and Candida albicans. Clin Infect Dis 1999; 29:926–8.
17. Joanne L. May, Anna King and Christine A. Warren. Fluconazole disc diffusion testing for the routine laboratory. *Journal of Antimicrobial Chemotherapy* 1997; 40, 511–516.
18. P Badiee, A Alborzi. Susceptibility of clinical Candida species isolates to antifungal agents by E-test, Southern Iran: A five year study. Iran J Microbiol 2011; 3(4): 183–188.

19. Bauters TG, Dhont MA, Temmerman MI, Nelis HJ. Prevalence of vulvovaginal candidiasis and susceptibility to fluconazole in women. Am J Obstet Gynecol. 2002; 187:569–574.

20. Citak S, Ozçelik B, Cesur S, Abbasoğlu U. In vitro susceptibility of *Candida* isolated from blood culture to some antifungal agents. Jpn J Infect Dis 2005; 58:44–46.