## Prevalence of Candida and Its Antifungal Susceptibility In Patients of Urinary Tract Infections

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Abstracts: Background & Objective: The present study was conducted to assess prevalence of Candida in patients of urinary tract infections. Methods: This retrospective study was carried out over period of 5 months from June 2016 to October 2016 at B.J Medical College, Civil Hospital Ahmedabad, Gujarat. Patients who presented with signs and symptoms of urinary tract infections were included. Urine samples were received from the patients clinically suspected of urinary tract infection. Isolation and identification of pathogen was done by standard microbiological method. Antifungal susceptibility testing for amphotericin-B, itraconazole, clotrimazole, fluconazole was carried out using out standard methods. Result: Out of total 4785 urine samples tested, 168(3.51%) showed growth of Candida species. Out of these 168 positive patient for Candida, 68(40.4%) was positive for Candida albicans,56(33.3%) was positive for Candida tropicalis,10(5.95%) was positive for Candida parapsilosis,27(16%) was positive for Candida krusei,7(4.16%) was positive for Candida dublinensis. The Candida isolates were more susceptible to Amphotericin-B(81.47%) and Itraconazole(60.30%) compared to Clotrimazole(59.60%) and Fluconazole(51.67%). Conclusion: Based on present study there is need to consider candiduria as an important entity in today's scenario. The presence of candiduria represents therapeutic challenge and should be verified by second clean catch urine culture. It is of utmost importance not only to identify candida species but also to conduct its antifungal profile. [Aarushi A NJIRM 2017; 8(2):44-47]

Key Words: Candiduria, Antifungal susceptibility testing

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Introduction: Candida urinary tract infections are an increasingly prevalent nosocomial problem with uncertain significance. The presence of Candida species in urine samples presents the physician with a challenge as to whether the candiduria represents colonization or lower or upper respiratory tract urinary infection including ascending pyelonephritis and renal candidiasis with sepsis. Candiduria is rarely seen as a community acquired infection in a structurally normal urinary tract and in healthy people. (Zakeya Abdulbaqi Bukhary) Candida albicans and non-C.albicans Candida (NACA) species colonize on the external side of the urethral opening in premenopausal and healthy females. Immune deficiencies may lead to an imbalance between C.albicans, NACA yeasts and the other host normal flora. In this condition, the commensal yeasts of Candida may convert into opportunistic pathogenic microorganisms creating candidal UTIs in the host( Payam Behzadi).<sup>2</sup> It is increasingly becoming an important subgroup of nosocomial urinary tract infections (10-15 %).1 (Zakeya Abdulbaqi Bukhary).It is common in the patients admitted in intensive care units, individuals with multiple predisposing factors, including diabetes mellitus, indwelling urine catheter, exposure antibiotics long term to

immunosuppressive therapy. The emergence of drug resistant Candida species, which is largely attributed to use of prolonged and inappropriate empirical therapy, has further complicated the patient management. Candiduria not properly diagnosed and treated has been source of morbidity and mortality (Yashavanth R.). So, the present study was carried out to know prevalence of candida species causing UTIs and their antifungal susceptibility pattern in a tertiary care hospital.(Yashavanth R).<sup>3</sup>

**Method:** This retrospective study was carried out over period of 5 months from June 2016 to October 2016 at B.J Medical College, Civil Hospital Ahmedabad, Gujarat. Mid stream urine samples were received from the patients clinically suspected of urinary tract infection.

Inclusion criteria: Male and female patients of all age groups were considered for our study. Both outpatients and inpatients who presented with signs and symptoms of urinary tract infections were included. Mid stream urine samples were received from the patients clinically suspected of urinary tract.. Urine wet mount examination was done to look for the presence of pus cells, red blood cells, casts,

crystals or any bacterial or fungal elements. The urine samples were inoculated on Mac Conkey agar and blood agar by calibrated wire loop technique delivering 0.001ml of urine as per standard protocol for urine culture. The culture plates were incubated aerobically at 37°C for 16-24hours. From growth, gram stain and LCB were done to identify Candida. Yeast isolates were identified on the basis colony characteristics and further by germ tube production, morphology on corn meal agar, carbohydrate fermentation tests and assimilation tests using yeast nitrogen base agar as per standard recommended procedures. Candida were also inoculated on to CHROM agar (HiMedia -HiCrome Candida differential Agar) for identification of Candida species 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. The Candida strains isolated were tested for antifungal susceptibility by disc diffusion method (M 44-A2, CLSI, USA). The inoculum was prepared by suspending five colonies in 5ml of sterile saline and matching the turbidity to 0.5 Mc Farland standard. A sterile cotton swab was dipped into the inoculum suspension and rotated several times and pressed firmly against the inside wall to remove excess fluid. The dried surface of sterile Mueller Hinton agar with 2% glucose and 0.5µg/ml of Methylene Blue agar plate was inoculated by evenly streaking the swab over the entire surface. This procedure is repeated by streaking two more times rotating the plates approximately 60°C each time to ensure an even distribution of inoculums. Discs containing fluconazole (25µg), voriconazole (1μg), amphotericin B(10 μg), itraconazole (1μg) and ketoconazole(15µg) were placed on the inoculated plates. Zones of inhibition around the disk were measured after incubating the plates for 24 hours at 35-37°C.

**Result: Table 1: Distribution of Candida species** 

| Candida species      | Total no | Total No % |  |
|----------------------|----------|------------|--|
| Candida albicans     | 68       | 41%        |  |
| Candida tropicalis   | 56       | 33%        |  |
| Candida parapsilosis | 10       | 6%         |  |
| Candida krusei       | 27       | 16%        |  |
| Candida dublinensis  | 7        | 4%         |  |
| Total                | 168      | 100%       |  |

Out of total 4785 urine samples tested, 168(3.51%) showed growth of Candida species. Out of these 168 positive patient for Candida, 68(41%) was positive for Candida albicans, 56(33%) was positive for Candida tropicalis,10(6%) was positive for Candida parapsilosis,27(16%) was positive for Candida krusei,7(4%) was positive for Candida dublinensis.

Table 2: Age and Gender wise distribution of Candida isolates

| Age group | Male       | Female    | Total      |  |
|-----------|------------|-----------|------------|--|
| 1-15      | 27(25%)    | 32(35.1%) | 59(30%)    |  |
| 16-30     | 30(27.7%)  | 31(34%)   | 61(30.65%) |  |
| 31-45     | 24(22.2%)  | 17(18.6%) | 41(20.60%) |  |
| 46-60     | 27(25%)    | 11(12%)   | 38(19.09%) |  |
| Total     | 108(54.2%) | 91(45.7%) | 199(100%)  |  |

Out of total 168 isolates, the rate of Candida species were more in males 108(54.2%) than in females 91(45.7%) with M:F ratio 1:0.9. Out of 168 isolates, highest isolation rate of Candida species found in age group of 16-30years in males were 30(27.7%) and in age group 1-15years in females were59(29.6%).

Table 3: Antifungal susceptibility testing pattern of Candida species

| Candida        | Total | IT            | KT             | VRC            | Amp-B            | NS         | FLC           |
|----------------|-------|---------------|----------------|----------------|------------------|------------|---------------|
| species        |       | (Itraconzole) | (Ketoconazole) | (Voriconazole) | (Amphotericin-B) | (Nystatin) | (Fluconazole) |
| C.albicans     | 68    | 49            | 35             | 34             | 67               | 34         | 39            |
|                |       | 72%           | 51.40%         | 50%            | 98.50%           | 50%        | 57.30%        |
| C.tropicalis   | 56    | 24            | 26             | 38             | 39               | 28         | 25            |
|                |       | 42.80%        | 46.40%         | 67.80%         | 69.60%           | 50%        | 44.60%        |
| C.parapsilosis | 10    | 8             | 9              | 10             | 12               | 9          | 8             |
|                |       | 80%           | 90%            | 100%           | 120%             | 90%        | 80%           |
| C.krusei       | 27    | 0             | 0              | 0              | 2                | 12         | 0             |
|                |       | 0.0%          | 0.0%           | 0.0%           | 7.40%            | 4.40%      | 0.0%          |
| C.dublinensis  | 7     | 4             | 4              | 4              | 4                | 4          | 4             |
|                |       | 51.10%        | 51.10%         | 51.10%         | 51.10%           | 51.10%     | 51.10%        |
| Total          | 168   | 85            | 74             | 86             | 124              | 87         | 76            |
|                |       | 50.6%         | 44.0%          | 51.19%         | 73.80%           | 51.70%     | 45.23%        |
| P-Value        |       | 0.000352      | 0.000167       | 0.000155       | 0.001129         | 0.000105   | 0.000191      |

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Out of 68 C.albicans, 49(72%), 35(51.4%), 34 (50%), 67(98.5%), 34(50%), 39(57.3%) antifungal sensitivity seen in Itraconazole, Ketoconazole, Voriconazole, Amphotericin-B, Nystatin, Fluconazole respectively. Out of 56 C.tropicalis ,24(42.8%), 26(46.4%), 38 (67.8%), 39(69.6%), 28(50%), 25(44.6%) antifungal sensitivity seen in Itraconazole, Ketoconazole, Voriconazole, Amphotericin-B, Nystatin, Fluconazole. Out of 10 C.tropicalis, 8(80%), 9(90%), 10 (100%), 12 (120%), 9(90%), 8(80%) antifungal sensitivity seen in Itraconazole, Ketoconazole, Voriconazole. Amphotericin-B, Nystatin, Fluconazole.

Out of 27 C.krusei, antifungal sensitivity seen only with Amphotericin-B, Nystatin 2(7.4%), 12(4.4%). Out of total 7 C.dublinensis, 4(51.1%), 4(51.1%), 4(51.1%), 4(51.1%), antifungal sensitivity seen in Itraconazole, Ketoconazole, Voriconazole, Amphotericin-B, Nystatin, Fluconazole.

**Discussion:** Community acquired urinary tract infections (UTIs) are a frequent problem worldwide which are caused by microbial invasion to different tissues of the urinary tract. In the last 2.5 decades the fungal UTIs due to Candida genus yeast has increased significantly.4 (Payam 2010) Pathogenic yeast from the genus Candida can cause serious infections in humans and are now recognized as a major agent of hospital acquired (nosocomial) infections.<sup>5</sup> (Parvez). The presence of candida species in urine, candiduria, an asymptomatic condition that results contamination during urine collection in patients with bladder colonization or upper urinary tract infection and haematogenous spread from other sites. (Zarei Mahmoudabadi).

In the last few years various factors like immunocompromised status, immunosuppressive therapy, prolonged hospital stay, prolonged antibiotic therapy, catherisation have all contributed for increase in number of cases of candiduria.<sup>3</sup>(Yashavanth)

In the present study, isolation rate of Candida species from urine samples was 3.51%, which is slightly higher than the observation of Ragini et al. (1.37%) and Yashavanth et al (2.27%). The reason behind this may be due to more number of catheterized and indoor patients in our study.<sup>7,3</sup>

In our study ,the isolation rate of non albicans Candida was 59.6%, which is higher than C.albicans 40.4%. This finding is in concordance with the studies done by Yashavanth R. et al which shows isolation rate of non albicans Candida and C.albicans, 69.7% and 30.3% respectively. <sup>3</sup>Changing trends in the aetiopathogenesis of urinary tract infections and considerable increase in number of non albicans Candida species is a matter of concern.

Surprisingly in our study, we found higher prevalence rate in male 108(54.2%) than female 91(45.7%) patients.

Identification of Candida species is important as non albicans Candida are more resistant to azoles compared to that of C.albicans. C.krusei and C.glabrata are known for their innate resistance to fluconazole.8(Ekta Joshi).The in vitro susceptibility testing of antifungal agents is becoming increasingly important because of the introduction antifungal agents and the recovery of clinical isolates that exhibit inherent or developed resistance to Amphotericin B, the Azole group of drugs during chemotherapy. (Lata Patel) Therefore clinicians need to be aware of these factors before taking decision on treatment of candiduria after repeating second sample of urine which is confirmatory especially in case of asymptomatic patients and also identification of candida yeast to the species level is now required.8(Ekta Joshi).

Conclusion: Non albicans is more important uropathogen causing candiduria than Candida albicans species. Speciation and susceptibility testing of the candida isolates plays an important role in the management of candidal infections. As increasing resistant to different Candida spp., these kinds of surveillances must be performed at regular intervals to follow any changes in the antifungal sensitivity pattern of the Candida which will help in further understanding of the problem in our population.

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