ORIGINAL RESEARCH

Prevalence of Candida Species in Urinary Tract Infections in a Tertiary Care Hospital, Bihar

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Abstract

Background: The presence of Candida spp. in urine, ‘Candiduria’, is an indicator of infectionofthearinarytractbyCandidaspecies. This conditioncanbeHazardousindiaeticpatients due to reduced immuneresponse. The aim of the present study was to explore in last two decades showed Candida associated in urinary tract infection along with change in its distribution. The overuse of antifungal drugs, especially azole group have contributed in emergence of resistant strains of Candida. Biofilm producing property of Candida also contributes to antifungal resistance.

Methods: We were included 1576 urine sample from different wards & ICU with Age group 0-80. This study was conducted in Department of Microbiology in Indria Gandhi Institute of Medical Sciences, Patna, Bihar. The duration of study was over a period of two year.

Results: The prevalence of candiduria caused by Candida albicantis more than that caused by other Candida species. The prevalence is more in female than male. The prevalence of age group is more in the age group between 21-30 years.

Conclusion: The increased prevalence of Candida albicanscandiduria which are also biofilm producers and resistant to commonly used drug fluconazole is a matter of concern. Therefore, the species identification of Candida isolates along with their antifungal susceptibility pattern should be routinely performed to help the clinicians in better treating the patients with candiduria.

Keywords: Candiduria, Urinary tract infection, Antifungal drug, CLED Agar

Background

It seems 10-15% cases of urinary tract infection are caused by candida species. It is the fourth most common pathogen of UTI especially in catheterized patients. It is reported that urinary catheters have been held responsible for 80% of hospital acquired UTI. Though 90% of severe infections are caused by Candida albicans but Non albicans Candida like Candida glabrata, Candida parapsilosis, Candida tropicalis and Candida krusei are increasingly important as causative agents of UTI. Non albicans Candida species are more resistant to antifungal drugs as compared to C. albicans.

It is observed that Candiduria is very commonly found in patients who are hospitalized, diabetic, and admitted in ICU. Catheterization process also increases more chances of UTI by allowing migration of the organisms into the bladder from external periurethral surface.
Though, the presence of Candida in urine may be a transient and asymptomatic condition. It may not meet the typical requirements for systemic antifungal therapy.\(^5\) The risk of morbidity and mortality associated with Candiduria in immunocompromised individuals indicated the clinical importance of this condition.\(^6\)

All over the world, diabetes is the most common endocrine disorder. \textit{Increased blood sugar level in patients with uncontrolled diabetes reduces the immunity of body and makes integumentary, gastrointestinal and urinary system and mucous membranes more susceptible for infections.}\(^7\)\(^8\)

In patients with urinary tract infection, Candida albicans the most common yeast isolated\(^\text{10}\) Still, there is changing pattern with a rising in prevalence of non albicans candida. The permanent resistance of non-albicans Candida to fluconazole is well recorded, making it necessary for the speciation of Candida in patients with UTI for initiation of appropriate therapy.\(^\text{11}\) The classification and identification of yeast in urine is essential to identify the etiology, since the pathogenicity and the susceptibility pattern to antifungal present variations according to species.

It is not easy to distinguish contamination of true infection without reliable diagnostic criteria for Candiduria. Predisposing factors such as diabetes mellitus, extremes of ages and female sex, prior antibiotic use, use of indwelling urinary devices, prolonged hospitalized stay have been reported to be associated with increased Candida growth in urine.\(^\text{12}\) Candida infection in humans has been found to be endogenous and through contaminated health care worker, infuscate and biomaterials, it may be acquired exogenously.\(^\text{13}\)

It has been observed that immune-compromised patient such as HIV-positive women have increase rates of vaginal colonization with Candida, often non-C. albicans species. Several studies also described that the higher colonization levels of Candida & non candidal species on almost all mucosal surfaces in HIV-positive patients, which (together with the general state of immunosuppression of the patient) may lead to higher levels of manifested Candida infections, including in the genitourinary tract (GI).\(^\text{14}\) Budding Yeasts generally have poor adherence to bladder mucosa and have no tropism regarding the tissues of the urinary system, therefore the importance of the abovementioned underlying factors (promoting obstruction in the urinary system) in the pathogenesis of candiduria (or funguria in general) is further highlighted. The epidemiology of Urinary tract infection associated with candiduria and Candida varies greatly by region, thus the estimation of local data is essential to evaluate trends over time and to reflect on the national situation compared to international data.

Candidaemia is the disseminated marker of candiduria, which may lead with a crude mortality of 30–40\%.\(^\text{15-16}\) The Candiduria is a defined as 104–105 CFU/ml of budding yeasts detected in the urine, while a Candida UTI is mainly characterized by 105< CFU/ml detected, which is usually corresponds with the sign &symptoms of the patient.

It is observed that the pathogenicity of Candida species may ascend to the urinary tract via a colonization focus, either near or directly at the urethra (retrograde infection route), though, they could be enter in the upper region of the urinary tract via the bloodstream (antegrade infection route). The risk factors of candiduria and Candida urinary tract infections are well reported, and include the female sex, extremes of age, diabetes mellitus, prolonged hospitalization, intensive care unit (ICU) admission, recent use of broad-spectrum antibiotics or immunosuppressants, dysfunction of the bladder and urinary stasis, nephrolithiasis, transplantation, congenital or structural abnormalities of the urinary tract, catheterization and simultaneous bacteriuria or bacterial UTIs.\(^\text{17}\)

An increased frequency of Candida infections with hospitalized cases has been reported for last past three decades. Different studies have observed that the prevalence of Urinary tract infections (UTIs) due to with Candida has risen. It seems, the 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. The patient therapeutic management has become intricate with the appearance of drug resistance in Candida species. Although, the morbidity rate due to Candida species is high and the mortality rate remains low. Candiduria is the condition which can be caused by Candida albicans as well as other Candida species. Candida albicans, once known as the leading causative yeast of UTI, is now being replaced by Non albicans Candida species, as the predominant pathogen. Non albicans Candida species are more resistant to antifungal drugs in comparison to Candida albicans. The present study was conducted to observe the prevalence of Candida species in UTIs.\textsuperscript{18-21} The 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. The fifth most common ranks of Candida species in hospital acquired infection in India. It has been seen that in present study the highest rate of candiduria in old aged patients i.e. patients above 60 years of age. Similar results were also 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. 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.\textsuperscript{22-23}

**Methods**

**Study Population**
We were included 1576 urine sample from different wards & ICU with Age group of 0-80.

**Study Area**
This study was conducted in Department of Microbiology in Indria Gandhi Institute of Medical Sciences, Patna, Bihar

**Study Duration**
The duration of study was over a period of two year.

**Study Design**

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Urine sample (1576 cases)
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Culture done on CLED Agar
↓
Incubate for 37°C for 24 hours
↓
Various Growth (786) Candida growth (176)
↓
Gram stain
↓
Microscopy (budding yeast like cells seen)
↓
Further culture done on SDA
↓
Microscopy (budding yeast like cells)
↓
Germ tube test
↓
Candida albicans Candida spp.
↓
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Procedure of study
Data Collection
This study was conducted during the two year in which we were included urine sample of 1576 cases from various departments, out of which 786 had various growth, from which 176 Candida strains were isolated. Mid stream urine sample collection technique was used. Patient’s demographic detail along with risk factor and co-morbid conditions were collected. Firstly we have done direct Gram staining, after that urine samples were streaked on CLED agar by calibrated loop (0.01 ml) method then incubated at 37ºC for 24-48 hour and reading was taking accordingly.

We had seen significant growth of budding yeast cells on CLED agar plate with significant colony count of \(>10^5\) colony forming units/ml and presence of budding yeast cells on direct microscopy confirm the presence of candiduria in urine. The amount of 100 CFU/ml, representing a single colony of yeast on a plate of CLED agar was regarded as a detection limit. Candida species were identified by germ tube formation in serum which was incubated at 37ºC. Chrome agar was also used to differentiate among different Candida species. Germ tube test was performed for differentiate Candida albicans from non candida albicans. Other method also used for identification by Chrom agar, sugar assimilation tests using commercially prepared sugar discs sucrose, maltose, dextrose, trehalose, lactose and dulcitol from HiMedia and studying micro morphology on corn meal agar.

Urine samples with other bacterial growth were excluded in the study. The basic culture media used in isolating Candida are CLED agar, Chrome agar, blood agar, sabouraud dextrose agar, yeast nitrogen base and yeast potato dextrose broth and cornmeal agar. Other media that can be used as a selective or differential media are Candida selective medium. Since C. albicans and C. dubliniensis are related species which are difficult to differentiate phenotypically, cultivation on Bird seed agar was found to be fast, sensible and reliable method to discriminate these two species.

Data Analysis
Data were analysed by using Statistics (Mean, Sensitivity & Prevalence).

Result
In this study we were included 1576 cases, out of them 176 cases had growth of Candida spp. Cases were included from 0-80 year of age group. Prevalence of age group we were seen 21-30 which was 59.6% followed by 31-40 (17.6%), 51-60 (5.6%), 61-70 (5.1%) then other age group. We observed that 92.1% diabetic cases found who had infection of Candida while 7.9% non diabetic We also had seen that most of the cases found in General Medicine then OBG, General surgery & other departments. The prevalence of Candiduria in this study was 10.2%. Among Candida spp. we were seen 61.9% Candida albicans. Cases we were found. Out of 176 cases 91.5% ICU & 8.5% Non-ICU cases were seen.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>6</td>
<td>3.4</td>
</tr>
<tr>
<td>11-20</td>
<td>6</td>
<td>3.4</td>
</tr>
<tr>
<td>21-30</td>
<td>105</td>
<td>59.6</td>
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<tr>
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<td>17.6</td>
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<td>61-70</td>
<td>9</td>
<td>5.1</td>
</tr>
<tr>
<td>71-80</td>
<td>4</td>
<td>2.2</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1. Distribution of Cases According to Age Group

\[
Z = L1+f1-f0/2f1-f0-f2×i
\]

\[
Z = 26.7
\]
Co-Morbidity | No. of Cases | Percentage
---|---|---
Diabetic | 162 | 92.1
Non-Diabetic | 14 | 7.9
Total | 176 | 100

Table 2. Distribution of Cases According to Co-Morbidity

ICU/Non ICU | No. of Cases | Percentage
---|---|---
ICU | 15 | 8.5
Non-ICU | 161 | 91.5
Total | 176 | 100

Table 3. Distribution of Cases According to Sample Received from ICU and NON-ICU Cases

| Department          | No. of Cases | Percentage |
---|---|---|
General Medicine | 73 | 45.3 |
General surgery | 25 | 15.5 |
Pediatrics | 7 | 4.3 |
OBG | 56 | 31.8 |
Total | 161 | 100 |

Table 4. Distribution of Cases According to Sample Received from Different Departments

Prevalence of Candida spp. | No. of Cases | Percentage
---|---|---
Candida albicans | 109 | 61.9 |
Other Candida spp. | 67 | 38.1 |
Total | 176 | 100 |

Table 5. This Table Shows Prevalence of Candida spp

Prevalence=61.9%

Discussion

The present study was a retrospective study. It was conducted at T. S, Misra medical college from January 2018 to January 2020. The sample size of the present study was 1576 patients of various departments of which 786 had growth, from which 176 Candida strains were isolated under the guidance of microbiology Department. A patient with or without symptoms of candiduriarequires a careful evaluation. It is reported that the candiduria is more commonly found in women than men. Candida albicans and C. non-albicans species are considered to be the important parts of microbial normal flora in the oral cavity, alimentary canal and vagina in a vast range of the healthy people. Additionally, they colonize on the external side of the urethral opening in premenopausal and healthy females. It may convert into opportunistic pathogenic microorganisms creating candidal UTIs in the host Fungal UTIs are relatively uncommon in comparison to bacterial urinary tract infection (UTI). So the corresponding susceptibility profile is not as well characterized.

This study observed male and female ratio 17:33 in accordance to study by Paul et al., Results showed that candiduria was more prevalent in age range 21-30 years (59.6%) followed by 31-40 years (17.6%), 50-60 years. NaymanAlpat et al., had found that long duration of Hospital stay and ICU increase the prevalence of candiduria in patients. 24-27
World widely, Urinary tract infections are the major cause of morbidity and present a considerable economic burden is seen. The therapeutic treatment of urinary tract infections (especially in settings where healthcare related and human resources are scarce) might be based on epidemiological data and empiric antibiotic treatment. Although, carries is the risk of not considering budding yeasts as likely causative agents of UTIs, which in turn will alter local epidemiological data and more importantly, may hinder the patient in receiving appropriate antimicrobial therapy. In the routine laboratories they do not perform the identification or even culture & sensitivity of yeasts from urine samples. Many studies showed that Candida albicans is the most commonly isolated species yet, an higher in the occurrence of non-albicans Candida species (NACS) has been reported.

Fluconazole is the drug of choice for proven Candidal UTIs, due to advantageous pharmacokinetic parameters (the drug is concentrated in the urine) of this antifungal agent. A comparatively, other azoles (e.g. itraconazole, voriconazole), flucytosine and amphotericin B are less favorable therapeutic options (both due to pharmacokinetics and adverse events associated with their use) and should be considered in refractory infections with fluconazole-resistant strains. This observable fact might be explain the increase in the isolation of fluconazole non-susceptible NACS (especially C. glabrata), which have been linked with previous exposure to fluconazole. Hence Clinicians necessary to be aware of the etiological role of NACS species (namely C. glabrata, C. tropicalis, C. parapsilosis, C. guilliermondii, C. krusei and C. lusitaniae) as there are therapeutic consequences corresponding with their isolation. Based on the different studies results of this retrospective survey, the most prevalence isolates at our tertiary-care center remains C. albicans, although, a significant difference could be observed in the number of different species detected in the samples from IPD and OPD departments. Hospitalization, a pronounced female dominance (1.7–2.15-times higher) and the advanced age (~70 years) of many affected patients is in line with the findings in literature.

The occurrence of C. glabrata as a significant etiologic agent of urinary tract infections is noteworthy, mainly due to its increasing non-susceptibility to commonly used antifungal agents (acquired resistance is also more and more frequent), most importantly fluconazole. Although, the incidence of its isolation was constant from 2008–2017, with no relevant increasing tendencies.

This is the best of our knowledge the first and longest-spanning study reporting on the incidence of candiduria (and UTIs caused by Candida spp. by proxy) in Hungary. Based on our present results, a urine sample was received, where the significant growth of Candida species was isolated. In these cases, the continuous communication between physicians and the diagnostic microbiology laboratory is crucial. The role of the laboratory is to supply clinically relevant information in a precise and timely manner, which should be reciprocated by the feedback from the physicians, beginning from the submission of the sample, followed by information regarding the symptoms of the patient and the clinical picture. This way, the microbiologists can also consider the possibility of the isolated yeasts as contaminants or possible causative agents.18-33

**Conclusion**

This study concludes that the high incidence of candiduria in diabetic patients should be highlighted. The increased incidence of Candida albicans candiduria which are also biofilm producers and resistant to commonly used antifungal drug such as fluconazole is a matter of concern. Thus, the species identification of Candida isolates along with their antifungal susceptibility pattern should be routinely performed to help the clinicians in better treating the patients with candiduria. Candidiasis in UTI is known as the most frequent hospital
acquired infection worldwide. Candida albicans is the most common cause of Hospital acquired infection.

Considering the high incidence rate of candiduria in diabetic patients, efficient control of diabetes, predisposing factors, and causal relationships between diabetes and candiduria should be emphasized. In addition, as the non-albicans Candida species were isolated more than C. albicans, their intrinsic resistance to antifungal drugs should be noted. Antifungal susceptibility testing for determination of susceptibility/resistance profile of isolates could be helpful for appropriate treatment.

References