RESEARCH ARTICLE

SPECIES DISTRIBUTION AND ANTIFUNGAL SUSCEPTIBILITY PROFILE OF CANDIDA ISOLATED FROM URINE SAMPLES

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ABSTRACT

Background: Candiduria is a common finding in hospitalized patients. The isolation of Candida from urine is challenging for both clinician and microbiologist as to whether the candiduria represents colonization or, lower or upper urinary tract infection including ascending pyelonephritis and renal candidiasis with sepsis. Although Candida albicans is the major cause of candiduria, non-albicans Candida (NAC) has emerged as an important opportunist pathogen. The NAC spp. are not only well adapted to the urinary tract but also are difficult to eradicate than C. albicans.

Aims & Objective: The present study aimed to determine the clinico-mycological profile of candiduria in a tertiary care hospital.

Material and Methods: A total of 218 Candida spp. isolated from urine samples were included in the study. Speciation of Candida was done by conventional methods and colony colour on HICHROM Candida agar. Antifungal susceptibility testing of the isolates was performed by disc diffusion method on glucose methylene Mueller- Hinton agar (GM-MH).

Results: In both the sexes maximum patients belong to age group >50 years. Urinary catheterization, use of broad spectrum antibiotics and diabetes mellitus were the major risks. Isolation of NAC spp. was more. Maximum resistance was seen to fluconazole.

Conclusion: The shift towards the NAC spp. as the causative agent of candiduria has generated the concern. Since several NAC spp. are inherently resistant to common antifungal agents, the rapid identification of Candida isolates upto species level along with its in-vitro antifungal susceptibility pattern is important for treatment and management of candiduria.

Key-Words: Antifungal Susceptibility; Fluconazole; Non- Albicans Candida Species; Candida Albicans

Introduction

Urinary tract infection (UTI) is an extremely common disorder in clinical practice. It encompasses a wide variety of clinical entities whose common denominator is microbiological invasion of any tissue of urinary tract extending from the renal cortex to the uretheral meatus.[1] Candida UTI or candiduria is a common finding in hospitalized patients.[2] Anatomic defects of urinary tract, indwelling urinary drainage devices, abdominal surgery, ICU stay, broad spectrum antibiotic therapy, diabetes mellitus, increased age and female sex are risk factors associated with candiduria.[3]

As Candida spp. is a human commensal, its isolation from urine is challenging for both clinician and microbiologist. The isolation of Candida spp. from urine may give rise to variety of interpretation, from procurement contamination of sampling to renal infection and collection system to life-threatening, invasive candidiasis.[2]

Most observational studies of candiduria have reported predominance of C. albicans.[4] In recent years with the advent and increasing use of fluconazole, the emergence of non-albicans Candida (NAC) spp. is noted.[5] The NAC spp. are not only well adapted to the urinary tract but also are difficult to eradicate than C. albicans.[3]

The present study was conducted at the tertiary care hospital of New Delhi with an aim to study clinico-mycological profile of candiduria.

Materials and Methods

The present study was carried out in the department of microbiology, tertiary care teaching hospital, New Delhi. A total of 218 Candida spp. isolated from urine samples processed in the

Department of Microbiology were included in the study.

Quantitative cultures with Candida colony counts of > 10^4 colony forming unit (CFU)/ ml in patients without indwelling urinary catheter and of ≥ 10^3 CFU/ ml of urine in patients with indwelling urinary catheter were considered significant. Contamination was differentiated from infection by obtaining second urine sample. Only when the second specimen showed the growth of Candida, the further mycological workup was done.

Species identification of Candida isolates was done by conventional techniques and colony color on HiChrome Candida agar.[6]Antifungal susceptibility of the isolates for fluconazole, ketoconazole, itraconazole and amphotericin B was done by disc diffusion method on glucose methylene Mueller- Hinton agar (GM-MH).[7] The antifungal discs were procured from Himedia Laboratories Pvt. Limited, Mumbai. The zone diameters were interpreted as per the approved Clinical and Laboratory Standards Institute (CLSI) (formerly known as National Committee for Laboratory Standards (NCCLS)) M44-A guidelines.[8] C. albicans (ATCC 90028) and C. krusei (ATCC 6258) were used as control strains.

Results

As shown in figure 1, candiduria was more common in females. In both the sexes maximum patients belong to age group >50 years. In most of the patients there was more than one risk factor. Urinary catheterization followed by the use of broad spectrum antibiotics and diabetes mellitus were the major risks for the development of candiduria.

Out of 218, 80 (36.6%) isolates were C. albicans whereas 138 (63.4 %) belonged to NAC spp. Among NAC spp. C. tropicalis followed by C. glabrata were the major isolates (figure 2). Table 1 shows the antifungal resistance pattern of Candida isolates. 83(38.1%) of the isolates were resistant to fluconazole. Fluconazole resistance was more in C. tropicalis (42%) followed by C. albicans (40%) and C. kefyr (40%). Itraconazole resistance was seen in 78 (35.7%) Candida isolates. C. tropicalis (40%) and C. glabrata (40%) showed maximum resistance to itraconazole. Resistance to ketoconazole was common in C. krusei (36.8%) followed by C. albicans (36.2%). Only 11 (5.7%) Candida isolates showed resistance to amphotericin B. Amphotericin B resistance was maximum in C. albicans (7.5%) followed C. glabrata (6.6%). Resistance to amphotericin B was not in noted in C. kefyr, C. krusei, C. parapsilosis and C. guilliermondii.

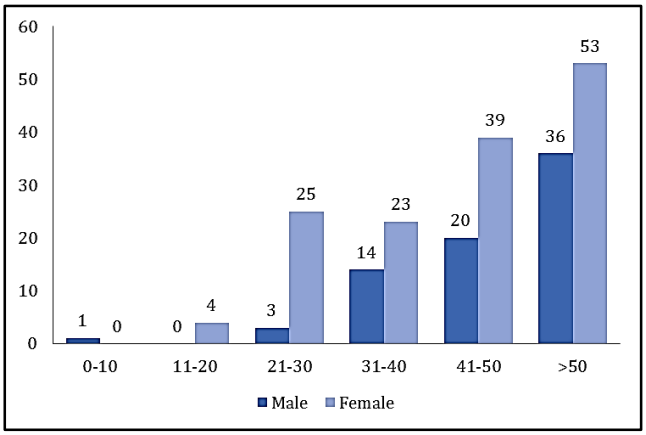

Figure-1: Age and Sex Distribution of Candiduria Patients

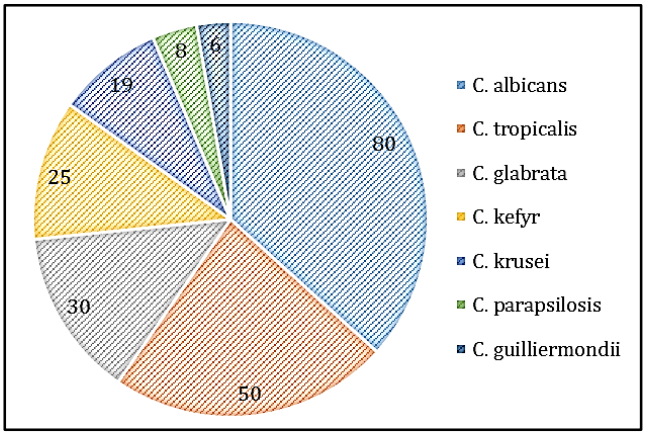

Figure-2: Species Distribution of Candida Isolates

Table-1: Antifungal Resistance Pattern of Candida Isolates

Candida spp.	Fluco-nazole (%)	Itraco-nazole (%)	Ketoco-nazole (%)	Amphote-ricin- B (%)	Total
C. albicans	32 (40)	28 (35)	29 (36.2)	06 (7.5)	80
C. tropicalis	21 (42)	20 (40)	15 (30)	03 (6)	50
C. glabrata	11 (36.6)	12 (40)	10 (33.3)	02 (6.6)	30
C. kefyr	10 (40)	08 (32)	09 (36)	_	25
C. krusei	06 (31.5)	07 (36.8)	07 (36.8)	_	19
C. parapsilosis	02 (25)	01 (12.5)	01 (12.5)	_	08
C. guilliermondii	01 (16.6)	02 (33.3)	02 (33.3)	_	06
Total	83 (38.1)	78 (35.7)	73 (33.4)	11 (5.1)	218

Discussion

In contrast to other uropathogenic micro-organism, Candida spp. rarely causes community acquired UTI.[4] About 10-15% of hospital

acquired UTI are due to Candida spp.[9] In our study Candiduria was common in female patients. Candida spp. is a frequent colonizer of vagina and facultatively may ascend to the bladder and/ or to the kidneys.[5] Studies of Strofer S et al.[10] and Sobel J et al.[11] also shows the gender difference in candiduria, where women outnumbered men.

In the present study more than one risk factor was identified in patient with candiduria. The most common associated risk factors were urinary catheterization, long term antibiotic therapy, diabetes mellitus and long hospital stay. Guler S et al.[9] reported that the risk of development of candiduria is increased 12-fold after use of urinary catheter. In the study conducted by Platt R et al.[12] candiduria was seen in 27% of all UTI related to indwelling catheters. Presence of catheter is identified as a significant risk factor for candiduria as Candida can easily colonize and form biofilm on the catheter surface. Candida biofilm consists of highly organized communities of yeast, hyphae and pseudohyphae attached to the biomaterial surfaces. High resistance to most of the antifungal drugs is seen in Candida biofilm.[13]

Long term antibiotic therapy or treatment with broad spectrum antibiotics possesses a risk of development of candiduria as it suppresses the population of commensal bacterial flora, favoring the colonization of Candida spp.[9] Phagocytosis and humoral immunity may also be negatively affected by long term antibiotic therapy. Community acquired candiduria is common in patients on antibiotics.[4]

Diabetes mellitus was one of the most common predisposing factors in our study. In diabetic patients the clinical manifestation of candiduria ranges from lower urinary tract colonization to asymptomatic infection, cystitis, pyelonephritis and perinephric abscess.[14] The exact role of diabetes in the development of candiduria is not known, but it is postulated that glucosuria predispose colonization of Candida spp. Impaired host resistance in diabetes also favors Candida infection.[4] Recent surgical procedures, ICU admission, urinary tract abnormalities, prolonged hospital stay and pregnancy were other risk factors identified to be associated with candiduria in our study.

The colonization and invasion of the urinary system by Candida spp. is favored by various virulence factors like phenotypic switching, dimorphism, galvanotropism and thigomo-tropism.[13] In the present study, a shift towards NAC spp. as a causative agent of candiduria was noted. In recent years the extensive prophylactic use of antifungal drugs in immunocompromised patients has increased colonization and infection of NAC spp.[5] In our study C. tropicalis and C. glabrata were the major isolates from the NAC spp. C. tropicalis has been identified as the most prevalent pathogenic yeast species of NAC group. Contributory factors in the emergence of C. tropicalis includes use of antifungal drugs, increase in the population of immunocompromised hosts, use of broad spectrum antibiotics and long term use of catheters.[15] About 10-15% of candiduria is caused by C. glabrata. C. glabrata adapts more efficiently to the urinary system than other members of NAC spp.[16] Studies have shown the increased ability of C. glabrata to form biofilm on silicon material in the presence of urine.[13]

The emergence of drug resistance in fungi has made antifungal sensitivity testing important for clinical mycology services. Since standard methods for antifungal sensitivity testing like broth dilution and E test are time consuming and costly, their use in routine practice is limited.[7,17] In the present study antifungal susceptibility profile of Candida was studied by using disk diffusion technique. Disk diffusion method is simple, economical and easy to perform simultaneously on large number of isolates.[17]

In our study, Candida isolates showed more resistance to fluconazole (38.1%) as compared to other antifungal agents. C. tropicalis (42%) showed maximum resistance to fluconazole. The resistance to fluconazole in Candida isolates is of significant concern. Fluconazole is useful because of a high concentration of active drug in the urine, cost effectiveness, safety, better tolerability and is less likely to become resistant during treatment.[4] Though the resistance to amphotericin B was less its use is limited due to a high frequency of renal toxicity and other adverse effects.[18]

Conclusion

The presence of Candida in urine is a diagnostic and therapeutic challenge for physicians' right from the general practioner to the specialist. Candiduria is becoming an important nosocomial infection. The shift towards the NAC spp. as the causative agent of candiduria has generated the concern. Since several NAC spp. are inherently resistant to common antifungal agents, the rapid identification of Candida isolates upto species level along with its in-vitro antifungal susceptibility pattern is important for treatment and management of candiduria.

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