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Antifungal drugs susceptibility towards candida albicans in female patients with UTI

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Abstract---Background: In women urinary tract infection is a growing concern clinically. The most common human fungal pathogens are candida species reportedly. The aim of the present study was to identify the Candida species causing UTIs and Antifungal susceptibility test. Methods: The study was conducted on 448 urine samples of female patients in Gurugram, Haryana. Urine sample of in-patients and out patients were collected during the period of 2 months for the diagnosis of candida species. Antifungal susceptibility test was done using disk diffusion method. Result: In the present study 13 Candida isolates were found. All the isolates found to be candida albicans (n=13) and Amphotericin B (100%) found to be the most effective drug against Candida albicans followed by voriconazole (92.3%) and fluconazole (61.53%) is the least sensitive drug against C. albicans. Conclusion: Study concluded that only C. albicans species found prevalent fungal species in female. It is also noticed that fungal UTI were less prevalent than bacteria UTI. amphotericin B was 100% sensitive drug towards all the isolates of C.albicans.

Keywords---Candida, Candiduria, UTI, antifungal, susceptibility, amphotericin B, fluconazole.

Introduction

The bacterial, fungi or viral inflammatory reaction is the cause of UTI. The most common and constant factor responsible for UTI is candida fungi about 10-30% (1). This is because Urethra and anus are very near to each other. However, *C. albicans* is found in 15-60% of the population because it the normal component of the body flora and in healthy humans oropharynx, colon, and vagina are frequently colonized (2). If candida species is present in urine it is called as candiduria and it is prevalent in the hospitalized patients (3). The colonization of the yeast in urinary catheter or cystitis or disseminated candidiasis is also a reason for the presence of candida in urine (4). The commensal yeasts of *Candida* can be convert to be pathogenic organism creating UTIs in the host due to the immune deficiencies which lead to an imbalance between *C. albicans* and non-*C. albicans* *Candida* yeasts and the other host normal flora (5). Candiduria can be both asymptomatic and symptomatic but mostly it is asymptomatic. However, the patients with renal candidiasis, pyelonephritis, cystitis, epididymorchitis, and prostatitis the candiduria is symptomatic (6). It is very difficult to distinguish between bacteriuria and candiduria that's because mostly patients diagnosed with candiduria don't show symptoms. Candiduria are considered as marker for invasive candidiasis so the it should not be neglected even if there is no symptoms (7).

Azoles, echinocandins, polyenes and flucytosine are the classic antifungal agents used for the treatment of fungal disease. Azole is the largest family of antifungal drugs and Azoles dislocate 14-b-demethylase (8). As many *non-ablicans Candida spp.* are integrally resistant to treatment with fluconazole that's why it is important to know the *Candida spp.* causing the UTI before starting the treatment (9). Caspofungin and Posaconazole are the antifungal drugs which show sensitivity against *candida species*. Caspofungin inhibit 1,3- β -D-glucan synthase to act against fungal growth. For different types of candidiasis, Caspofungin show less side effects and have favorable drug interaction profile due to which it is used as first line therapy (10). For the treatment of fungal infections, Fluconazole and Caspofungin are the agents of choice, both excreted as active forms primarily in the urine. Due to the disproportionate use of these antifungal agents, they have been led to higher selective pressure and development of resistance unfortunately (11).

Different ideas have been anticipated to increase the effect of *C. albicans* towards fluconazole so that we can deal with the failed treatment. Different Combinations like, fluconazole with non-antifungal agents such as antibacterial, calcineurin inhibitors, heat shock protein 90 inhibitors, regulators of calcium homeostasis and traditional Chinese medicine drugs also been applied for the better treatment. Collective effects were shown by many of these combinations against *C. albicans*, in particular resistant strains. These combinations helps in the enhancement of the membrane permeability, efflux diminish antifungal agents that hinder with intracellular ion homeostasis, inhibiting the activity of proteins and enzymes intended for the survival of fungi and inhibit the development of biofilms (12). The aim of this study was to determine the frequency of fungal UTI in female patients and isolated and identify *candida species* using culture technique, microscopic

method to diagnose fungal infections in patients and demonstrate the antifungal susceptibility test.

Materials and Methods

Patients

This cross-sectional study was conducted on 448 urine samples from in-patients and out-patients who were suspect for the UTI visiting Private hospitals and pathological laboratories of Delhi NCR regions, during the period of 2 months.

Urine collection

Mid-stream urine was collected in a sterile container and properly sealed. Demographic details of patients like age, gender, address and transfer to the laboratory for microscopic analysis and cultured for finding presence of any *fungi*.

Candida isolation and identification

All samples were cultured on CLED plate using streaking method. Incubation was done at 37°C aerobically for 12-24 hours and evaluated based on color and number of growth colonies. urine samples yielding pure growth of *Candida species* with more than 10⁵ CFU (colony forming units) were included in the study. If no growth was seen the media were incubated for several more days. For the further identification of the species microscopy was done using wet mount method.

Antifungal susceptibility testing

Antifungal susceptibility tests were done on the positive isolates using a standard method of agar disk diffusion technique on Muller Hinton Methylene Blue Agar (MHMB). A lawn culture of the suspension was made on the test medium using sterile cotton swab and discs were placed over the plate, then incubated at 35 °C for 24 hours. Antifungals tested were Fluconazole, Voriconazole and Amphotericin B. Results were represented as susceptible and resistant.

Results

In the present study, a total of 448 urine samples were collected from the hospitals who were suspected of UTI. Out of 127 positive urine culture, 2.90% (n=13) with the positive urine culture for *candida albicans* only, and rest 89.7% (n=114) are positive for bacteria. Amphotericin B 100% was the most susceptible drug for *C. albicans* followed Voriconazole 92.3% and Fluconazole 61.53%.

The prevalence is high in adult women within the age group of 20-45 years. *C. albicans* was the most common *Candida species* isolated from the urine samples. Isolates were identified with the help of microscopy, morphology and pigmentation of the colonies (table.1). *C. albicans* give tiny to small whitish colony on CLED agar (fig.1.) and under microscope *candida* appears budding yeast cells and Pseudo hyphae (fig.2 and fig.3).

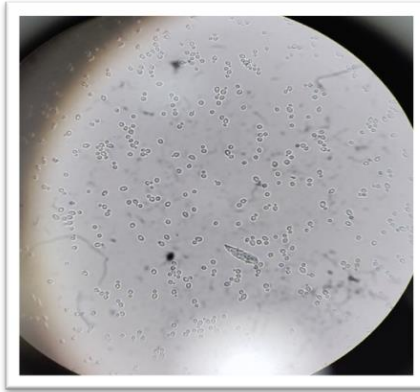


Fig 1. Whitish colony on CLED agar

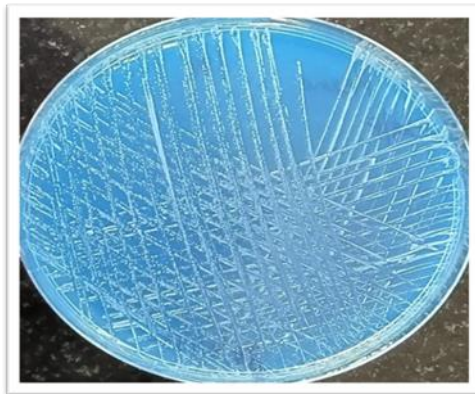


Fig 2. Budding yeast cells

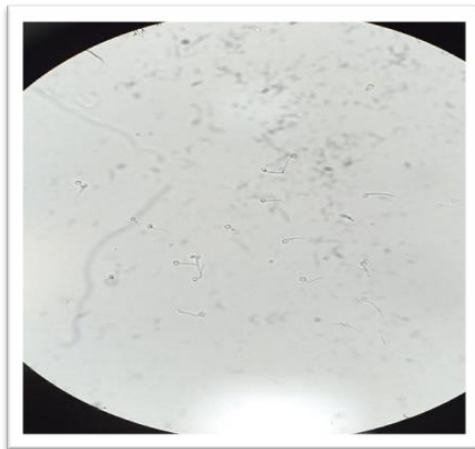


Fig 3. Pseudo hyphae

Table 1
Morphological diagnosis of candiduria on CLED agar

Candida species	Under microscope	Colony count in urine	Culture on CLED agar
<i>Candida albicans</i>	Budding yeast cells, Pseudo hyphae	$>10^5$	Tiny whitish colonies

Table 2
Susceptibility of *Candida.albicans* to antifungal drugs

Antifungal drugs	<i>Candida. Albicans</i> (n=13)	
	Susceptible	Resistant
Amphotericin B	13 (100%)	-
Voriconazole	12 (92.3%)	1 (7.69%)
Fluconazole	8 (61.53%)	5 (38.4%)

Discussion

A similar study on female by Tomczak H et al. reported that *C. albicans* (47%) are the most frequent species followed by *C. glabrata* (31%), *C. tropicalis* (6%), *C. krusei* (3%). As in our study only *C. albicans* is isolated, this limitation is due to the less sample size or it can be due to different study area (1). In a previous studies, *C. albicans* (59.4%) and *C. glabrata* (16.21) have been reported as the most frequent causes of candiduria and most influencing cause was diabetes (48.6%) (6,11,13–16). In a study conducted by Pramodhini et al, (2021) noticed that majority of the patients who were diagnosed with candiduria were within the age group of 61-75 (37.1%) and 22.9% was within the age group of 46-60 years. However occurrence was high in female patients (31.4%) than males. Incidence of *C. tropicalis* isolates was 65.7% and *C. albicans* isolates was 17.1% of the cases. Demonstration of AST show that amphotericin B (38.6%) was the most resistant drug followed by fluconazole (22.7%), caspofungin (15.7%) and voriconazole (12.3%), respectively. On the other hand the result of our study is totally different. (7)

It is found in the study by Fazeli A, et al, Zarei-Mahmoudabadi A et al and Nademi A, et al (4,17,18) that percentage of female is more (58.97% and 65.1%) than that of male (41.02% and 34.9%) and also that *C. albicans* is the mostly found species (68.42% and 53.3%). Main reason can be the shorter urethra and vaginal candidiasis in women. Study done by Gharanfoli A, et al similar results, where *C. albicans* are the most prevalent. In the present study, 2.90 % of urine specimens were positive for *Candida* spp. and this rate is low in comparison with some other studies (Fazeli A, et al, Gharanfoli A, et al) (4,6). Population and geographical region can be related to the occurrence rate. A study by Mehta Ret al. found highest number of *Candida* isolates from urine 43 (37.39%). Out of 43 (37.39%) isolates, *Candida* isolates were *Candida albicans* (n= 18) and non-*albicans Candida* species (n=25). Among non-*albicans Candida* species, *Candida tropicalis* (n=21) was the most predominant species (20).

A study by Almeida et al (21) reported that in urine *C. tropicalis* (38.8%) is the most prevalent isolate followed by *C. albicans* (29%). Through AST, it was demonstrated that *C. albicans* was sensitive to both fluconazole and amphotericin B but non-*C. albicans* show 31.2% sensitivity to fluconazole and only 3.1% were resistant to amphotericin B. However Seifi Z et al demonstrated that Except for fluconazole all the antifungal agents were susceptible for all *Candida* isolates from the urine of children (22). However, results of our study is quite different in case of isolates, therefore *C. albicans* are the only isolates present in the urine but result of AST were similar, amphotericin B was 100% sensitive drug towards all the isolates of *C. albicans*.

Conclusion

It is concluded from the present study that *C. albicans* was the most common isolated species causing nosocomial candiduria and requires early diagnosis and treatment. The decreased sensitivity of *Candida spp.* to fluconazole is may be due to long-term and widespread use of antifungals among the study subjects.

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Conflict of Interest

None

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