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To investigate the susceptibility of Candida isolates from the urine of hospitalized patients to antifungal agents

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ABSTRACT

Aim: To investigate the susceptibility of Candida isolates from the urine of hospitalized patients to antifungal agents. **Material and methods**: The study included a total of 2123 hospitalized patients who had their urine samples submitted for culture and sensitivity testing. Out of these, 100 patients were found to be positive for Candida species, and these 100 Candida-positive samples formed the basis of the study. For the culture, urine samples were cultured on Sabouraud Dextrose Agar (SDA) and incubated at 37°C for 24-48 hours. The colonies were further identified to the species level using chromogenic agar, germ tube test, and VITEK 2 system (bioMérieux, France). The antifungal susceptibility of the Candida isolates was determined using the Clinical and Laboratory Standards Institute (CLSI) M27-A3 broth microdilution method. The antifungal agents tested included Fluconazole, Itraconazole, Voriconazole, Amphotericin B, Caspofungin, and Micafungin. **Results**: - Candida tropicalis, Candida parapsilosis, and Candida krusei were less common, each representing 15%, 10%, and 10% of the isolates, respectively. For Candida albicans, 75% of the isolates were susceptible to fluconazole, while 25% were resistant. Itraconazole showed a 70% susceptibility rate, with 30% resistance. Voriconazole was effective against 88% of the isolates, and amphotericin B had the highest susceptibility rate at 95%. Candida glabrata had 40% resistance to fluconazole and 52% to itraconazole. However, it remained largely susceptible to voriconazole (80%), amphotericin B (88%), caspofungin (84%), and micafungin (92%). Candida tropicalis had 67% of isolates susceptible to fluconazole and 60% to itraconazole. Candida parapsilosis isolates showed 80% susceptibility to fluconazole, 70% to itraconazole, 90% to voriconazole, and 90% to both amphotericin B and micafungin. Candida krusei, had 70% susceptibility to itraconazole, voriconazole, and caspofungin, while amphotericin B and micafungin showed 70% and 80% susceptibility, respectively. **Conclusion**: The study revealed a 4.71% prevalence of Candida urinary tract infections among hospitalized patients, with a mean age of 55 years and a balanced gender distribution. Key risk factors identified were diabetes, catheter use, prior antibiotic use, immunosuppression, and renal failure. Candida albicans was the most common species, followed by Candida glabrata, Candida tropicalis, Candida parapsilosis, and Candida krusei. Antifungal susceptibility testing showed high susceptibility rates to amphotericin B, caspofungin, and micafungin across most species, though resistance to fluconazole and itraconazole was notable, particularly in Candida glabrata.

Keywords: Candida, urine, antifungal agents

INTRODUCTION

Candida species are among the most common opportunistic pathogens in clinical settings, frequently causing infections in hospitalized patients. These infections, known as candidiasis, can range from superficial mucosal and cutaneous infections to invasive diseases affecting the bloodstream and various internal organs. Urinary tract infections (UTIs) caused by Candida, known as candiduria, are particularly common in hospitalized patients, especially those in intensive care units (ICUs) and those with predisposing risk factors such as prolonged catheterization, diabetes, prior antibiotic use, immunosuppression, and renal failure. The growing prevalence of candiduria poses a significant challenge to healthcare providers due to the rising incidence of antifungal resistance among Candida species. Candiduria is often a result of either colonization or an actual infection of the urinary tract. Differentiating between these two conditions is crucial for effective management. Colonization refers to the presence of Candida in the urine without symptoms of infection, whereas an actual infection involves symptomatic urinary tract inflammation. Despite its frequent occurrence, the clinical significance of candiduria remains debated, as it can be an indicator of an underlying systemic candidiasis, particularly in high-risk patients. Thus, understanding the antifungal susceptibility patterns of Candida isolates is essential for guiding appropriate therapeutic interventions and improving patient outcomes.[1]The antifungal susceptibility of Candida species is of paramount importance due to the emergence of resistant strains, which complicates treatment options. Fluconazole, a widely used antifungal agent, has been the cornerstone of candidiasis treatment due to its oral availability, favorable safety profile, and broad-spectrum activity against various Candida species. However, resistance to fluconazole has been increasingly reported, particularly among non-albicans Candida species such as Candida glabrata and Candida krusei. The rising resistance necessitates the use of alternative antifungal agents, including echinocandins (e.g., caspofungin, micafungin) and polyenes (e.g., amphotericin B), which have shown efficacy against resistant strains.[2,3]The clinical management of candiduria involves a nuanced approach, often requiring a balance between treating true infections and avoiding unnecessary antifungal therapy for colonization. The decision to treat candiduria is influenced by factors such as the presence of symptoms, the patient's immune status, and the risk of progression to invasive candidiasis.[4] In many cases, removal or replacement of urinary catheters and addressing underlying risk factors can resolve candiduria without the need for antifungal treatment. However, in symptomatic patients or those at high risk of systemic infection, antifungal therapy becomes imperative.[5,6]Recent advancements in diagnostic techniques have improved the identification and susceptibility testing of Candida species. The use of chromogenic agar allows for the rapid identification of Candida species based on colony color, while molecular techniques and automated systems like the VITEK 2 provide precise species-level identification and susceptibility profiles. These advancements enable timely and accurate diagnosis, facilitating appropriate antifungal therapy.[7,8]Despite these advancements, challenges remain in the management of candiduria. The variability in antifungal susceptibility among different Candida species, coupled with the emergence of multi-drug resistant strains, underscores the need for continuous surveillance and research. Studies focusing on the antifungal susceptibility of Candida isolates from different clinical settings provide valuable insights into resistance trends and inform clinical practice.[9]The rising incidence of candiduria in hospitalized patients, particularly those with multiple risk factors, necessitates a comprehensive understanding of antifungal susceptibility patterns. The aim of this study is to assess the antifungal susceptibility of Candida isolates from the urine of hospitalized patients. By analyzing the susceptibility profiles of various Candida species, this study seeks to inform treatment strategies and contribute to the effective management of candiduria in clinical settings.

MATERIAL AND METHODS

This study was conducted in Department of Obstetrics and Gynaecology, Madhubani Medical College, India to assess the antifungal susceptibility of Candida isolates from the urine of hospitalized patients. It was carried out in the microbiology department of a tertiary care hospital. The study protocol was approved by the hospital's Institutional Review Board (IRB). Informed consent was obtained from all participants prior to sample collection. Patient confidentiality was maintained throughout the study. The study included a total of 2123 hospitalized patients who had their urine samples submitted for culture and sensitivity testing. Out of these, 100 patients were found to be positive for Candida species, and these 100 Candida-positive samples formed the basis of the study.

Inclusion and Exclusion Criteria

The inclusion criteria for the study were hospitalized patients aged 18 years and above, those who provided urine samples for culture, and patients with a positive identification of Candida species in the urine culture. The exclusion criteria were patients with mixed infections in the urine sample and those who had received antifungal treatment in the past 30 days.

Methodology

Urine samples were collected from the patients using standard aseptic techniques. Midstream urine samples were preferred to minimize contamination. The samples were transported to the microbiology laboratory within one hour of collection and processed immediately. For the culture, urine samples were cultured on Sabouraud Dextrose Agar (SDA) and incubated at 37°C for 24-48 hours. Positive growth was identified by the appearance of creamy, smooth colonies. The colonies were further identified to the species level using chromogenic agar, germ tube test, and VITEK 2 system (bioMérieux, France). The antifungal susceptibility of the Candida isolates was determined using the Clinical and Laboratory Standards Institute (CLSI) M27-A3 broth microdilution method. The antifungal agents tested included Fluconazole, Itraconazole, Voriconazole, Amphotericin B, Caspofungin, and Micafungin. The minimum inhibitory concentrations (MICs) were interpreted according to the CLSI guidelines. Quality control strains of Candida albicans ATCC 90028 and Candida parapsilosis ATCC 22019 were used to ensure the accuracy of the antifungal susceptibility testing.

Statistical Analysis

Patient demographic data, clinical history, and antifungal susceptibility results were recorded. Data were analyzed using SPSS version 25.0. Descriptive statistics were used to summarize the data. The prevalence of Candida species and their antifungal susceptibility profiles were reported in frequency tables and charts. The Chi-square test was used to compare categorical variables, and a p-value of <0.05 was considered statistically significant.

RESULTS

The study included a total of 2123 hospitalized patients who had their urine samples submitted for culture and sensitivity testing. Among these patients, 100 were found to be positive for Candida species, resulting in a prevalence rate of 4.71%. The mean age of the Candida-positive patients was 55 years with a standard deviation of 18 years, indicating a wide age range among the affected individuals. The gender distribution among the Candida-positive patients was fairly balanced, with 45 males and 55 females.

The clinical parameters of the Candida-positive patients were examined to identify any common underlying conditions or risk factors. It was found that 40% of the patients had diabetes, which is known to be a significant risk factor for Candida infections. Catheter use

was prevalent in 70% of the patients, highlighting the association between urinary catheterization and the risk of developing Candida urinary tract infections. Prior antibiotic use was reported by 50% of the patients, which can disrupt the normal microbial flora and predispose individuals to fungal infections. Additionally, 30% of the patients were immunosuppressed, and 20% had renal failure, both of which are known to increase susceptibility to infections.

The distribution of different Candida species among the 100 positive isolates was analyzed. Candida albicans was the most commonly isolated species, accounting for 40% of the cases. Candida glabrata was the second most prevalent species, found in 25% of the isolates. Candida tropicalis, Candida parapsilosis, and Candida krusei were less common, each representing 15%, 10%, and 10% of the isolates, respectively. This distribution is consistent with the known prevalence of these species in clinical settings, with Candida albicans typically being the most frequent.

The antifungal susceptibility testing revealed varying levels of resistance among the different Candida species. For Candida albicans, 75% of the isolates were susceptible to fluconazole, while 25% were resistant. Itraconazole showed a 70% susceptibility rate, with 30% resistance. Voriconazole was effective against 88% of the isolates, and amphotericin B had the highest susceptibility rate at 95%. Caspofungin and micafungin also showed high susceptibility rates of 90% and 95%, respectively.

Candida glabrata displayed higher resistance rates compared to Candida albicans, with 40% resistance to fluconazole and 52% to itraconazole. However, it remained largely susceptible to voriconazole (80%), amphotericin B (88%), caspofungin (84%), and micafungin (92%).

Candida tropicalis had 67% of isolates susceptible to fluconazole and 60% to itraconazole. It showed better susceptibility to voriconazole (80%) and very high susceptibility to amphotericin B (93%), caspofungin (87%), and micafungin (93%).

Candida parapsilosis isolates were generally susceptible to the tested antifungal agents, with 80% susceptible to fluconazole, 70% to itraconazole, 90% to voriconazole, and 90% to both amphotericin B and micafungin. Caspofungin susceptibility was slightly lower at 80%.

Candida krusei, known for its inherent resistance to fluconazole, had 70% susceptibility to itraconazole, voriconazole, and caspofungin, while amphotericin B and micafungin showed 70% and 80% susceptibility, respectively.

Table 1: Demographic Parameters

Parameter	Value
Total Patients	2123
Prevalence	4.71
Candida Positive Patients	100
Age (mean ± SD)	55 ± 18
Gender (M/F)	45/55

Table 2: Clinical Parameters

Clinical Parameter	Number of Patients	Percentage (%)
Diabetes	40	40
Catheter Use	70	70
Prior Antibiotic Use	50	50
Immunosuppressed	30	30

Renal Failure	20	20

Table 3: Prevalence of Candida Species

Candida Species	Number of Isolates	Percentage (%)
Candida albicans	40	40
Candida glabrata	25	25
Candida tropicalis	15	15
Candida parapsilosis	10	10
Candida krusei	10	10

Table: 4 Antifungal Susceptibility of All Isolated Species

Candida Species	Fluconazole (S)	Fluconazole (R)	Itraconazole (S)	Itraconazole (R)	Voriconazole (S)	Voriconazole (R)	Amphotericin B (S)	Amphotericin B (R)	Caspofungin (S)	Caspofungin (R)	Micafungin (S)	Micafungin (R)
Candida albicans	30 (75%)	10 (25%)	28 (70%)	12 (30%)	35 (88%)	5 (12%)	38 (95%)	2 (5%)	36 (90%)	4 (10%)	38 (95%)	2 (5%)
Candida glabrata	15 (60%)	10 (40%)	12 (48%)	13 (52%)	20 (80%)	5 (20%)	22 (88%)	3 (12%)	21 (84%)	4 (16%)	23 (92%)	2 (8%)
Candida tropicalis	10 (67%)	5 (33%)	9 (60%)	6 (40%)	12 (80%)	3 (20%)	14 (93%)	1 (7%)	13 (87%)	2 (13%)	14 (93%)	1 (7%)
Candida parapsilosis	8 (80%)	2 (20%)	7 (70%)	3 (30%)	9 (90%)	1 (10%)	9 (90%)	1 (10%)	8 (80%)	2 (20%)	9 (90%)	1 (10%)
Candida krusei	7 (70%)	3 (30%)	6 (60%)	4 (40%)	8 (80%)	2 (20%)	7 (70%)	3 (30%)	7 (70%)	3 (30%)	8 (80%)	2 (20%)

DISCUSSION

In this study, 2123 hospitalized patients had their urine samples tested for fungal infections, out of which 100 were positive for Candida species, yielding a prevalence rate of 4.71%. The mean age of the patients was 55 years, indicating a middle-aged demographic, with a nearly equal gender distribution (45 males and 55 females). This prevalence rate aligns with previous studies, such as one conducted by Blumberg et al.[10], which reported a prevalence rate of 4.8% in a similar hospital setting. Another study by Kauffman et al.[11] found a slightly higher prevalence of 5.2% among hospitalized patients, suggesting variations might be due to different hospital populations and sampling methods.The clinical parameters highlighted key

risk factors associated with Candida infections. Diabetes was present in 40% of the patients, catheter use in 70%, prior antibiotic use in 50%, immunosuppression in 30%, and renal failure in 20%. These findings are consistent with other studies. For instance, a study by Pappas et al.[5]identified diabetes, antibiotic use, and catheterization as significant risk factors for candiduria. Similarly, Kauffman et al.[11] also emphasized the high prevalence of catheter use and prior antibiotic therapy among their Candida-positive patients. These commonalities underline the importance of monitoring these risk factors in hospitalized patients to prevent fungal infections.

The most commonly isolated species in this study was Candida albicans, accounting for 40% of the cases, followed by Candida glabrata (25%), Candida tropicalis (15%), Candida parapsilosis (10%), and Candida krusei (10%). This distribution is similar to that reported by Blumberg et al.[10], who found Candida albicans to be the predominant species, followed by Candida glabrata. Another study by Pfaller et al.[4] also reported Candida albicans as the most frequent isolate, although they noted a rising incidence of non-albicans species, particularly Candida glabrata and Candida tropicalis. These results emphasize the shifting landscape of Candida infections, highlighting the need for continuous surveillance and updated antifungal strategies.The antifungal susceptibility testing revealed significant resistance patterns. Candida albicans showed high susceptibility to amphotericin B (95%), voriconazole (88%), and micafungin (95%), but lower susceptibility to fluconazole (75%) and itraconazole (70%). Candida glabrata displayed notable resistance to fluconazole (40%) and itraconazole (52%) but remained largely susceptible to other antifungals. These findings are corroborated by the study conducted by Pfaller et al.[4], which reported similar susceptibility patterns, with Candida glabrata showing high resistance rates to fluconazole.Candida tropicalis exhibited 67% susceptibility to fluconazole and 60% to itraconazole, but high susceptibility to amphotericin B (93%), caspofungin (87%), and micafungin (93%). Candida parapsilosis showed 80% susceptibility to fluconazole, 70% to itraconazole, and high susceptibility to voriconazole, amphotericin B, and micafungin (all 90%). These susceptibility profiles are in line with findings from Kauffman et al.[11], who reported high susceptibility rates of Candida parapsilosis to most antifungal agents but noted emerging resistance to fluconazole.Candida krusei, known for its inherent resistance to fluconazole, showed 70% susceptibility to itraconazole, voriconazole, and caspofungin, and 70-80% susceptibility to amphotericin B and micafungin. These results are consistent with the study by Pappas et al.[5], which highlighted the inherent resistance of Candida krusei to fluconazole and variable susceptibility to other antifungals. When comparing the results with other studies, it becomes evident that the prevalence and antifungal resistance patterns of Candida species can vary based on geographic location, patient demographics, and hospital settings. The study by Blumberg et al.[10] and Pfaller et al.[4] both support the findings of this study, indicating that Candida albicans remains the most common species, but there is a noticeable rise in non-albicans species like Candida glabrata and Candida tropicalis.

CONCLUSION

The study revealed a 4.71% prevalence of Candida urinary tract infections among hospitalized patients, with a mean age of 55 years and a balanced gender distribution. Candida albicans was the most common species, followed by Candida glabrata, Candida tropicalis, Candida parapsilosis, and Candida krusei. Antifungal susceptibility testing showed high susceptibility rates to amphotericin B, caspofungin, and micafungin across most species, though resistance to fluconazole and itraconazole was notable, particularly in Candida glabrata.

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