e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(9); 266-270

Original Research Article

Emerging Trends in Candiduria and Susceptibility to Antifungal Drugs among Cancer Patients at a Tertiary Care Hospital

Karekar Bhagyashree[1], Salunke Gaurav[2], Biswas Sanjay[3]

[1]Senior Resident, Bharatratna Atal Bihari Vajpayee Medical College, Pune, Maharashtra, India
[2]Associate Professor, Tata Memorial Hospital, HBNI University, Mumbai, Maharashtra, India
[3]Professor & Head of Department of Microbiology, Tata Memorial Hospital, HBNI University, Mumbai, Maharashtra, India

Received: 01-06-2026 / Revised: 15-07-2026 / Accepted: 21-08-2026
Corresponding author: Dr. Bhagyashree Karekar
Conflict of interest: Nil

Abstract

Background: Hospitalized patients often suffer from urinary fungal infections. With the increasing burden of patients with fungal infections, our study aims at determining susceptibility of *Candida* species in urinary isolates along with treatment outcome.

Methods: A retrospective observational study was conducted spanning from January 2022 to December 2023. A total of 41 *Candida* isolates were studied from urine samples of cancer patients. Relevant information was obtained using the hospital electronic medical record system.

Findings: Amongst the 41 patients, study population ranged from 10 months to 79 years of age. Female preponderance was seen (56.1%). *Candida tropicalis* (34.1%) was the most frequently isolated *Candida* species, followed by *Trichosporon asahii* (17%) & *C. albicans* (17%). Fluconazole (46.3%) was most commonly used antifungal agent. *Candida albicans* isolates were susceptible to all the antifungals under study. *Candida tropicalis* exhibited susceptibility to most drugs, though Posaconazole and Itraconazole showed highest frequencies of resistance at 10 and 5, respectively.

Interpretation: Since candiduria is an important cause of morbidity in neutropenic patients, accurate identification of *Candida* species can be useful for the appropriate selection of antifungal agents.

Keywords: Cancer patients, *Candida tropicalis, Candida albicans*, Fluconazole, Posaconazole, Itraconazole.
DOI: 10.25258/ijcpr.18.9.39

Introduction

Candiduria is a nonspecific finding that can occur with contamination of a urine sample, colonization of an indwelling catheter and/or the bladder, symptomatic cystitis and invasive upper tract infection (hematogenous seeding of kidney cortex secondary to disseminated course of candidiasis) [1]. Many of the asymptomatic patients are colonized and hence there is no need of antifungal therapy. In patients with indwelling catheters, candiduria gets cleared simply by removing predisposing factors, i.e. the catheters [1]. There has been a rising incidence of *Candida* species causing urinary tract infections, reflecting a changing trend driven by an increasing number of at-risk patients

Although *Candida albicans* is a common pathogen and standard treatment for candidiasis is Fluconazole, there is a growing concern over the emergence of innately azole - resistant non-albicans *Candida* species (*C. glabrata* & *C. kruzei*), highlighting a shift in the epidemiological landscape. Therefore, infections by these strains may mandate an alternative treatment with Amphotericin B or Itraconazole [2]. Also simply identifying or ruling out *Candida* species is no longer sufficient [3]. Thus, this study was carried to study various *Candida* species causing urinary tract infections amongst the immunocompromised individuals suffering from cancer and to analyse their susceptibility pattern.

Methodology

An observational study was conducted spanning from January 2022 to December 2023. A total of 41 *Candida* isolates were studied from urine samples of cancer patients.

Initially, the germ tube test was performed on each of the isolates to differentiate between *C. albicans* and non-albicans. Then, the *Candida* isolates were cultured on CHROMagar for speciation. Species identification was confirmed by automated

identification using Vitek machine. Broth microdilution was performed for antifungal susceptibility testing. The MIC (minimum inhibitory concentrations) was assessed using CLSI & EUCAST guidelines for *Candida* isolates. Relevant clinical and microbiological information was obtained using the hospital electronic medical record system.

Results

The study included 41 cancer patients with a median age of 53 years (IQR = 24 years).

The minimum age was 10 months and the maximum age was 79 years. Among the participants, (Chart 1) 56.1% were female (n = 23) and 43.9% were male (n = 18).

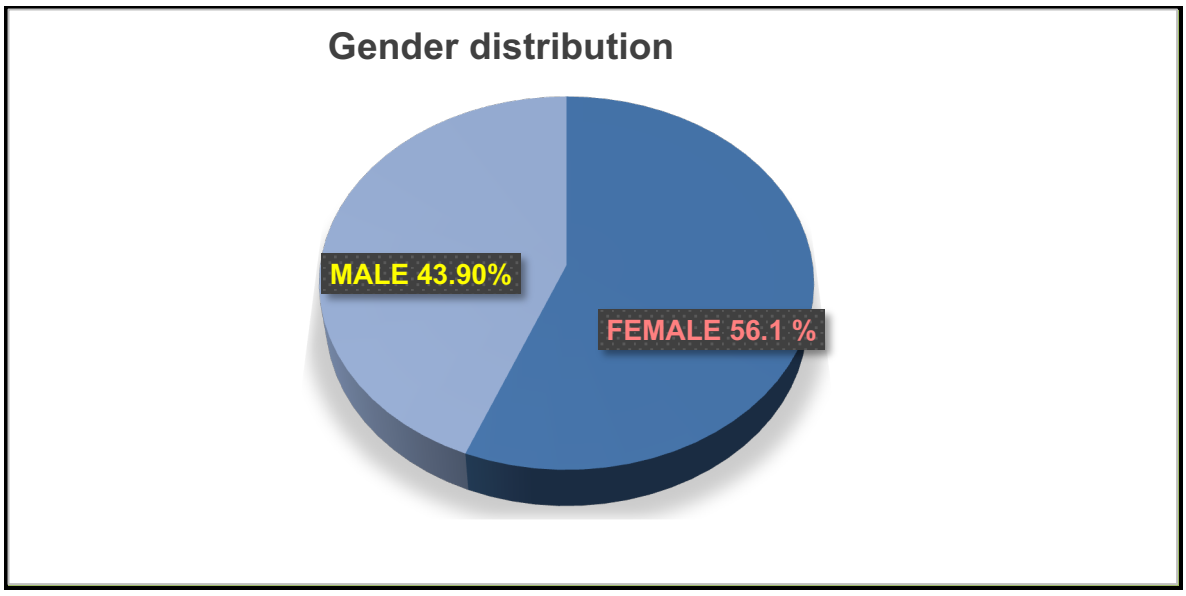

Figure 1: Gender distribution

The distribution of cancer types was diverse (Chart 2), with the most common being Gynaec-Oncology (36.6%), followed by Uro-Oncology (17.073%) and Paediatric Solid Tumour (14.6%).

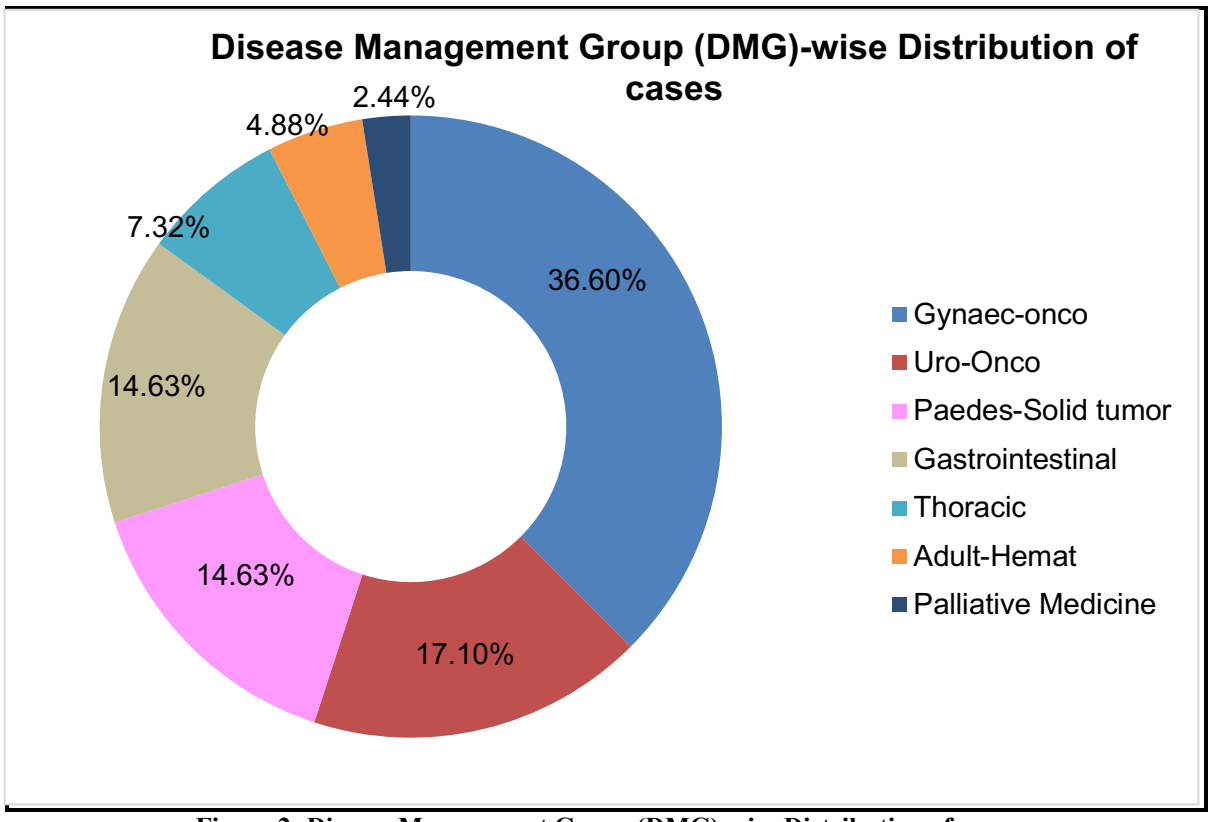

Figure 2: Disease Management Group (DMG)-wise Distribution of cases

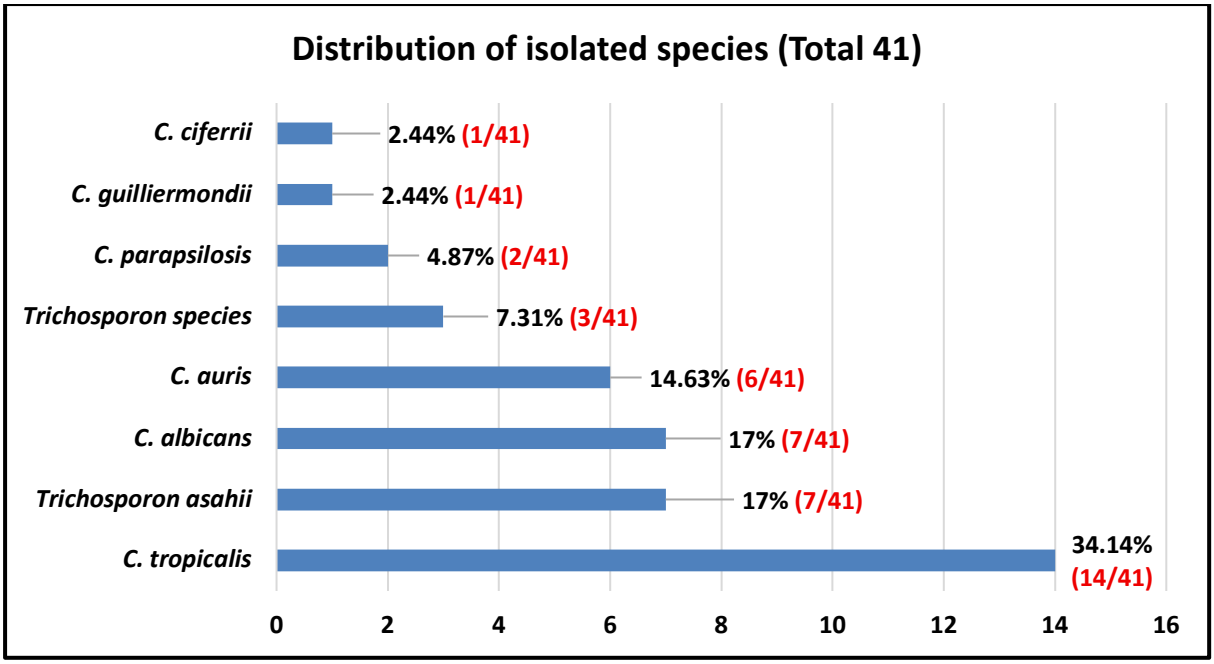

Figure 3: Distribution of isolated species (Total 41)

The most frequent isolates identified were *Candida tropicalis* (34.1%) (Chart 3) followed by *Trichosporon asahii* (17%) & *Candida albicans* present in 17% of cases. Various antifungal treatments were administered, with fluconazole being the most common (46.3%), followed by voriconazole (19.5%) and caspofungin (14.6%).

Susceptibility patterns varied across different species. *Candida tropicalis* exhibited susceptibility to most drugs, though posaconazole and itraconazole exhibited considerable amount of resistance, 71.42% (10/14) and 35.71% (5/14), respectively. *Candida albicans* isolates were susceptible to all the antifungals under study i.e., Anidulafungin, Fluconazole, Voriconazole, Amphotericin B, Caspofungin, Micafungin, Posaconazole, and Itraconazole. *Candida auris* and *Trichosporon asahii* had varying MIC (Minimum Inhibitory Concentration) values.

Discussion

The most common nosocomial infections among the hospitalized patients are urinary tract infections (UTIs) and their incidence has been on a rise during the recent decades [4]. There are many microorganisms which are associated with UTIs including, bacteria, viruses, filamentous fungi, and yeasts. However, 10-15% of them are caused by *Candida* species which constitute the most common fungal mycoflora [5]. In our study, females (56.1%) were more affected than males, with a male: female ratio of 0.78. Datta et al. [6] reported 54% females in their study population whereas Georgiadou et al. [4] reported 88% females to be suffering from candiduria. This could be due to the fact that *Candida* species form important constituent of the normal flora of the vagina, as it colonizes on outer side of the urethral opening in healthy females, but in the case of immunodeficiency, they can convert into opportunistic pathogenic microorganisms [4]. Additionally, the presence of shorter urethra in women than in men facilitates reaching the bladder via ascending route [5]. The current study showed that maximum number of patients belonged to Gynaec-Oncology [36.6% (15/41)], followed by Uro-Oncology patients. This could be attributed to the alteration of the microbial flora after surgical interventions in both the type of patients.

In the literature, *C. albicans* has been reported as the most common cause of candiduria (50-70%) followed by *C. glabrata* (20%) and *C. tropicalis* (3.7%) [10,14]. However, during the last decade whims change have been seen whereby, incidence rate of non-albicans *Candida* species like *C. parapsilosis, C. lusitaniae, C. guilliermondii* and *C. krusei* have been increasing [11]. This can be clearly seen in this study, where *C. tropicalis* [34.14% (14/41)] was the most commonly isolated yeast from cases of candiduria followed by *C. albicans* [17% (7/41)]. The results of our study are equally supported by Paul et al. [9], who has also reported the incidence of *C. tropicalis* with an incidence rate of 30.5%. Although coinfection with bacteria is more common among patients, polymicrobial infections with several yeast species were reported in 5-10% of *Candida*-related UTIs. Interestingly, in most cases, *C. glabrata* appears to be a frequent pathogen in combination with other species. There are various degrees of susceptibility of *Candida* species to frequently used antifungal drugs across various studies [12]. They have shown that non-albicans species such as *Candida glabrata, C. tropicalis, C. krusei, C. parapsilosis,* and *C. lusitaniae* exhibit higher resistance to fluconazole

compared to *Candida albicans* [12]. In the present study, only one isolate of *C. tropicalis* has shown resistance to fluconazole while another one isolate was reported to be susceptible dose-dependent. *C. parapsilosis* and *C. albicans* were sensitive to fluconazole. This finding is more or less similar to findings of other studies owing to the lower sample size. In a study by Seifi et al, [15] the tested isolates were resistant to fluconazole. This finding is contradictory to the finding in our study, wherein maximum number of isolates tested susceptible to fluconazole except for two isolates of *C.tropicalis*. Varying MIC values were observed in case of other *Candida* isolates such as *C. ciferii, C. auris, C. guilliermondii, Trichosporon asahii* and *Trichosporon* species with regards to fluconazole as there are no available guidelines to determine their susceptibility pattern. Susceptibility to voriconazole exhibited analogous findings to that of fluconazole. The pathogenic potential of *Candida tropicalis* is driven by a range of virulence factors, including the production of extracellular enzymes such as phospholipase, haemolysin, coagulase, and proteinase, as well as its ability to form biofilms and resist antifungal agents. [13] These secreted enzymes play a crucial role in tissue invasion, helping the fungus to damage host cells, evade immune responses, and facilitate its spread—particularly by enhancing escape mechanisms following phagocytosis by macrophages. [13] A high level of resistance to posaconazole was observed in *Candida tropicalis* isolates, with 71.42% (10 out of 14) demonstrating maximum resistance. This signifies the increase in azole resistant strains of *Candida* species. In a study by Mahmoudabadi et al. [17], the *C. tropicalis* isolates were totally susceptible to posaconazole, whereas resistance to it was observed in strains of *C. albicans* and *C. glabrata*. This finding is not consistent with the findings of the present study which could be due to geographical variations.

Additionally, a notable proportion of isolates—35.71% (5 out of 14)—also exhibited resistance to itraconazole in the current study. In a study by Law et al. [16], itraconazole was found to be resistant in 17% of the C. tropicalis isolates. In the current study, the percentage of itraconazole resistant isolates of C.tropicalis is slightly higher as compared to the study by Law et al. [16].

All *Candida* isolates under study were susceptible to anidulafungin, caspofungin and micafungin. Axner-Elings et al. [18], reported that one of the eight *Candida tropicalis* isolates recovered from a patient undergoing caspofungin therapy exhibited MIC values indicative of resistance—specifically, 1 µg/mL for anidulafungin (at 24 h) and 2 µg/mL (at 48 h), and 4 µg/mL and 8 µg/mL for caspofungin at 24 and 48 hours, respectively. The isolate also showed intermediate susceptibility to micafungin (0.5 µg/mL at both time points). Sequence analysis of the FKS1 gene revealed a heterozygous S80P mutation in the Fks1p protein, a known marker associated with echinocandin resistance [18]. This is contradictory to the findings of the present study, which may be because the patient was previously being treated with caspofungin and had later developed resistance to it.

Amphotericin B, was also found to be susceptible to all the isolates of *C. albicans, C. parapsilosis* and *C. tropicalis*. Varying MIC values were obtained for other fungal isolates as they did not have pre-defined breakpoints. Amanati et al. [19], observed that 93.1% of the *C. albicans*, 100% of *C. parapsilosis* & *C. tropicalis* isolates were sensitive to Amphotericin B. This is a finding which is more or less similar to the observations in the current study. Thus, the evaluation of susceptibility patterns of the *Candida* isolates is highly important as it helps in providing appropriate antifungal therapy to the patient, thereby improving the prognosis.

Conclusion

Candiduria is an important cause of morbidity in patients with underlying malignancies or other immunosuppressed state. Accurate identification of *Candida* species is of utmost importance for administering antifungal therapy. Determining susceptibility pattern for the different *Candida* isolates has also become a matter of concern in the view of increase in resistance to the antifungal agents during recent years. Also, early and accurate diagnosis will help in improving prognostic outcome.

Acknowledgement: We thank Mrs. Charusheela and Mr. Pramod Chavan for their help and co-operation during the study.

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