

# Species Distribution, Drug Resistance, and Risk Determinants of *Candida* UTIs: A Five-Year Retrospective Study in Beijing

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**Objective:** The *Candida* genus has become an important pathogen of urinary tract infections (UTIs). Systemic infections caused by *Candida* could result in high mortality and significant medical costs, presenting an increasingly severe clinical challenge. This five-year retrospective study was designed to investigate the species distribution, antifungal resistance patterns and clinical risk factors associated with *Candida* urinary tract infections, it is critical to guide the rational selection of antifungal agents and optimize clinical management strategies.

**Methods:** This retrospective study analyzed 229 cases of *Candida* UTIs diagnosed at the Third Medical Center of the Chinese PLA General Hospital between 2020 and 2024. Species distribution and antifungal susceptibility were evaluated using chi-square tests, while multivariate logistic regression was employed to identify independent risk factors.

**Results:** 1. A total of 230 *Candida* strains were isolated from 229 patients (138 males and 91 females). The detection rate of *C. albicans* decreased from 47.06% in 2020 to 39.22% in 2024, with a corresponding rise in non-*albicans* species. 2. Among the 199 strains tested for antifungal susceptibility, all isolates remained fully susceptible to amphotericin B and 5-fluorocytosine (0.00% resistance). In contrast, resistance to azole antifungals was notably higher. *C. tropicalis* exhibited significantly greater resistance to triazole agents compared to *C. albicans* ( $P < 0.05$ ), while *C. glabrata* demonstrated a high resistance rate to itraconazole (44.00%), indicating a growing resistance concern. 3. Univariate analysis showed that hospital stays  $\geq 14$  days, urinary catheterization  $\geq 7$  days, and broad-spectrum antibiotic use were significantly associated with *Candida* UTIs ( $P < 0.05$ ). Multivariate logistic regression identified prolonged hospitalization and catheterization as independent risk factors ( $P < 0.05$ ).

**Conclusion:** The increasing prevalence of non-*Candida albicans* species and rising azole resistance—particularly among *Candida tropicalis*—underscore the importance of routine species identification and antifungal susceptibility testing. Early urine culture screening and individualized antifungal selection are crucial, especially for patients with prolonged hospital stays or indwelling catheters, promoting the transition from empirical medication use to individualized treatment in clinical practice.

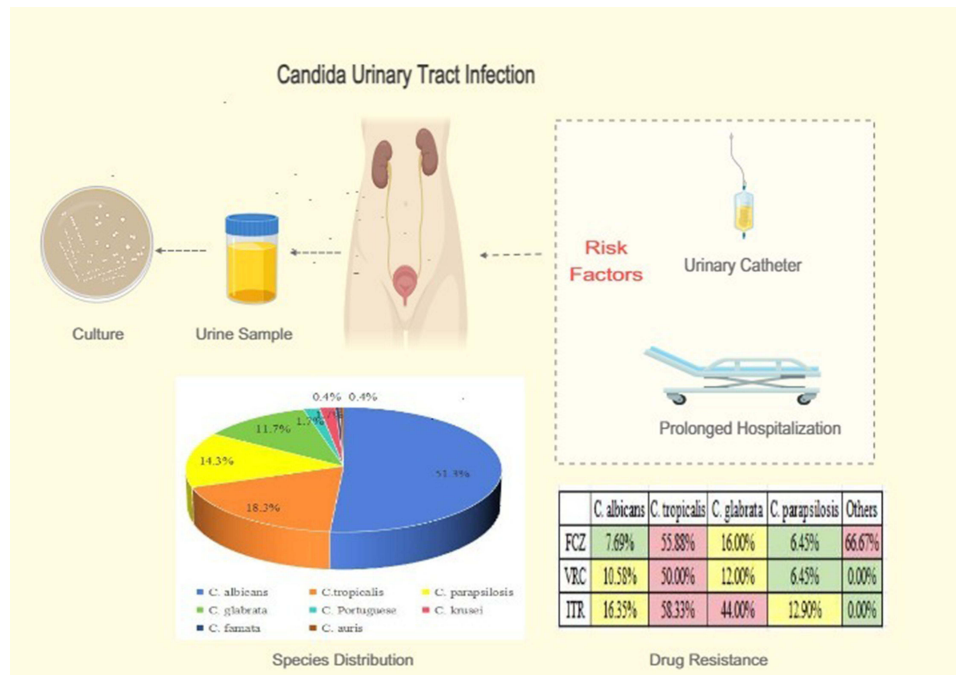
**Keywords:** urinary tract infections, *Candida*, antifungal resistance, risk factors

## Introduction

Urinary tract infections (UTIs) are among the most common infectious diseases in clinical settings, second only to respiratory tract infections in incidence.<sup>1</sup> *Candida* species, as opportunistic pathogens, primarily affect hospitalized patients and individuals with compromised immune systems. Reports on *Candida* urinary tract infections indicate a continuous rise in incidence with the widespread use of broad-spectrum antibiotics, immunosuppressive therapies, and invasive procedures globally.<sup>2</sup> The prevention and monitoring of *Candida* UTIs, along with meticulous nursing care, should be prioritized for high-risk patients with prolonged hospitalization, catheter use, comorbidities and compromised immunity.



## Graphical Abstract



*Candida* species are now isolated in approximately 10% of urine culture-positive cases, with a growing proportion of infections caused by non-*Candida albicans* species.<sup>3</sup> The emergence and spread of these non-*C. albicans* species were not merely simple changes in the types of pathogens, but exacerbated global antifungal resistance through complex drug-resistant mechanisms and strong environmental adaptability.<sup>4</sup> Treatment options are limited by the toxicity and pharmacokinetic constraints of antifungal drugs, and the emergence of antifungal resistance further complicates therapeutic strategies.<sup>5</sup> Therefore, continuous surveillance of species distribution and antifungal resistance patterns is essential to inform clinical decision-making. However, there is still limited research in this regard.

Although some short-term studies have given significant attention to fungal resistance at present.<sup>6,7</sup> Our study offers a comprehensive five-year retrospective analysis of *Candida* UTIs in a tertiary hospital in Beijing to fully reveal the long-term dynamic evolution of strain distribution and drug resistance. The distribution of species, the trends in antifungal resistance, and associated clinical risk factors for *Candida* UTIs in this region were characterized systematically, these findings provided important basis for formulating personalized empirical treatment schemes for local resistance patterns.

## Methods

### Clinical Data Collection

A retrospective analysis was conducted on 229 patients diagnosed with *Candida* urinary tract infections (UTIs) at our hospital between 2020 and 2024. The study protocol was approved by the Ethics Committee of the Third Medical Center of the Chinese PLA General Hospital, and informed consent was obtained from all participants.

### Inclusion Criteria Were as Follows

Patients included in the study must meet following three criteria simultaneously.

1. Microbiological Confirmation: Positive urine culture yielding *Candida* at concentrations  $>1 \times 10^5$  CFU/mL from midstream urine samples, in accordance with the diagnostic criteria described in the Clinical Practice Guideline for the Management of *Candida* UTIs.<sup>8</sup>

2. Abnormal urinalysis results: at least one of the following: a positive leukocyte esterase result, a positive nitrite result, or pyuria (>10 WBC/HP), along with the presence of yeast-like spores observed during urine microscopy.
3. Clinical symptoms consistent with UTI: including lower urinary tract symptoms such as urinary frequency, urgency, dysuria, or other systemic symptoms (including but not limited to fever >38.0°C), without another identifiable source of infection.

### Exclusion Criteria Included

1. Repeated isolation of the same *Candida* strain from the same patient.
2. Incomplete demographic information or antifungal susceptibility testing results.

All data are retrieved through the system firstly, and then independently reviewed and cross-verified by two researchers to ensure the integrity and accuracy of the data.

For comparison, a control group was established, comprising patients with bacterial UTIs who were identified from the same patient pool and during the same period as the *Candida* UTI group. These control patients were matched to the *Candida* cases based on age and gender. This matching strategy eliminated these demographic confounders, thereby facilitating the identification of risk factors uniquely associated with *Candida* UTIs.

## Microbiological Methods

### Strain Isolation and Identification

According to the standard operating procedure,<sup>9</sup> midstream morning urine samples were aseptically collected from patients using sterile catheters. A 5 µL aliquot of midstream urine was aseptically inoculated onto ChromAgar medium after mixing and incubated aerobically at 37°C for 24–48 hours. Preliminary species identification was based on colony color and morphology on ChromAgar. It has greatly shortened the time for pathogen identification, providing preliminary basis for early empirical treatment. Strains that could not be conclusively identified via chromogenic reaction were further analyzed using the VITEK 2 COMPACT system with YST identification cards.

### Antifungal Susceptibility Testing

Antifungal susceptibility testing was performed using the ATB FUNGUS 3 broth microdilution method. The antifungal agents tested included fluconazole (FCZ), voriconazole (VRC), itraconazole (ITR), amphotericin B (AMB), and 5-fluorocytosine (5FC). The minimum inhibitory concentration (MIC) for each drug was determined by visual reading of the dilution series. The isolates were then assigned to susceptibility categories (S or R) in accordance with the interpretive breakpoints provided by the Clinical and Laboratory Standards Institute.<sup>10</sup> *Candida albicans* ATCC 14053 served as the quality control strain.

## Statistical Analysis

Statistical analyses were conducted using SPSS version 27.0. Categorical variables were expressed as frequencies and percentages, and intergroup comparisons were performed using the chi-square ( $\chi^2$ ) test. Multivariate logistic regression analysis was applied to identify independent risk factors associated with *Candida* UTIs. A two-tailed P-value of <0.05 was considered statistically significant.

## Results

### General Information

Between 2020 and 2024, a total of 230 *Candida* strains were isolated from 229 patients diagnosed with urinary tract infections, including 138 males and 91 females. The average age of male patients was  $72.20 \pm 15.87$  years, while that of female patients was  $72.27 \pm 18.92$  years. No statistically significant differences were observed in gender or age distribution ( $P > 0.05$ ) (Table 1). The results indicated that over the past five years, the age and gender distribution of *Candida* UTIs patients has remained relatively stable in our hospital. This demographic stability of the cohort over time provided a crucial foundation for the subsequent analysis of risk factors and antifungal resistance trends.

**Table 1** Age and Gender Distribution of Patients with *Candida* UTIs

|           | Total | 2020 | 2021 | 2022 | 2023 | 2024 | $\chi^2$ | P     |
|-----------|-------|------|------|------|------|------|----------|-------|
| Gender    |       |      |      |      |      |      |          |       |
| Male      | 138   | 19   | 31   | 27   | 26   | 35   | 3.345    | 0.502 |
| Female    | 91    | 15   | 21   | 17   | 23   | 15   |          |       |
| Age Group |       |      |      |      |      |      |          |       |
| ≤39       | 11    | 4    | 3    | 2    | 1    | 1    | 18.151   | 0.111 |
| 40-59     | 29    | 6    | 7    | 3    | 5    | 8    |          |       |
| 60-79     | 100   | 10   | 19   | 21   | 20   | 30   |          |       |
| ≥80       | 89    | 14   | 23   | 18   | 23   | 11   |          |       |

**Notes:**  $\chi^2$ -test was used to compare the distribution of gender and age in *Candida* UTIs patients across different years; The results indicated that no statistically significant differences were observed in gender or age distribution ( $P > 0.05$ ).

## Isolation of *Candida*

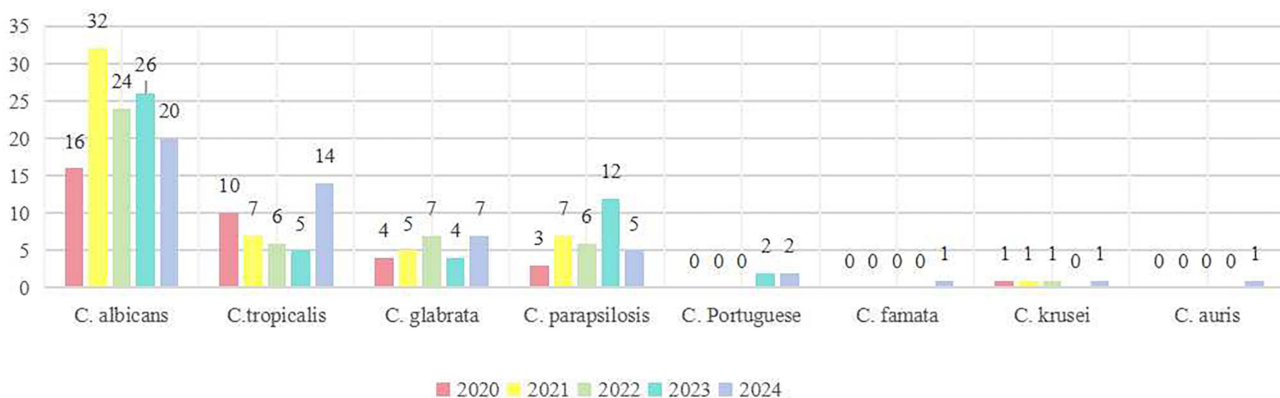
During the study period, 230 *Candida* strains were isolated. The annual distribution was as follows: 34 strains (14.8%) in 2020, 52 (22.6%) in 2021, 44 (19.1%) in 2022, 49 (21.3%) in 2023, and 51 (22.2%) in 2024. *C. albicans* was the most frequently isolated species, accounting for 118 strains (51.3%). The remaining 112 strains (48.7%) were non-*albicans* species, including 42 *C. tropicalis*, 33 *C. parapsilosis*, and 27 *C. glabrata*. Together, these four species represented 95.65% of all isolates.

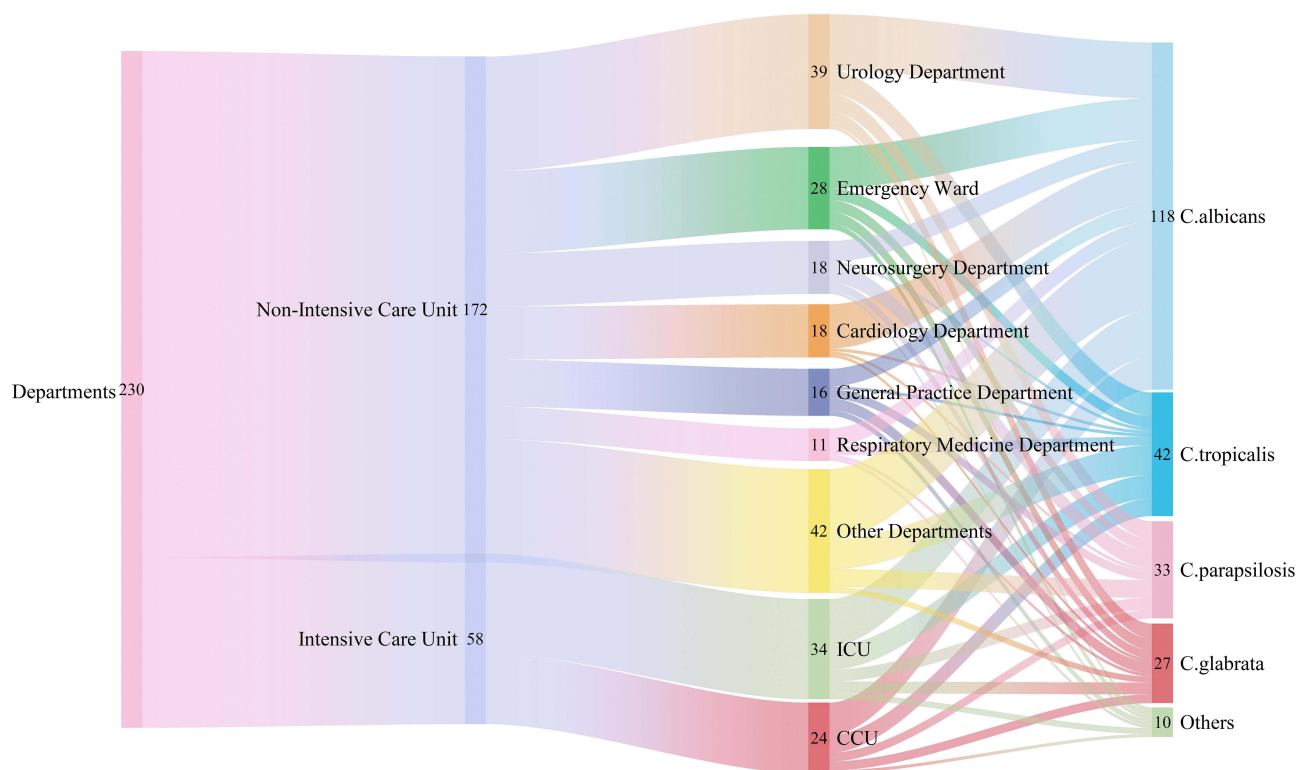
Notably, the detection rate of *C. albicans* showed a declining trend, decreasing from 47.06% in 2020 to 39.22% in 2024, while the proportion of non-*albicans* *Candida* increased correspondingly over the same period (Figure 1). This epidemiological shift posed a significant clinical challenge, as it resulted in a more challenging formulation of empirical treatment strategies, increased complexity in the execution of clinical practice, and heightened the risk of adverse patient outcomes.

## Departmental Distribution

Of the 230 *Candida* isolates, the highest proportions were recovered from patients in the Intensive Care Unit (25.22%) and the Department of Urology (16.96%), underscoring the increased risk of *Candida* infections in these clinical settings.

A total of 58 strains were isolated from Intensive Care Unit patients (Including both the ICU and CCU in our hospital) and 172 from non- Intensive Care Unit wards, with *C. albicans* accounting for 46.55% and 52.91%, respectively. There were no statistically significant differences in species distribution between emergency and non-emergency areas or between ICU and non-ICU wards ( $P > 0.05$ ) (Figure 2), suggesting that it is not possible to simply determine the specific type of *Candida* infection based solely on the patient's department.

**Figure 1** Distribution of *Candida* in Patients with Urinary Tract Infections.



**Figure 2** Distribution of *Candida* Isolates Across Departments.

## Antifungal Susceptibility

### Overall Susceptibility Profile

Due to the discharge of 17 patients and incomplete data for another 14, antifungal susceptibility testing was performed on 199 strains. All tested strains were fully susceptible to amphotericin B and 5-fluorocytosine, with no resistance observed (0.00%).

However, resistance to azole antifungals was comparatively higher: 26.63% for itraconazole, 17.59% for fluconazole, and 16.58% for voriconazole. Resistance rates varied significantly among *Candida* species (Figure 3). Notably, *C. glabrata* exhibited a 44.00% resistance rate to itraconazole, which was significantly higher than that of *C. albicans* ( $\chi^2 = 5.158$ ,  $P = 0.023$ ). Likewise, *C. tropicalis* demonstrated significantly greater resistance to triazole drugs compared to *C. albicans* ( $\chi^2 = 20.441$ ,  $P < 0.0001$ ;  $\chi^2 = 13.241$ ,  $P = 0.003$ ;  $\chi^2 = 11.991$ ,  $P = 0.0005$ ).

### Temporal Trends in Resistance

An assessment of resistance trends in *C. albicans* and *C. tropicalis* from 2020 to 2024 revealed fluctuations in triazole resistance rates over time. However, these variations were not statistically significant ( $P > 0.05$ ) (Figure 4). The results indicated that the resistance of these two main types of *Candida* to triazole drugs remained relatively stable. Continuous monitoring remains crucial to promptly detect any potential resistance turning points.

## Factors Associated with *Candida* Urinary Tract Infections

Significant differences were observed between patients with *Candida* UTIs and bacterial UTIs in terms of hospital stay duration, indwelling urinary catheter use, and administration of broad-spectrum antibiotics ( $P < 0.05$ ) (Table 2). And these indicated that *Candida* UTIs was related to medical interventions to some extent. For patients with these risk factors, clinicians should be highly alert and screen for *Candida* UTIs timely.

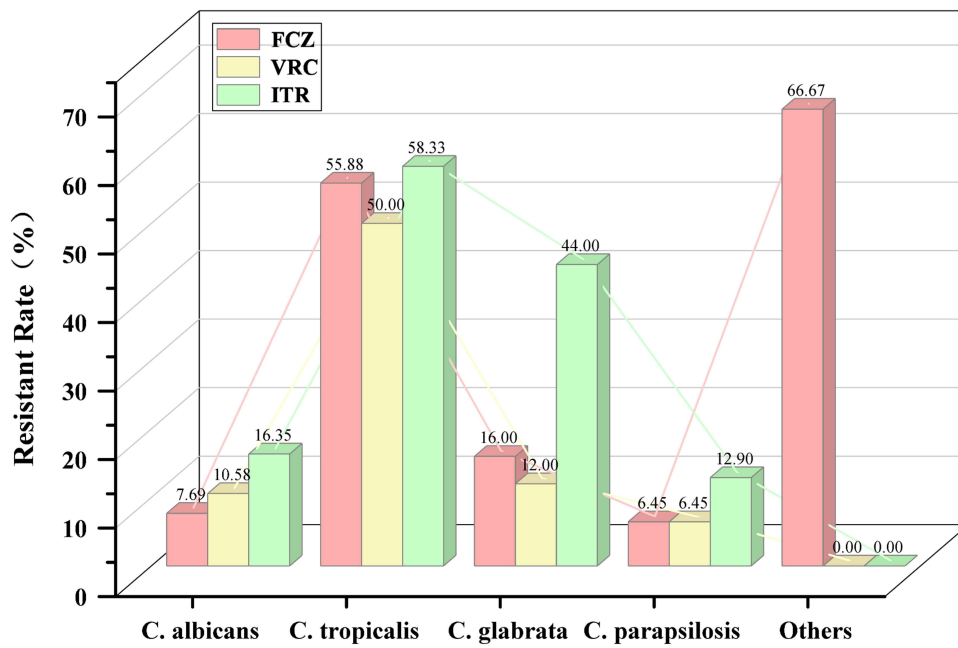


Figure 3 Antifungal Drug Resistance in *Candida* Strains.

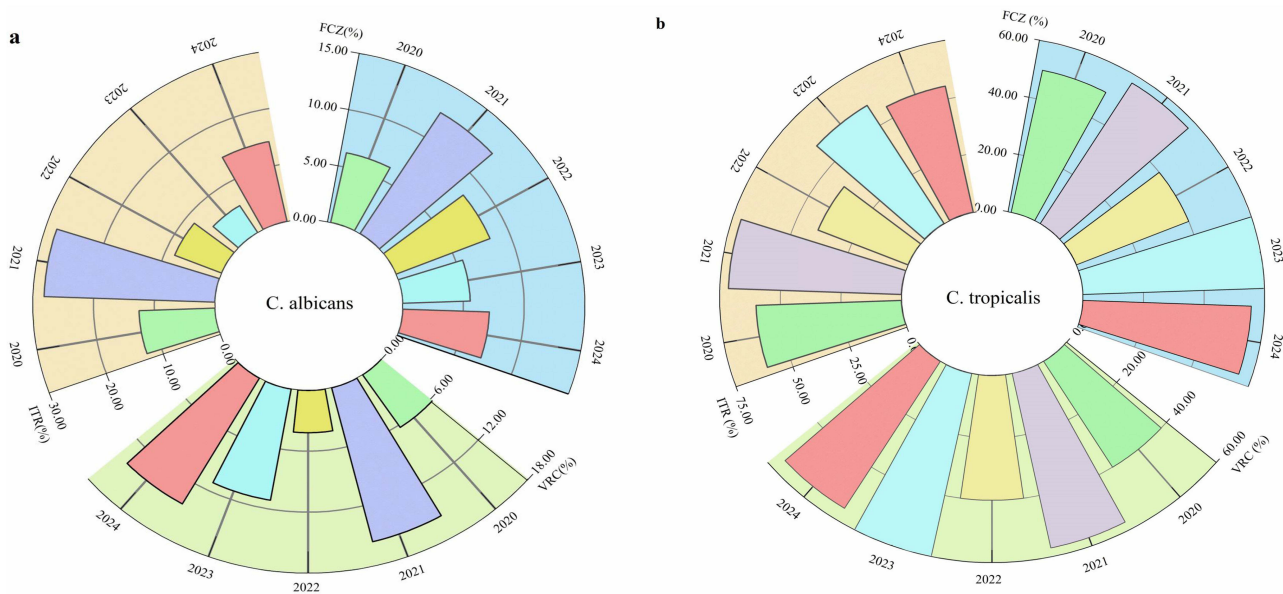


Figure 4 Antifungal Resistance of *C. albicans* and *C. tropicalis* Over the Years. (a) Antifungal Resistance of *C. albicans* (b) Antifungal Resistance of *C. tropicalis*.

### Independent Risk Factors

Multivariate logistic regression analysis identified hospital stay duration ( $\geq 14$  days) and indwelling urinary catheter use ( $\geq 7$  days) as independent risk factors for the development of *Candida* urinary tract infections. The use of broad-spectrum antibiotics did not retain statistical significance in the multivariate model ( $P < 0.05$ ) (Table 3), demonstrating that on the basis of ensuring therapeutic effect, strictly controlling the hospital stay duration and maximizing the reduction of catheter dwell time were core intervention measures to lower the risk of *Candida* UTIs.

**Table 2** Factors Associated with *Candida* Urinary Tract Infections

| Factors                    |          | <b>Candida UTI Patients (n=229)</b> | <b>Bacterial UTI Patients (n=229)</b> | $\chi^2$ | <b>P</b> |
|----------------------------|----------|-------------------------------------|---------------------------------------|----------|----------|
| Gender                     | Male     | 138                                 | 141                                   | 0.082    | 0.774    |
|                            | Female   | 91                                  | 88                                    |          |          |
| Age                        | ≥70      | 148                                 | 130                                   | 2.965    | 0.085    |
|                            | <70      | 81                                  | 99                                    |          |          |
| Hospital stay duration     | ≥14 days | 155                                 | 93                                    | 33.801   | 0.0001   |
|                            | <14 day  | 74                                  | 136                                   |          |          |
| Diabetes                   | Yes      | 85                                  | 70                                    | 2.194    | 0.139    |
|                            | No       | 144                                 | 159                                   |          |          |
| Catheter time              | ≥7 days  | 161                                 | 124                                   | 12.721   | 0.0004   |
|                            | <7 day   | 68                                  | 105                                   |          |          |
| Broad-spectrum Antibiotics | Yes      | 193                                 | 173                                   | 5.441    | 0.020    |
|                            | No       | 36                                  | 56                                    |          |          |
| Immunosuppression          | Yes      | 11                                  | 6                                     | 1.527    | 0.216    |
|                            | No       | 218                                 | 223                                   |          |          |

**Notes:**  $\chi^2$ -test was used to identify potential risk factors associated with *Candida* UTIs compared to bacterial UTIs; The results indicated that the hospital stay duration, indwelling urinary catheter use and administration of broad-spectrum antibiotics were associated with *Candida* UTIs significantly ( $P < 0.05$ ).

**Table 3** Independent Risk Factors for *Candida* Urinary Tract Infections

|                                   | <b>B</b> | <b>Wald</b> | <b>OR (95% CI)</b> | <b>P</b> |
|-----------------------------------|----------|-------------|--------------------|----------|
| Female                            | -0.121   | 0.352       | 0.886(0.596–1.320) | 0.553    |
| Age≥70                            | 0.022    | 0.011       | 1.023(0.672–1.555) | 0.917    |
| Hospital stay duration≥14 days    | 0.860    | 13.997      | 2.364(1.506–3.704) | 0.0001   |
| Use of broad-spectrum antibiotics | 0.185    | 0.420       | 1.203(0.688–2.102) | 0.517    |
| Diabetes                          | 0.214    | 1.015       | 1.237(0.817–1.876) | 0.314    |
| Catheter time≥7 days              | 0.657    | 7.537       | 1.931(1.206–3.086) | 0.006    |
| Immunosuppression                 | 0.600    | 1.193       | 1.822(0.621–5.345) | 0.275    |

## Discussion

*Candida* species have emerged as increasingly important fungal pathogens in urinary tract infections, particularly among patients with compromised immunity, prolonged antibiotic exposure, or indwelling urinary catheterization.<sup>11</sup> In immunocompromised hosts, *Candida* UTIs can escalate into candidemia and systemic candidiasis, severe conditions associated with high mortality rates and considerable healthcare expenditures.<sup>12</sup> Hence, early diagnosis and targeted antifungal therapy remains pivotal for enhancing patient prognosis and reducing disease burden. Although bacterial UTIs have been extensively studied, research on *Candida* UTIs remains relatively limited. In our hospital, *Candida* has emerged as the fourth most common causative agent of UTIs, with especially high detection rates in intensive care and urology departments, which aligns with previous reports.<sup>13</sup> This likely reflects the enhanced vulnerability of patients in these units, which can be attributed to their critical illness status and associated immune dysfunction.

Notably, our five-year surveillance data revealed a decline in the detection rate of *C. albicans* and a corresponding increase in non-*albicans* species. This trend aligns with findings from previous studies: Arastehfar et al<sup>14</sup> reported a similar pattern in critically ill patients in Iran, while Mesini et al<sup>15</sup> observed analogous shifts in pediatric populations. Furthermore, regional variations in *Candida* species distribution, as illustrated by Hu Ailing et al,<sup>16</sup> emphasize the critical need for localized surveillance to inform and optimize targeted antifungal therapy.

In our cohort, two key patient characteristics may have contributed to the elevated detection rate of non-*albicans* *Candida* species: a high proportion of elderly patients (with a mean age of 72.2 years) and a substantial prevalence of

chronic comorbidities. These comorbidities included malignancy (21.4%), diabetes mellitus (20.5%), cerebrovascular disease (17.0%), pneumonia (14.0%), and cardiovascular disease (10.5%). Age-related immunosenescence and structural urinary tract changes render this population more vulnerable to drug-resistant fungal infections.<sup>17</sup>

For symptomatic *Candida* UTIs, fluconazole continues to be recommended as first-line therapy, primarily due to its excellent urinary excretion.<sup>18</sup> However, our antifungal susceptibility testing of 199 isolates uncovered two key findings: species-specific resistance patterns and year-to-year variability in susceptibility. While all isolates remained fully susceptible to amphotericin B and 5-fluorocytosine (resistance rate: 0.00%), resistance to azoles—particularly triazoles—was prominent.

*C. albicans* and *C. parapsilosis* exhibited relatively low azole resistance, which aligns with prior studies.<sup>19</sup> In contrast, *C. tropicalis* showed significantly higher triazole resistance ( $P < 0.05$ ); this is likely due to its robust biofilm-forming capacity, a trait that enhances antifungal tolerance.<sup>20</sup> The historically low detection of *C. tropicalis* may have led to its under recognition in clinical practice and the overuse of fluconazole as empirical therapy. This could have facilitated the emergence of azole-resistant *C. tropicalis* strains.<sup>21</sup> Notably, *C. glabrata* also displayed concerning itraconazole resistance (44.00%), a finding consistent with results reported by Pramodhini et al<sup>22</sup> from a tertiary care center in South India. This further reinforces the importance of species-level identification in managing *Candida* infections. Consequently, significant variation in susceptibility to triazole antifungals drugs existed among *Candida* species. Relying solely on empiric therapy may not only be ineffective but also potentially exacerbate drug resistance. It is imperative to obtain species identification and antifungal susceptibility testing to guide targeted treatment. For critically ill or high-risk patients without available antifungal susceptibility results, therapy could be informed by local epidemiological data and antifungal resistance surveillance findings.

Our analysis identified prolonged hospitalization ( $\geq 14$  days) and long-term catheterization ( $\geq 7$  days) as independent risk factors for *Candida* UTIs, corroborating previous studies.<sup>1,23</sup> Extended hospital stays and indwelling urinary catheters can disrupt both the natural physical barrier of the urinary tract and the local mucosal immune microenvironment, elevating the risk of *Candida* colonization and subsequent UTIs development. Therefore, in clinical practice, efforts should prioritize minimizing unnecessary urinary catheterization and closely monitoring infection-related indicators in hospitalized patients; these measures are critical to reduce the occurrence of *Candida* UTIs. Interestingly, in contrast to some earlier studies,<sup>24</sup> the use of broad-spectrum antibiotics was not found to be an independent risk factor for *Candida* UTIs in our cohort. This discrepancy may be attributable to limitations in our sample size, which could have constrained the statistical power to detect such an association if it exists.

This study had several limitations. Firstly, antifungal susceptibility was determined using the ATB™ FUNGUS 3 system, which lacks susceptibility assessment for echinocandin. Secondly, some eligible patients were excluded from the drug resistance analysis, potentially affecting result generalizability. Future research could aim to expand the sample size, incorporate echinocandin susceptibility testing, and establish long-term resistance surveillance, thereby offering more comprehensive evidence to guide clinical treatment strategies.

In summary, our five-year analysis revealed an increasing prevalence of non-*C. albicans* species among *Candida* UTIs, with *C. tropicalis* showing notable azole resistance. Notably, amphotericin B and 5-fluorocytosine remained viable treatment options. Risk factor analysis further emphasized the critical role of hospitalization duration and catheter use in increasing susceptibility to *Candida* UTIs. This study highlighted routine species identification and antifungal susceptibility testing are essential to guide tailored therapy, improve treatment efficacy, and alleviate patient burden. For high-risk patients or those with fluconazole-resistant infections, first-line therapy with echinocandins or amphotericin B is recommended; additionally, immediate involvement of infection control teams is advised upon detection of rare or highly resistant strains. Future research warrants the establishment of a multicenter prospective surveillance network. This network would enable dynamic monitoring of regional antifungal resistance patterns, ultimately providing evidence to inform the development of localized, tailored empirical therapy strategies.

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Ethics Approval and Informed Consent

The study protocol was approved by the Ethics Committee of The Third Medical Centre of Chinese PLA General Hospital (KY2024-018), and the patients provided written informed consent at the time of entering this study. We confirmed that the data was anonymized or maintained with confidentiality in line with the Declaration of Helsinki.

## Consent for Publication

All authors confirm that the details of any images, videos and recordings can be published.

## Funding

This study was supported by Beijing Natural Science Foundation (7252170) and Beijing Novo Program (20250484960).

## Disclosure

The authors declare no conflicts of interest in this work.

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