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ORIGINAL RESEARCH

Clinical Characteristics and Risk Factors for Mortality in Candidemia: A Retrospective Single-Center Study in China

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Purpose: Candidemia is a major cause of hospital-acquired bloodstream infections and is associated with high mortality. This study evaluated clinical characteristics, pathogen distribution, antifungal susceptibility, and factors associated with 28-day outcome in patients with candidemia.

Methods: We retrospectively analyzed 169 patients with confirmed candidemia at Guangdong Provincial People's Hospital from January 2021 to December 2023. Patients were classified as survivors (n = 81) or non-survivors (n = 88) according to 28-day outcome. Species distribution, time to positivity (TTP), antifungal susceptibility, clinical features, and prognostic factors were compared. Variables significant in univariate analysis were entered into a multivariable logistic regression model.

Results: Most patients were admitted to the intensive care unit (70.41%), and the 28-day mortality rate was 52.07%. The main causative species were *Candida albicans* (38.46%), *Candida parapsilosis* (27.22%), *Candida glabrata* (15.98%), and *Candida tropicalis* (15.98%). TTP differed significantly among species; *C. tropicalis* showed the shortest median TTP (18.73 h), whereas *C. parapsilosis* and *C. glabrata* showed longer TTPs (38.34 h and 37.15 h, respectively; $P < 0.0001$). *C. tropicalis* showed high resistance rates to fluconazole and voriconazole, at 33.33% and 37.04%, respectively. Univariate analysis showed that age, coronary heart disease, respiratory disease, concomitant bacterial bloodstream infections, septic shock, APACHE II score, catheter insertion, mechanical ventilation, glucocorticoid use, antifungal treatment within 48 h, and antifungal therapy duration ≥14 days were associated with 28-day mortality. Multivariate logistic regression further demonstrated that only antifungal therapy lasting ≥14 days emerged as an independent risk factor for 28-day mortality.

Conclusion: Candidemia entails severe infection and poor prognosis, with *C. albicans* predominating. Clinicians should maintain vigilant monitoring and interventions targeting identified risks while tracking evolving resistance patterns.

Keywords: Candidemia, *Candida albicans*, mortality risk factors, epidemiology, in vitro antifungal susceptibility

Introduction

The widespread use of broad-spectrum antimicrobials, corticosteroids, immunosuppressants, cancer therapies, invasive catheterization, and organ transplantation has substantially increased the immunocompromised population at risk for fungal infections.[1,2] Invasive candidiasis (IC) is increasingly prevalent worldwide, representing a significant threat to patient health. Candidemia, the most common manifestation of IC, ranks as the fourth most frequent hospital-acquired

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bloodstream infection.[3] It frequently results in a prolonged hospitalization and poor clinical outcomes, with mortality rates reaching 35% to 70%.[4–7] The increase in mortality may be associated with the rise in non-*Candida albicans Candida* (NCAC) infections.[5,8] Current diagnostic challenges for candidemia include non-specific clinical manifestations and the suboptimal performance of blood cultures characterized by low sensitivity and prolonged turnaround times. Compounding these issues, certain *Candida* species exhibit escalating resistance rates and demonstrate healthcare-associated transmission.[6] Notably, the rising prevalence of azole-resistant *C. tropicalis* strains with significant cross-resistance further complicates both early diagnosis and effective antifungal intervention.[7,9–11] Moreover, the species distribution and drug susceptibility profiles of *Candida* vary by geographic region and over time.[12,13]

Given these challenges, it is imperative to investigate the species distribution, in vitro antifungal susceptibility profiles, clinical characteristics of candidemia patients, and particularly mortality risk factors. Such insights will provide critical evidence for early targeted therapy and optimized clinical interventions. Accordingly, this single-center retrospective study analyzed clinical data from patients with candidemia at our institution between January 2021 and December 2023. We systematically examined the demographic and clinical characteristics, pathogen distribution patterns, in vitro antifungal susceptibility results, and prognostic determinants. This comprehensive analysis aims to establish evidence-based guidance for improving candidemia management through early diagnosis and precision treatment.

Materials and Methods

Study Population

This study population included 169 patients diagnosed with candidemia at Guangdong Provincial People's Hospital between January 2021 and December 2023. All patients met the diagnostic criteria for candidemia as outlined in the 2016 IDSA Clinical Practice Guidelines for the Management of Candidiasis. Inclusion criteria were as follows: i) at least one positive blood culture for *Candida*, with the first positive culture used for patients with multiple positive cultures; ii) exclusion of bacteremia alone, filamentous fungemia, cryptococcal fungemia, missing records of time to positivity (TTP), and duplicated strains; iii) availability of complete clinical data, including symptoms, signs, auxiliary diagnostic results, laboratory tests, and medical records.

Data Collection

Data collected included clinical characteristics, risk factors, in vitro antifungal susceptibility (AFST) results, treatment methods, and prognosis. Based on the 28-day prognosis following the first positive blood culture, patients were categorized into survival and non-survival groups. TTP was defined as the time interval from the start of blood culture incubation to the automated positive signal indicating organism growth. If both aerobic and anaerobic bottles were positive, the shorter TTP was used for analysis. If a patient had persistent candidemia with multiple positive blood cultures, only the TTP of the first positive blood culture episode was recorded. APACHE II scores were assessed at admission date; (1,3)-β-D-glucan (BDG) levels were measured at blood culture date.

Candida Isolation and Identification

Bilateral venous blood was collected aseptically using the BD BACTEC™ Plus Aerobic/F Culture Vials (Becton Dickinson, USA). After inoculation, the blood culture bottles were placed in the BD BACTEC^{TM} FX system (Becton Dickinson, USA) for incubation and automatic detection of positivity. Gram staining was performed on positive culture vials. If yeast-like fungi were observed, the cultures were inoculated onto Sabouraud Agar (SDA) and CHROM agar and incubated at 35 °C for 24–48 hours. Species identification was conducted using the VITEK MS (IVD 3.2) mass spectrometer (bioMérieux, France). AFST was performed using the ATB FUNGUS 3 kit (bioMérieux, France), strictly adhering to the manufacturer's instructions.

Antifungal Susceptibility Testing

AFST of *Candida* spp. to antifungal antibiotics were performed on ATB Fungus 3 kit, strictly adhering to the manufacturer's instructions: i) pick a single isolated colony and suspend it in 0.9% sterile saline to match the 2.0 McFarland standard; ii) add 20 μL to each lyophilized ampoule and vortex well; iii) add 135 μL to each microtiter well. Incubate the plate aerobically at 35 °C ± 2 °C in a humidified incubator for 24 ± 2 hours. Use *C. parapsilosis* ATCC 22019 as the quality control strain. Minimum inhibitory concentrations (MICs) for all antifungal drugs were recorded after 24 hours of incubation. AFST results were interpreted according to CLSI M59 and CLSI M60 standards.[14,15] Based on the recommended clinical breakpoints (CBPs), results were classified as susceptible (S), intermediate (I), susceptible-dose dependent (SDD), or resistant (R). Epidemiological cutoff values (ECVs) were also applied: isolates with MICs ≤ ECVs were classified as wild-type (WT), and those with MICs > ECVs were classified as non-wild-type (NWT). Due to the lack of recommended CBPs and ECVs for 5-fluocytosine, its susceptibility results were not analyzed in this study.

Statistical Analysis

Statistical analysis was performed using SPSS 23.0 software. Normally distributed continuous variables were expressed as mean ± standard deviation and compared using independent samples t-tests. Non-normally distributed variables were expressed as median and interquartile range [M (P_{25}, P_{75})] and compared using the Mann–Whitney *U*-test. Categorical variables were expressed as percentages (%) and compared using the chi-square (χ^2) test. Variables with statistical significance in univariate analysis were included in a multivariate logistic regression model to calculate odds ratios (OR) and 95% confidence intervals (CI). A P-value < 0.05 was considered statistically significant. Variables with collinearity or clinical overlap were excluded from the multivariable model after model diagnostics.

Results

Pathogen Detection and Related Findings

Among 169 *Candida* isolates, *C. albicans* accounted for 38.46% (65/169) while NCAC species represented 61.54% (104/169), demonstrating a statistically significant predominance of NCAC (χ^2 = 17.09, P < 0.0001). NCAC distribution comprised: *C. parapsilosis* (27.22%, 46/169), *C. glabrata* (15.98%, 27/169), *C. tropicalis* (15.98%, 27/169), and other species (2.37%, 4/169) (Figure 1A). Most patients originated from intensive care units (70.41%, 119/169), with surgical wards contributing 17.75% (30/169) (Figure 1B). Temporal analysis revealed a significant epidemiological shift: The isolation rate of *C. parapsilosis* increased progressively from 18.18% (12/66) in 2021 to 28.26% (13/46) in 2022 and further to 36.84% (21/57) in 2023, whereas that of *C. albicans* declined from 48.48% (32/66) in 2021 to 32.61% (15/46) in 2022 and subsequently to 31.58% (18/57) in 2023. (Figure 1C). The median TTP for all isolates was 31.08 hours (IQR 23.23–45.63), with only 26.03% (44/169) yielding TTPs < 24 hours. Significant interspecies variation was observed (Kruskal–Wallis Z = 35.90, P < 0.0001): *C. tropicalis* demonstrated the shortest TTP (18.73 hours, IQR 14.70–26.22), followed by *C. albicans* (28.70 hours, IQR 23.23–47.12), while *C. parapsilosis* (38.34 hours, IQR 30.04–46.45) and *C. glabrata* (37.15 hours, IQR 25.65–62.27) exhibited the longest TTP (Figures 1D). Figure 2 shows that *C. glabrata* and *C. tropicalis* showed the highest mortality rates, both at 66.67%. *C. albicans* showed an intermediate mortality rate of 52.31%, whereas *C. parapsilosis* had the lowest mortality rate, at 36.96% (P < 0.05). This gradient distribution reveals distinct pathogenic differences among strains, notably with *C. glabrata* and *C. tropicalis* showing nearly 30 percentage points higher mortality than *C. parapsilosis*. These findings provide key insights for clinical precision medicine, underscoring an urgent need to strengthen rapid identification of high-risk strains and develop differentiated treatment strategies.

Morphological Characteristics of Candida Species on Blood Smears and CHROM Agar

All four *Candida* species exhibited yeast-like blastoconidia with predominantly oval-to-spherical morphology on smears prepared from positive blood culture vials (Figure 3A–D). Distinctive morphological features were observed: *C. parapsilosis* demonstrated elongated oval blastoconidia (Figure 3C), while *C. glabrata* displayed significantly smaller cellular dimensions compared to other species (mean diameter 2.1 ± 0.3 μm vs 4.5 ± 0.6 μm in *C. albicans,* P < 0.001)

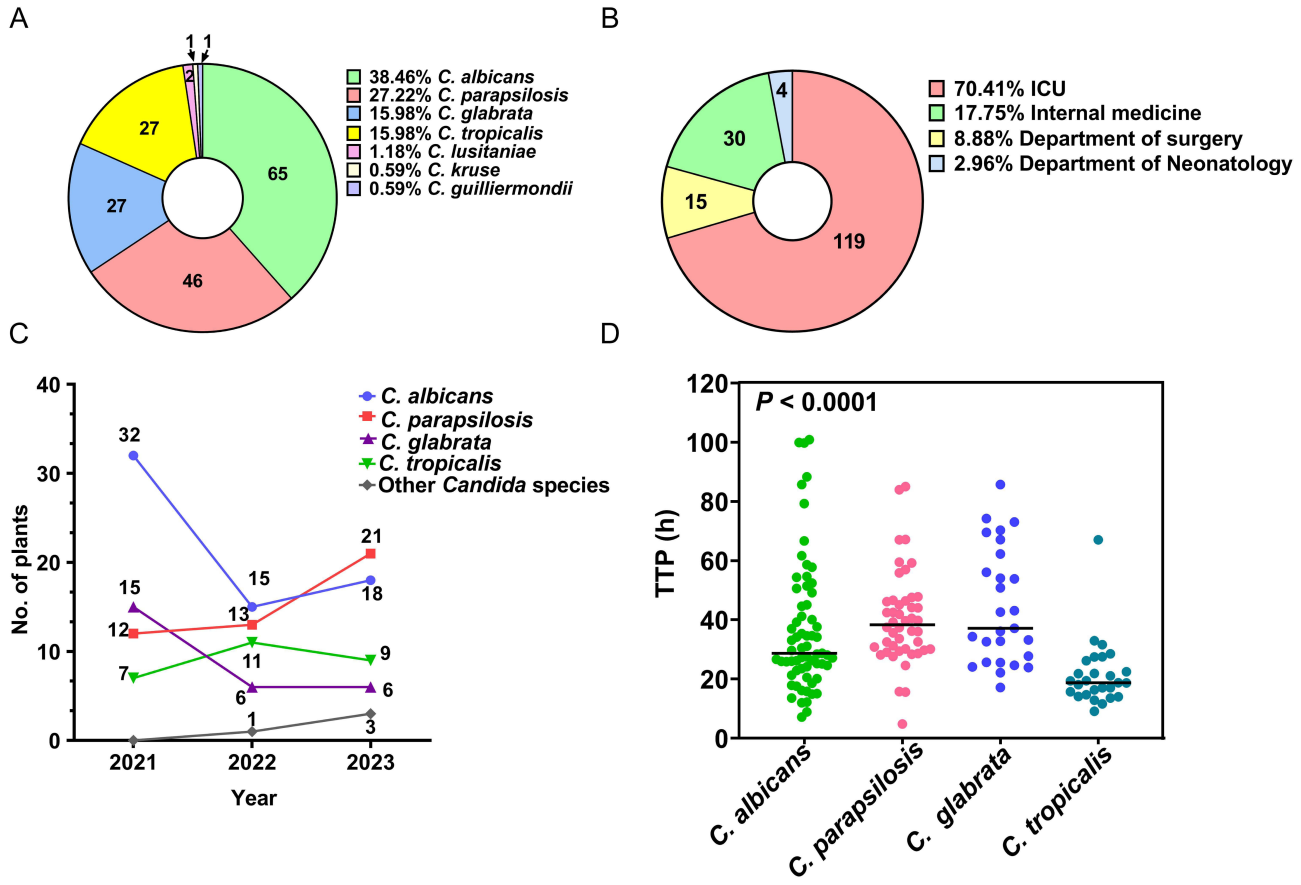

Figure 1 Etiological distribution and clinical characteristics of candidemia. (**A**) Species distribution of *Candida* isolates (n = 169); (**B**) distribution across hospital wards; (**C**) temporal trends in species distribution from 2021 to 2023; (**D**) comparison of time to positivity among predominant *Candida* species ($P < 0.0001$).

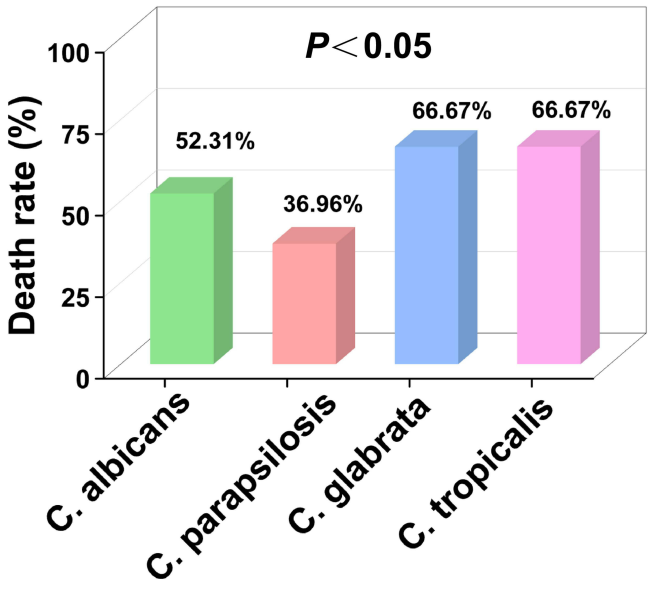

Figure 2 Mortality rates among patients infected with different *Candida* species.

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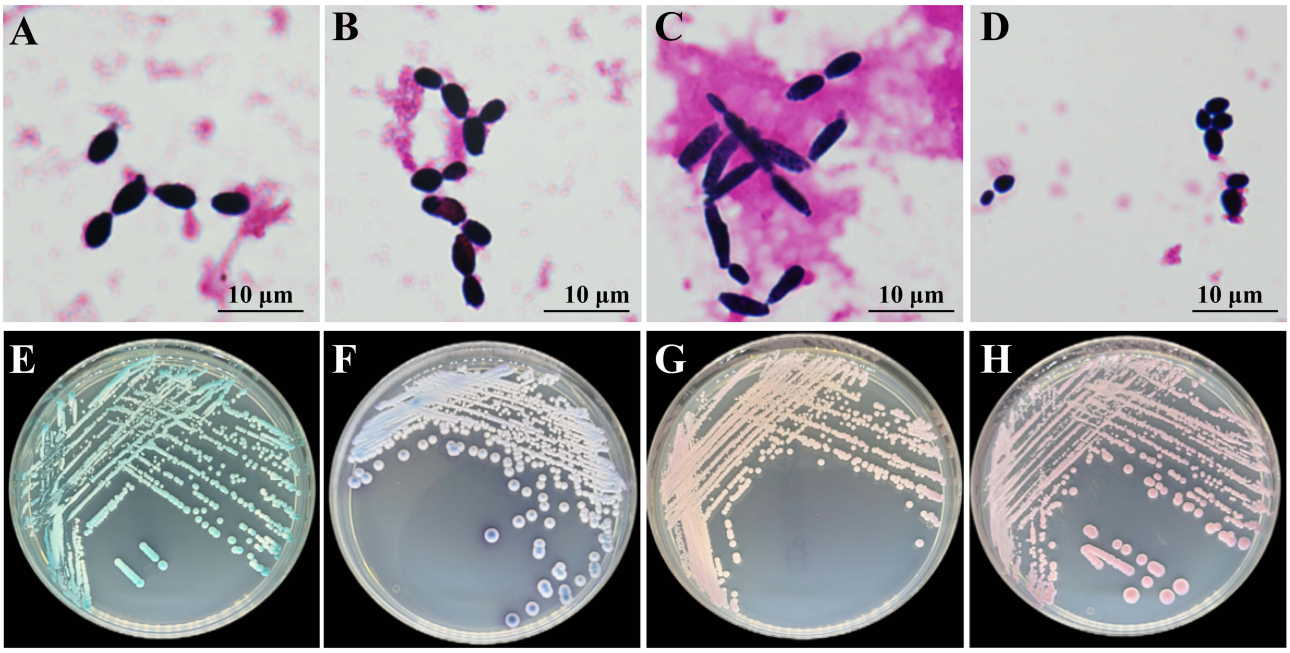

Figure 3 Morphological and chromogenic characteristics of predominant *Candida species*. (**A–D**) Gram-stained blood culture smears (×1000): (**A**) *C. albicans*; (**B**) *C. tropicalis*; (**C**) *C. parapsilosis*; (**D**) *C. glabrata*. (**E–H**) CHROMagar *Candida* colonies (37 °C, 24 h): (**E**) *C. albicans* (emerald green); (**F**) *C. tropicalis* (slate-gray); (**G**) *C. parapsilosis* (pale pink); (**H**) *C. glabrata* (purple center, white periphery).

(Figure 3D). After 24 hours of incubation at 37 °C on CHROM agar, chromogenic differentiation yielded species-specific colony pigmentation: *C. albicans* formed emerald green colonies; *C. tropicalis* produced slate-gray colonies with a metallic sheen; *C. parapsilosis* developed pale pink colonies exhibiting smooth margins; and *C. glabrata* displayed central purple pigmentation surrounded by a white periphery (representative microscopic and macroscopic appearances are shown in Figure 3E–H, respectively).

AFST Results for Four Common Candida Species

C. albicans exhibited low resistance rates to fluconazole (4.62%; 3/65) and voriconazole (4.62%; 3/65). Similarly, *C. parapsilosis* showed low resistance to voriconazole (4.35%; 2/46) and fluconazole (8.70%; 4/46), along with a low NWT rate to itraconazole (4.35%; 2/46). In contrast, *C. tropicalis* demonstrated high resistance rates to both fluconazole (33.33%; 9/27) and voriconazole (37.04%; 10/27), with an MIC_{90} of 128 μg/mL and a geometric mean (GM) of 34.48 μg/mL for fluconazole. *C. tropicalis* also exhibited a high NWT rate to itraconazole (33.33%; 9/27). While *C. glabrata* had a higher resistance rate to voriconazole (18.52%; 5/27), no resistance or NWT isolates were observed for fluconazole or itraconazole. No NWT strains of amphotericin B were detected. Overall, *C. albicans, C. tropicalis*, and *C. parapsilosis* displayed varying degrees of resistance to fluconazole and voriconazole (Table 1).

Clinical Characteristics of Candidemia Patients

The cohort comprised 169 patients (111 males, 65.68%; 58 females, 34.32%) with a mean age of 65.13 ± 20.35 years. Most patients had invasive devices: indwelling urinary catheters (124/169, 73.37%), catheter insertion (111/169, 65.68%), and mechanical ventilation (135/169, 79.88%). Based on 28-day mortality following initial blood culture positivity, patients were stratified into survival (n=81) and non-survival (n=88) groups, yielding a 28-day mortality rate of 52.07% (88/169).

Univariate analysis showed that age, coronary heart disease, respiratory disease, bacterial bloodstream infections (BSIs), septic shock, APACHE II score, catheter insertion, mechanical ventilation, glucocorticoid use, antifungal treatment within 48 h, and duration of antifungal therapy (≥ 14 days) were factors associated with 28-day outcome in patients with candidemia ($P < 0.05$) (Table 2).

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Table 1 In vitro Antifungal Susceptibility Testing Results of Four Prevalent *Candida* Species Isolated from Bloodstream Samples [N]

Antifungal Agents	MIC_{50}	MIC_{90}	GM	MICs (μg/mL)												
				0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	R/NWT%
C. albicans (n=65)																
Amphotericin B	0.5	0.5	0.5				65									0.00
Fluconazole	1	1	6.86					62							3	4.62
Itraconazole	0.125	0.125	0.26		62			1		2						—
Voriconazole	0.06	0.06	0.4	61		1					3					4.62
C. parapsilosis (n=46)																
Amphotericin B	0.5	0.5	0.51				45	1								0.00
Fluconazole	1	4	4.3					34	5	3	2			2		8.70
Itraconazole	0.125	0.125	0.23		44			1		1						4.35
Voriconazole	0.06	0.125	0.2	40	3	1			1	1					4.35	
C. tropicalis (n=27)																
Amphotericin B	0.5	0.5	0.5				27									0.00
Fluconazole	1	128	34.48					17	1		2				7	33.33
Itraconazole	0.125	4	0.91		15	1	3	3	1	4						33.33
Voriconazole	0.06	8	2.36	14	2		1	2		1	7					37.04
C. glabrata (n=27)																
Amphotericin B	0.5	0.5	0.5				27									0.00
Fluconazole	4	4	3.11					8	4	13	2					0.00
Itraconazole	0.25	1	0.49		11	3	6	6	1							0.00
Voriconazole	0.125	0.5	0.25	10	3	9	3	2								18.52

Notes: MIC_{50}: MIC required to inhibit the growth of 50% of the strains; MIC_{90}: MIC required to inhibit the growth of 90% of strains; GM: geometric mean of MIC; R: resistance; NWT: non-wild strains; —: There are no clinical and epidemiological breakpoint. Due to the lack of recommended CBPs and ECVs for 5-fluocytosine, its susceptibility results were not analyzed in this study.

Table 2 Univariate Analysis of Prognostic Factors for Candidemia [n(%)]

Risk Factors	Total Number of Cases	Survival Group	Death Group	χ^2/t/Z value	*P* value
	(n=169)	(n=81)	(n=88)		
Male	111 (65.68)	51 (62.96)	60 (68.18)	0.51	0.475
Female	58 (34.31)	30 (37.03)	28 (31.82)		
Age	65.13±20.35	61.09±20.41	68.79±19.72	−2.453	0.015*
ICU stay >14 days	88 (52.07)	36 (44.44)	52 (59.09)	3.625	0.057
Diabetes	51 (30.18)	20 (24.69)	31 (35.22)	2.222	0.136
Coronary heart disease	56 (33.14)	17 (20.98)	39 (44.31)	10.362	0.001*
Cardiovascular disease	102 (60.36)	44 (54.32)	58 (65.90)	2.367	0.124
COPD	11 (6.51)	5 (6.17)	6 (6.81)	0.029	0.865
Respiratory disease	93 (55.03)	33 (40.74)	60 (68.18)	12.834	0.000*
Cerebrovascular disease	45 (26.62)	20 (24.69)	25 (28.40)	0.298	0.585
Chronic liver disease	11 (6.51)	5 (6.17)	6 (6.81)	0.506	0.477

(*Continued*)

Table 2 (Continued).

Risk Factors	Total Number of Cases (n=169)	Survival Group (n=81)	Death Group (n=88)	χ^2/t/Z value	*P* value
Chronic renal disease	32 (18.93)	16 (19.75)	16 (18.18)	0.068	0.795
Hematological disease	9 (5.32)	3 (3.70)	6 (6.81)	0.811	0.368
Autoimmune disease	2 (1.18)	1 (1.23)	1 (1.13)	0.003	0.953
Malignant solid tumor	32 (18.93)	17 (20.98)	15 (17.04)	0.427	0.513
MODS	14 (8.28)	6 (7.40)	8 (9.09)	0.157	0.692
Three or more comorbidities	64 (37.87)	29 (35.80)	35 (39.77)	0.283	0.595
Concomitant BSIs	22 (13.02)	6 (7.40)	16 (18.18)	4.324	0.038*
Septic shock	43 (25.44)	10 (12.34)	33 (37.50)	14.068	0.000*
APACHE II	23.72±8.32	20.08±7.34	25.87±8.45	−2.982	0.004*
Recent surgical history	87 (51.47)	46 (56.79)	41 (46.59)	1.757	0.185
Catheter insertion	111 (65.68)	41 (50.61)	70 (79.54)	15.658	0.000*
Mechanical ventilation	135 (79.88)	57 (70.37)	78 (88.63)	8.756	0.003*
Indwelling catheter	124 (73.37)	59 (72.83)	65 (73.86)	0.023	0.88
Indwelling drainage tube	92 (54.43)	50 (61.72)	42 (47.72)	3.334	0.068
Use of glucocorticoids	88 (52.07)	34 (42.00)	54 (61.36)	6.353	0.012*
1,3-β-D-glucan (pg/mL)	108.20 (38.75, 346.75)	100.05 (29.65, 311.20)	131.00 (53.7, 430.35)	−1.489	0.137
Prophylactic antifungal	77 (45.56)	35 (43.20)	42 (47.72)	0.347	0.556
Antifungal treatment within 48 h	116 (68.64)	63 (77.77)	53 (60.22)	6.035	0.014*
Type of initial antifungal therapy					
Echinocandins	37 (21.89)	19 (23.45)	18 (20.45)	0.705	0.703
Triazoles	58 (34.31)	34 (41.97)	24 (27.27)		
Polyenes	20 (11.83)	10 (12.34)	10 (11.36)		
Treatment adequacy	67 (39.64)	41 (50.61)	26 (29.54)	3.717	0.054
Use of echinocandins	49 (28.99)	23 (28.39)	26 (29.54)	1.032	0.310
Catheter removal	55 (32.54)	30 (37.03)	25 (28.40)	0.104	0.748
Duration of antifungal therapy (≥14 days)	61 (36.09)	43 (53.08)	18 (20.45)	19.198	<0.001*

Note: *$P < 0.05$.
Abbreviations: MODS, multiple organ dysfunction syndrome; APACHE II, Acute Physiology and Chronic Health Scoring System, 2nd Edition; BSIs, bacterial bloodstream infections.

Multivariable Logistic Regression Analysis of 28-Day Mortality

Multivariate logistic regression analysis indicated that the duration of antifungal therapy (≥ 14 days) was a statistically significant independent risk factor for the outcome (OR = 6.875; 95% CI: 2.194–21.549; $P = 0.001$). In contrast, APACHE II score, presence of coronary heart disease, catheter insertion, and glucocorticoid, age, underlying respiratory disease, BSIs, and initiation of antifungal therapy within 48 hours showed no statistically significant association with the study outcome (all $P > 0.05$) (Table 3).

Table 3 Multivariate Logistic Regression Model Analysis of Prognostic Risk Factors in Patients with Candidemia

Risk Factors	β value	SE	OR value	Wald	95% CI	*P* value
Age	−0.003	0.021	0.997	0.019	0.957–1.039	0.890
Coronary heart disease	−1.224	0.658	0.294	3.458	0.081–1.068	0.063
Respiratory disease	−0.727	0.623	0.484	1.359	0.142–1.641	0.244
Concomitant BSIs	−0.248	0.621	0.780	0.160	0.231–2.635	0.690

(*Continued*)

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Table 3 (Continued).

Risk Factors	β value	SE	OR value	Wald	95% CI	*P* value
APACHE II	−0.069	0.036	0.933	3.771	0.871–1.001	0.052
Catheter insertion	−1.260	0.651	0.284	3.751	0.079–1.015	0.053
Use of glucocorticoids	−1.161	0.605	0.313	3.674	0.096–1.026	0.055
Antifungal treatment within 48 h	0.175	0.675	1.191	0.067	0.317–4.476	0.796
Duration of antifungal therapy (≥14 days)	1.928	0.583	6.875	10.941	2.194–21.549	0.001*

Note: *$P < 0.05$. Septic shock and mechanical ventilation were excluded from the multivariable model because of collinearity/clinical overlap with APACHE II score or disease severity indicators.
Abbreviation: BSIs, bacterial bloodstream infections.

Discussion

Candidemia is a bloodstream infection caused by *Candida* spp. In recent years, the incidence and mortality of candidemia have been increasing year by year, and it has become a serious public health problem worldwide.[5,16] At the same time, the composition of candidemia species is also changing. *C. albicans* remains the leading species, whereas NCAC species are increasing.[17] In this study, it was found that the causative agent of candidemia in our hospital was still represented by *C. albicans* (38.46%), *C. parapsilosis* (27.22%), *C. glabrata* (15.98%), and *C. tropicalis* (15.98%). This distribution is generally consistent with recent Chinese multicenter surveillance data, in which *C. albicans* remains the most common species (approximately 33.8%–46.0%), while *C. parapsilosis* (15.6%-22.0%), *C. tropicalis* (17.6%-21.5%), and *C. glabrata* (11.2%-14.8%) are the predominant NCAC species.[18] We found that *C. parapsilosis* rose from 18.18% to 28.26% to 36.84% over the same period. The rising incidence of *C. parapsilosis* infections warrants focused clinical and microbiological attention, given its growing epidemiological prominence and documented association with the emergence and dissemination of azole-resistant isolates. In recent years, *C. parapsilosis* has emerged as a leading cause of candidemia in multiple geographic regions, with several outbreaks linked to clonal expansion of fluconazole-resistant strains.[2,13]

Blood culture is still the gold standard for the diagnosis of candidemia, but it has been reported that blood culture has low sensitivity, a long TTP, with a reported median of 48 h, and species differences.[19] This study found that *C. tropicalis* had the shortest median TTP (18.73 h), followed by *C. albicans* (28.70 h), while *C. parapsilosis* (38.34 h) and *C. glabrata* (37.15 h) showed the longest TTP, which is consistent with relevant reports.[20] In their report, TTPs of *C. tropicalis* and *C. glabrata* were 21.26 ± 3.20 h and 66.84 ± 30.87 h, respectively. A Korean single-center study also observed that *C. tropicalis* isolates were associated with shorter TTPs compared with other common *Candida* species.[11] Current studies have clarified that TTPs variation is predominantly determined by the intrinsic growth rate of different *Candida* species, rather than the initial fungal load in peripheral blood.[11] This characteristic endows TTPs with important practical value in clinical practice. Before formal species identification results are available, clinicians may preliminarily infer the probable pathogen based on TTPs: a TTP shorter than 24 hours may suggest *C. tropicalis*. Therefore, TTPs may aid in the initial clinical characterization of fungal isolates prior to definitive species identification. In addition, mortality varied markedly by *Candida* species: *C. glabrata* and *C. tropicalis* had the highest mortality at 66.67%, followed by *C. albicans* (52.31%), and *C. parapsilosis* had the lowest rate at 36.96%. Clinicians should prioritize intensive monitoring for patients suspected of being infected with these two high-risk strains according to TTPs.

Following the acquisition of identification and AFST results, therapeutic regimens should be adjusted based on susceptibility profiles and resistance patterns. This study found no NWT isolates of amphotericin B were detected. However, *C. albicans, C. tropicalis*, and *C. parapsilosis* exhibited varying degrees of resistance to fluconazole and voriconazole. Notably, *C. tropicalis* demonstrated resistance rates of 33.33% to fluconazole and 37.04% to voriconazole, consistent with relevant reports.[4] Globally, *C. tropicalis* has exhibited prominent azole resistance, with its fluconazole resistance rate reported at 30%–35% and voriconazole resistance rate at 35%-40%.[5,6] This trend is particularly concerning: azoles remain the cornerstone of first-line antifungal therapy, and increasing azole resistance in *Candida* spp. not only undermines the efficacy of empirical treatment but is also independently associated with higher rates of treatment

failure and adverse clinical outcomes. Therefore, it is necessary to actively send blood cultures for clinical testing, and laboratories should carry out in vitro antifungal susceptibility tests to grasp the changes in drug susceptibility of *Candida*. Clinically, for patients with extremely short TTPs suggestive of *C. tropicalis*, echinocandins are recommended as initial antifungal therapy in settings with prevalent azole resistance to mitigate the risk of treatment failure.

The overall 28-day mortality rate of 52.07% in our cohort falls within the global mortality range of 35%-70% for candidemia.[5] We found that age, coronary heart disease, respiratory disease, bacterial bloodstream infections, septic shock, APACHE II score, catheter insertion, mechanical ventilation, glucocorticoid use, antifungal treatment within 48 h, and duration of antifungal therapy (≥ 14 days) were the variables associated with non-survival in univariate analysis at 28 days, which were slightly different from those reported in related studies, mainly in the association of age and chronic cardiopulmonary diseases with mortality.[1,7,21] These discrepancies may be related to the differences in medical environment and level in different regions.

At present, it is believed that the main causes of candidemia are low immunity and damaged mucosal barrier, and most of the patients (70.41%) are distributed in ICU, and such patients have a long hospital stay, often with urinary catheters (73.37%), central venous catheters (65.68%), mechanical ventilation (79.88%), and glucocorticoids (52%), etc., which make it difficult for the patients' digestive tract to be used normally, and the physiological barrier is destroyed. *Candida* and bacteria colonizing the body surface and environment are prone to invasion of the bloodstream, often complicated by respiratory diseases and septic shock, resulting in a high mortality rate (52.07%), which is similar to that reported in the literature.[19] The APACHE II scoring system is widely used in the ICU, and its score is proportional to the patient's prognosis. In this study, we found that the APACHE II score in the dead group was higher than that in the survival group (25.87 ± 7.57 vs 20.08 ± 7.18), indicating that the patients in the death group were more severely ill and had a worse prognosis. As documented in the relevant report, the APACHE II score strongly predicts ICU mortality, with higher scores in deceased than in surviving patients.[1,2] Additionally, univariate analysis identified antifungal treatment within 48 hours as a notable prognostic factor: patients who received timely antifungal intervention within 48 hours after the first positive blood culture achieved a higher survival rate. This finding is consistent with multiple previous studies, which also confirmed that early antifungal intervention within 48 hours was significantly associated with improved survival outcomes in patients with *Candida* bloodstream infections.[1,9,18] Delayed initiation of antifungal therapy may exacerbate fungal dissemination, amplify systemic inflammatory responses, and further deteriorate organ function, ultimately increasing the risk of death.[2,11]

Nonetheless, our study confirmed that survivors were more likely than non-survivors to receive antifungal therapy for ≥14 days (53.08% vs. 20.45%), largely because patients who died early were unable to complete a full treatment course. Accordingly, long-course antifungal therapy was identified as an independent risk factor for 28-day mortality in the regression model, rather than a protective factor. In the multivariable model, duration of antifungal therapy ≥14 days was independently associated with higher 28-day mortality. This finding is largely explained by the fact that patients who died early could not complete a full course of antifungal treatment. Clinicians should determine treatment duration dynamically according to disease severity, microbiological clearance, source control, and clinical response. Recent research also indicates that the standard 14-day regimen is primarily indicated for complicated candidemia, while shortened treatment courses may be applicable to patients with uncomplicated cases.[21,22] A 16-year retrospective study conducted in Argentina further verified that severe illness and complicated clinical conditions are strongly linked to unfavorable prognosis in candidemia patients.[19] Thus, clinicians should assess severity and response dynamically and tailor therapy to avoid unnecessary prolongation.

In summary, the patients with candidemia in our hospital are mainly intensive care patients, who are seriously ill and have a poor prognosis. *C. albicans* remains the predominant pathogen in candidemia, while *C. parapsilosis* isolation rates showed an increasing trend over the study period. Bloodstream infections caused by *Candida* species exhibit species-specific differences in TTPs, which may provide early supportive information while awaiting definitive identification. Moreover, a substantial proportion of these isolates demonstrate reduced susceptibility, or outright resistance, to fluconazole and voriconazole. Clinical monitoring and intervention should be focused on risk factors, and changes in

drug resistance of *Candida* should be grasped in a timely manner to improve the prognosis of patients and reduce mortality.

This study has several limitations. First, its retrospective design at a single center limits generalizability. Second, incomplete records may introduce bias, and the modest sample size reduces statistical power. Third, AFST used the ATB Fungus 3 kit rather than the gold standard broth microdilution method, which may result in lower accuracy for certain fungi and azoles, with variable reproducibility across different species and drug combinations.

Conclusions

Our study highlights shifting *Candida* epidemiology dominated by NCAC species and rising azole resistance. Concomitant BSIs and glucocorticoid exposure were associated with outcome in univariate analysis, demanding intensified surveillance in critical care settings. TTP may provide valuable preliminary information for early species prediction while awaiting definitive identification, supporting antifungal stewardship in this higher-risk cohort. Clinicians should prioritize early detection of co-infections, judicious corticosteroid use, and tailored antifungal therapy guided by local resistance patterns to improve outcomes. Special attention should be paid to patients requiring prolonged antifungal treatment, as this factor was linked to poor 28-day outcomes.

Ethical Statement

This study received ethical approval from the Ethics Committee of Guangdong Provincial People's Hospital (KY2025-106-01) and Suzhou Ninth People's Hospital Affiliated to Soochow University (KYLW2025-025-01) in accordance with the Declaration of Helsinki. Due to the retrospective nature of this study, the requirement for written informed consent was waived by the ethics committees while maintaining strict confidentiality of patient data.

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Disclosure

The authors declare no conflict of interest in this work.

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