

Identification and antifungal susceptibility patterns of *Candida* species isolated from blood cultures

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Received: June 2026, Accepted: August 2026

ABSTRACT

Background and Objectives: Candidemia is an important cause of healthcare-associated bloodstream infection, and changes in the distribution of *Candida* species may influence antifungal treatment strategies. This study aimed to determine the species distribution of yeasts isolated from blood cultures and evaluate their antifungal susceptibility profiles.

Materials and Methods: This retrospective study included 269 yeast isolates recovered from blood cultures between December 2017 and December 2021. Species identification was performed using the VITEK 2 YST system. Antifungal susceptibility testing was performed using Sensititre YeastOne for 215 (79.9%) isolates and VITEK 2 AST-YS08 for 54 (20.1%). Minimum inhibitory concentration results were interpreted according to applicable CLSI species-specific clinical breakpoints.

Results: Of the 269 isolates, 112 (41.6%) were *Candida albicans* and 157 (58.4%) were non-*albicans Candida*. The most frequent non-*albicans* species were *C. parapsilosis* (n=73, 27.1%), *Nakaseomyces glabrata* (*C. glabrata*) (n=37, 13.8%), and *C. tropicalis* (n=34, 12.6%). Fluconazole MIC₅₀/MIC₉₀ values were 0.5/256 mg/L for *C. albicans*, 1/16 mg/L for *C. parapsilosis*, 8/32 mg/L for *C. glabrata*, and 1/4 mg/L for *C. tropicalis*.

Conclusion: The predominance of non-*albicans Candida*, particularly *C. parapsilosis*, highlights the importance of continuous local surveillance. Methodological differences between commercial susceptibility testing systems should be considered when interpreting antifungal susceptibility results.

Keywords: Candidemia; Microbial sensitivity tests; Antifungal agents; Drug resistance; Fungal

INTRODUCTION

Candida albicans and non-*albicans Candida* (NAC) species are important causes of healthcare-associated bloodstream infections and are associated with substantial morbidity and mortality (1-3). The risk of candidemia increases with broad-spectrum antimicrobial exposure, intensive care unit ad-

mission, immunosuppression, invasive procedures, central venous catheterization, and total parenteral nutrition (1-3). Species distribution and antifungal susceptibility patterns vary among institutions and geographical regions, and an increasing contribution of NAC species has been reported in many surveillance studies (4-7). This shift is clinically relevant because antifungal susceptibility differs among *Can-*

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*did*a species (8, 9).

Rapid and reliable species-level identification combined with local antifungal susceptibility surveillance is therefore important for empirical treatment and antifungal stewardship. Automated and commercial systems such as VITEK 2 and Sensititre YeastOne are widely used in routine laboratories, but method-dependent differences may occur for selected species-antifungal combinations (10-15). Susceptibility categories should consequently be assigned only when applicable species-specific clinical breakpoints are available.

The present study aimed to determine the distribution of *Candida* species isolated from blood cultures in a tertiary training and research hospital and to evaluate antifungal susceptibility testing performed as part of the routine laboratory workflow.

MATERIALS AND METHODS

Study design and ethics. Ethical approval for this study was obtained from the Clinical Research Ethics Committee of Istanbul Bakırköy Sadi Konuk Training and Research Hospital (Decision No. 2022/45). Blood culture records of patients managed at the hospital between December 2017 and December 2021 were retrospectively evaluated.

Isolation of strains. Blood samples collected aseptically from adult and pediatric patients were incubated at 37°C for up to 7 days in BACTEC 9240 or BACTEC™ FX (Becton Dickinson, USA) automated blood culture systems. Bottles yielding a positive signal were examined by Gram staining, and samples showing yeast cells were subcultured onto Sabouraud dextrose agar (Oxoid, UK) and 5% sheep blood agar (bioMérieux, France). For patients with multiple positive blood cultures during the same candidemia episode, only one representative isolate was included. Multiple positive blood-culture bottles yielding the same *Candida* species within the same episode were considered a single isolate; thus, the denominator represents non-duplicate bloodstream *Candida* isolates rather than individual positive blood-culture bottles.

Species identification and antifungal susceptibility testing. Species identification was performed using the VITEK 2 YST identification system

(bioMérieux, France).

Antifungal susceptibility testing was performed as part of the routine diagnostic laboratory workflow using Sensititre YeastOne or VITEK 2 AST-YS08 (bioMérieux, France). Of the 269 isolates, 215 (79.9%) were tested using Sensititre YeastOne and 54 (20.1%) using VITEK 2 AST-YS08. Testing was performed according to the procedures of the commercial systems in routine use during the study period.

The two susceptibility platforms were used on different subsets of isolates and were not applied in parallel to the same isolates. Therefore, the present study was not designed as a direct comparison of the two methods, and no method-to-method agreement analysis was performed.

The principal antifungal agents evaluated in the present analysis were amphotericin B, fluconazole, voriconazole, caspofungin, micafungin, and anidulafungin. MIC distributions were summarized separately for each species-antifungal combination. MIC range, MIC₅₀, and MIC₉₀ values were calculated from the available MIC results. MIC₅₀ and MIC₉₀ were defined as the MICs inhibiting 50% and 90% of the tested isolates, respectively. Because not every antifungal agent was tested against every isolate, the denominator was reported separately for each species-antifungal combination.

MIC results were interpreted according to the applicable CLSI species-specific clinical breakpoints provided in CLSI M60, where available (16). Clinical breakpoints and epidemiological cutoff values were not considered interchangeable, and categorical susceptibility interpretations were not assigned to species-antifungal combinations for which an applicable clinical breakpoint was unavailable (13-17). Because the two commercial susceptibility platforms were used on non-identical subsets of isolates, pooled susceptibility findings were interpreted cautiously (10-15).

Quality control. For each testing series, *Candida albicans* ATCC 90028, *Candida parapsilosis* ATCC 22019, and *Candida krusei* ATCC 6258 were used as quality control strains.

Statistical analysis. Data were analyzed using SPSS version 26.0 (IBM Corp., USA). Descriptive statistics were expressed as numbers and percentages. MIC distributions were summarized using MIC ranges and MIC₅₀/MIC₉₀ values, where appropriate.

RESULTS

A total of 269 bloodstream *Candida* isolates were included in the study. Of these, 112 (41.6%) were identified as *C. albicans* and 157 (58.4%) as non-*albicans Candida*. The non-*albicans Candida* isolates consisted of *C. parapsilosis* (n=73), *C. glabrata* (n=37), *C. tropicalis* (n=34), *C. krusei* (n=10), and *C. kefyr* (n=3) (Tables 1 and 2).

Antifungal MIC distributions varied according to *Candida* species and antifungal agent (Table 3). Because susceptibility testing was performed retrospectively as part of the routine diagnostic laboratory workflow, not all antifungal agents were tested against every isolate; therefore, species–drug-specific denominators are provided.

Among *C. albicans* isolates with available results, fluconazole MICs ranged from 0.12 to 256 mg/L (n=108), with MIC₅₀ and MIC₉₀ values of 0.5 and 256 mg/L, respectively. Voriconazole MICs ranged from 0.008 to 8 mg/L (n=108), with MIC₅₀ and MIC₉₀ values of 0.12 and 8 mg/L, respectively. Caspofungin, micafungin, and anidulafungin MIC₅₀ values were

0.03, 0.015, and 0.06 mg/L, respectively.

For *C. parapsilosis*, fluconazole MICs ranged from 0.25 to 32 mg/L among isolates with available results (n=60), with MIC₅₀ and MIC₉₀ values of 1 and 16 mg/L, respectively. Micafungin and anidulafungin showed higher MIC distributions than those observed for *C. albicans*, with MIC₅₀ values of 2 mg/L for both agents.

Among *C. glabrata* isolates tested with fluconazole (n=25), the MIC range was 0.5–32 mg/L, with MIC₅₀ and MIC₉₀ values of 8 and 32 mg/L, respectively. In *C. tropicalis*, fluconazole MICs ranged from 0.5 to 4 mg/L (n=25), with MIC₅₀ and MIC₉₀ values of 1 and 4 mg/L, respectively.

Results for the less frequently isolated species were interpreted descriptively because of their small sample sizes.

MIC₅₀ and MIC₉₀ represent the minimum inhibitory concentrations inhibiting 50% and 90% of tested isolates, respectively. Values were calculated from the available MIC distributions for each species–antifungal combination. Because not every antifungal agent was tested against every isolate, denominators vary among species and antifungal agents. MIC₉₀ values were not reported for species–drug combinations with fewer than 10 tested isolates. Categorical susceptibility interpretation was performed only where applicable CLSI species-specific clinical breakpoints were available.

DISCUSSION

In this single-centre retrospective study, non-*albicans Candida* species constituted the majority of bloodstream isolates, with *C. parapsilosis* being the

Table 1. Distribution of *Candida* species isolated from blood cultures.

Species	n	%
<i>Candida albicans</i>	112	41.6
<i>Candida parapsilosis</i>	73	27.1
<i>Nakaseomyces glabrata</i> (<i>C. glabrata</i>)	37	13.8
<i>Candida tropicalis</i>	34	12.6
<i>Pichia kudriavzevii</i> (<i>C. krusei</i>)	10	3.7
<i>Kluyveromyces marxianus</i> (<i>C. kefyr</i>)	3	1.1
Total	269	100.0

Table 2. Distribution of *Candida* isolates according to the antifungal susceptibility testing method used.

Species	Sensititre YeastOne, n (%)	VITEK 2 AST-YS08, n (%)	Total, n
<i>C. albicans</i>	85 (75.9)	27 (24.1)	112
<i>C. parapsilosis</i>	60 (82.2)	13 (17.8)	73
<i>N. glabrata</i> (<i>C. glabrata</i>)	30 (81.1)	7 (18.9)	37
<i>C. tropicalis</i>	30 (88.2)	4 (11.8)	34
<i>P. kudriavzevii</i> (<i>C. krusei</i>)	8 (80.0)	2 (20.0)	10
<i>K. marxianus</i> (<i>C. kefyr</i>)	2 (66.7)	1 (33.3)	3
Total	215 (79.9)	54 (20.1)	269

Percentages in individual species rows represent the proportion of isolates of each species tested using the corresponding method.

Table 3. Antifungal MIC distributions among bloodstream *Candida* isolates

Species	Antifungal	n tested	MIC range (mg/L)	MIC ₅₀ (mg/L)	MIC ₉₀ (mg/L)
<i>C. albicans</i>	Amphotericin B	102	≤0.25–8	1	2
	Caspofungin	96	0.01–0.5	0.03	0.5
	Fluconazole	108	0.12–256	0.5	256
	Micafungin	108	0.008–2	0.015	2
	Voriconazole	108	0.008–8	0.12	8
	Anidulafungin	66	0.03–0.12	0.06	0.06
<i>C. parapsilosis</i>	Amphotericin B	65	0.25–1	0.5	1
	Caspofungin	70	0.25–1	0.5	1
	Fluconazole	60	0.25–32	1	16
	Micafungin	70	0.5–4	2	2
	Voriconazole	70	0.008–0.25	0.12	0.25
	Anidulafungin	60	1–8	2	2
<i>C. glabrata</i>	Amphotericin B	30	0.5–1	0.5	1
	Caspofungin	35	0.03–0.5	0.12	0.5
	Fluconazole	25	0.5–32	8	32
	Micafungin	35	0.015–2	0.015	2
	Voriconazole	30	0.015–1	0.015	1
	Anidulafungin	27	0.015–0.5	0.12	0.5
<i>C. tropicalis</i>	Amphotericin B	25	0.5	0.5	0.5
	Caspofungin	25	0.06–0.25	0.12	0.25
	Fluconazole	25	0.5–4	1	4
	Micafungin	25	0.06	0.06	0.06
	Voriconazole	25	0.12–0.5	0.12	0.5
	Anidulafungin	15	0.25	0.25	0.25
<i>C. krusei</i>	Amphotericin B	9	0.12–1	1	—
	Caspofungin	9	0.06–0.5	0.06	—
	Micafungin	8	0.015–0.12	0.03	—
	Voriconazole	9	0.008–1	0.5	—
	Anidulafungin	9	0.03–0.12	0.06	—
<i>C. kefyr</i>	Amphotericin B	3	1	—	—
	Fluconazole	3	0.12	—	—
	Voriconazole	3	0.008	—	—
	Anidulafungin	3	0.25	—	—

most frequently identified non-*albicans* species. This distribution represents the epidemiology observed in our institution and should not be interpreted as evidence of a broader regional epidemiological shift. *Candida* species distribution may vary substantially according to geographical region, institution, patient population, and surveillance methodology (5-7).

The MIC distributions demonstrated species-specific variation in antifungal susceptibility. Broad fluconazole and voriconazole MIC distributions were observed among *C. albicans* isolates, while elevated fluconazole MIC values were also observed among

C. parapsilosis and *C. glabrata*. Species-dependent variation in azole susceptibility has also been described in surveillance studies (5, 8). These findings support the importance of local antifungal susceptibility surveillance (25).

The relatively higher echinocandin MIC distributions observed for *C. parapsilosis*, particularly for micafungin and anidulafungin, should be interpreted in the context of the known species-specific susceptibility characteristics of this organism and should not automatically be equated with acquired resistance (4, 9, 17). Similarly, categorical interpretations were

avoided for species–antifungal combinations for which applicable CLSI clinical breakpoints were unavailable (16).

Recent multicentre data from Türkiye provide important regional context, particularly regarding *C. parapsilosis* and fluconazole resistance (18-20). The emergence and interhospital spread of fluconazole-resistant *C. parapsilosis* have also been reported in other settings, including Spain, further emphasizing the importance of continued local and regional surveillance (21-23). However, direct comparison with the present findings should be made cautiously because the current study was conducted at a single centre and susceptibility testing was performed using routine commercial methods rather than a standardized multicentre reference protocol.

An additional methodological consideration is that Sensititre YeastOne and VITEK 2 AST-YS08 were used on different subsets of isolates as part of routine diagnostic practice. The two methods were not performed in parallel on the same isolates; therefore, the study was not designed to assess agreement between the two systems. Published studies have demonstrated that agreement may vary according to *Candida* species, antifungal agent, and testing method (10-15). Consequently, the susceptibility findings in the present study should be interpreted as retrospective routine-laboratory surveillance data rather than as results of a formal method-comparison study.

Species identification was based on the routine VITEK 2 YST system. Although this approach reflects routine laboratory practice during the study period, the absence of MALDI-TOF MS or molecular confirmation limits the resolution of species-level identification, particularly for closely related, cryptic, or emerging yeast species (24). Therefore, species-level findings should be interpreted within the context of the identification method used.

The principal limitations of this study include its single-centre and retrospective design. Antifungal susceptibility testing was performed as part of routine diagnostic practice using two commercial platforms on different subsets of isolates, and the same isolates were not tested in parallel by both methods. Furthermore, not every antifungal agent was tested against every isolate, resulting in different denominators among species–drug combinations. Reference broth microdilution confirmation was not available for all isolates. Species identification was performed using VITEK 2 YST without MALDI-TOF MS or

molecular confirmation, which may limit discrimination of closely related or emerging yeast species. Finally, the relatively small numbers of some less frequently isolated *Candida* species limited species-specific statistical interpretation. These limitations should be considered when interpreting the MIC distributions and when comparing the present findings with multicentre or reference-method-based surveillance studies.

CONCLUSION

This single-centre retrospective study provides institutional surveillance data on bloodstream *Candida* isolates. Non-albicans *Candida* species predominated, with *C. parapsilosis* being the most frequent non-albicans species. Antifungal MIC distributions varied among species, emphasizing the importance of continued local susceptibility surveillance.

The susceptibility findings should be interpreted in the context of the commercial testing platforms used, differences in the number of isolates tested for individual species–antifungal combinations, and the availability of applicable CLSI clinical breakpoints (13-17). Confirmation by a reference broth microdilution method should be considered for unusual or clinically important susceptibility profiles (17, 24, 25).

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