

Species Distribution and Antifungal Resistance in Candida Bloodstream Infections

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ABSTRACT

Introduction: Candidemia is a serious infection with high morbidity and mortality. This study evaluated the distribution of *Candida* species, antifungal susceptibility outcomes, and variables associated with mortality in cases of candidemia.

Methods: Patients aged ≥ 18 years with candidemia diagnosed between 2024 and 2025 were retrospectively analyzed. Associations between clinical variables and 30-day mortality were examined using logistic regression analyses, including both univariable and multivariable models.

Results: The mean age of the 132 patients who developed candidemia was 68.7 ± 15.4 years, and 46.2% were female. The dominant strain was *Candida albicans*, followed in order of frequency by *C. glabrata* and *C. auris*. The 30-day mortality rate was 55.3%. The highest mortality rate was observed in *C. auris* isolates (72.4%). In univariable analysis, intensive care unit (ICU) stay [odds ratio (OR): 17.26, 95% confidence interval (CI): 6.08-49.01; $p < 0.001$], fluconazole resistance (OR: 2.92, 95% CI: 1.42-6.01; $p = 0.005$), and amphotericin B resistance (OR: 3.57, 95% CI: 1.33-9.55; $p = 0.009$) were significantly associated with mortality. All *Candida albicans* isolates were susceptible to fluconazole and echinocandins. All *C. auris* isolates were susceptible to echinocandins, while high rates of resistance to fluconazole (82.8%) and amphotericin B (89.7%) were observed. Evaluation of time to blood culture positivity showed that growth was detected in more than 90% of patients within the first two days.

Conclusion: Candidemia is associated with a high mortality rate. ICU stay emerged as an independent predictor of 30-day mortality, while resistance to fluconazole and amphotericin B may also be associated with mortality. The identification of *Candida auris* as the third most common pathogen, along with its high resistance rates to fluconazole and amphotericin B, is particularly noteworthy. The finding that all isolates, including *C. auris*, were susceptible to echinocandins supports an echinocandin-based empirical treatment approach in patients with suspected candidemia.

Keywords: Candidemia, mortality, *C. auris*, antifungal susceptibility, resistance

Introduction

Candidemia is among the leading causes of nosocomial bloodstream infections and is associated with substantial mortality, particularly in patients in intensive care units (ICUs). Despite advances in microbiological identification methods and antifungal therapy, mortality among patients with candidemia remains approximately 60%. Recent studies have demonstrated substantial inter-center variability in terms of candidemia incidence, species distribution, antifungal resistance, and mortality, and awareness of local epidemiology has been reported to reflect treatment success (1-3).

Another important epidemiological shift is the increasing prominence of non-*albicans Candida* species. Although *C. albicans* continues to be reported as the most common pathogen in many series, a notable rise has been observed in the proportions of *C. glabrata*, *C. parapsilosis*, and particularly *Candida auris*. This shift is clinically significant, as these species often exhibit reduced susceptibility to azoles or broader multidrug resistance to antifungal agents, which may complicate empirical treatment approaches and adversely affect clinical outcomes (1,2,4). Current knowledge regarding these infections in Türkiye is largely derived from a limited number of studies, leaving substantial gaps in



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the evidence required to support clinical practice and public health decision-making.

This study aims to provide in-depth epidemiological insights into candidemia over a two-year period (2024-2025) at Haydarpaşa Numune Training and Research Hospital, one of the leading hospitals in İstanbul. Through detailed multivariable analyses, it seeks to identify the key risk factors associated with candidemia-related mortality. In addition, the antifungal susceptibility patterns of the isolated *Candida* species were evaluated. By providing contemporary data from Türkiye, this study may help address existing knowledge gaps and support evidence-based decisions in both clinical practice and public health.

Methods

The study protocol received institutional ethical approval from the Ethics Committee of Haydarpaşa Numune Training and Research Hospital (decision number: 2026/33, date: February 17, 2026). All research activities were carried out in accordance with internationally accepted ethical standards, including those described in the 2013 revision of the Declaration of Helsinki. Given the retrospective design of the study and the use of anonymized patient data, the requirement for obtaining individual informed consent was waived by the ethics committee.

This retrospective observational study was conducted at Haydarpaşa Numune Training and Research Hospital, in İstanbul. Patients aged ≥ 18 years who were hospitalized in inpatient wards and ICUs between January 1, 2024, and December 31, 2025, and had *Candida* spp. isolated from blood cultures were included. Patients with *Candida* isolates obtained from non-blood clinical specimens, patients in whom species-level identification could not be performed, and patients with incomplete microbiological data were excluded.

Cases were classified as candidemia when *Candida* species were identified in blood culture samples. When *Candida* was recovered again within 30 days of the initial episode, the event was classified as a continuation of the initial episode. Isolates detected after an interval greater than 30 days were considered to represent a separate episode. The survival rates of patients diagnosed with candidemia were examined during the first 30 days, and deaths within this period were considered as 30-day mortality. Data on demographic variables (age and sex), site of hospitalization, species identification, antifungal susceptibility results, time to blood culture positivity, time to initiation of empirical antifungal therapy after detection of yeast on Gram staining, administered antifungal treatment, and 30-day mortality were recorded.

Blood cultures were processed with the BD BACTECT™ FX automated detection platform (Becton Dickinson, Franklin Lakes, NJ, USA). Following a positive growth signal, Gram-stained smears were examined microscopically. Specimens containing yeast cells were then cultured on 5% sheep blood agar (Oxoid, UK) and Sabouraud dextrose agar (RTA, Türkiye) for fungal isolation. After inoculation, the culture media were maintained at 35 ± 2 °C for 24-48 hours to allow yeast growth. Isolates obtained from the cultures were subsequently identified by MALDI-TOF MS. Antifungal susceptibility was determined with the VITEK 2 Compact platform using the AST YS08 card (bioMérieux, France). Interpretation of results was based on CLSI M27M44S criteria. To ensure the reliability

of susceptibility testing, *Candida parapsilosis* (ATCC 22019) and *Candida krusei* (ATCC 6258) were incorporated as quality control reference strains. Results were retrospectively evaluated using laboratory records with categorical reporting (susceptible, intermediate, and resistant).

Time to initiation of antifungal therapy was categorized as: treatment initiated within the first 24 hours or treatment initiated after 24 hours. Time to blood culture positivity was categorized by the day on which a positive blood culture signal was detected after blood culture collection.

Statistical Analysis

All statistical analyses were performed using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria). According to the distributional characteristics of the variables, continuous variables were presented as mean $\pm$ standard deviation or median (minimum-maximum), whereas categorical variables were expressed as numbers and percentages. Comparisons between patients who died within 30 days and those who survived were performed using the Student's *t* test or the Mann-Whitney *U* test for continuous variables and Fisher's exact test or the chi-square test for categorical variables. Univariable logistic regression analysis was initially performed to identify variables associated with 30-day mortality. Variables with a *p* value < 0.05 in the univariable analysis were subsequently included in a multivariable logistic regression model to identify independent risk factors associated with mortality. The results of the univariable logistic regression analyses were reported as odds ratios (ORs), whereas the results of the multivariable logistic regression analyses were presented as adjusted ORs (aORs) with corresponding 95% confidence intervals (CIs). A *p* value < 0.05 was considered statistically significant.

Results

A total of 132 patients with candidemia were included in the study. The mean age was 68.7 ± 15.4 years; the mean age was 67.3 ± 14.9 years in survivors and 69.9 ± 15.9 years in patients who died ($p = 0.331$). Among the patients, 61 (46.2%) were female and 71 (53.8%) were male; no significant association was found between sex and mortality ($p = 0.484$). The overall 30-day mortality rate was 55.3% (73/132). A total of 94 patients (71.2%) were followed in the ICU; the rate of ICU stay was 93.2% among patients who died vs. 44.1% among survivors, and this difference was statistically significant ($p < 0.001$).

When antifungal susceptibility profiles were evaluated, fluconazole non-susceptible isolates were more frequent among patients who died than among survivors (56.2% vs. 30.5%; $p = 0.005$). Similarly, resistance to amphotericin B was higher among patients who died than among survivors (28.8% vs. 10.2%; $p = 0.009$). No echinocandin resistance was detected. There was no statistically significant difference in mortality between initiation of empirical antifungal therapy within the first 24 hours and later initiation (100.0% vs. 94.5%, respectively; $p = 0.128$). Blood culture positivity was detected within the first two days in 95.5% of cases; this finding was not associated with mortality (98.3% vs. 93.2%, respectively; $p = 0.224$) (Table 1, Figure 1).

The most frequently isolated species from blood cultures was *Candida albicans* (32.6%), followed by *C. glabrata* (23.5%) and *C. auris* (22.0%). *C. parapsilosis* (15.2%) was identified less frequently, while *C. tropicalis*

(6.1%) and *C. krusei* (0.8%) were the least frequently isolated species (Figure 2).

All *C. auris* isolates were susceptible to echinocandins, whereas high rates of fluconazole (82.8%) and amphotericin B (89.7%) resistance were observed. In contrast, none of the *Candida albicans* isolates examined showed resistance to fluconazole or echinocandins; all strains were susceptible.

Species-specific mortality rates were 39.5% for *Candida albicans*, 54.8% for *C. glabrata*, 72.4% for *C. auris*, 65.0% for *C. parapsilosis*, 50.0% for *C.*

tropicalis, and 100.0% for *C. krusei*. Although the highest mortality was observed in *C. auris* isolates, the mortality rate calculated for *C. krusei* was not interpretable because *C. krusei* was represented by a single isolate. Overall, the association between *Candida* species and mortality was not statistically significant ($p=0.093$) (Table 2).

In univariable analysis, ICU stay (OR: 17.26, 95% CI: 6.08-49.01; $p<0.001$), fluconazole resistance (OR: 2.92, 95% CI: 1.42-6.01; $p=0.005$), and amphotericin B resistance (OR: 3.57, 95% CI: 1.33-9.55; $p=0.009$) were significantly associated with mortality. In multivariable logistic regression analysis, only ICU stay was identified as an independent

Table 1. Baseline characteristics according to 30-day mortality

Variable	Overall (n=132)	Alive (n=59)	Died (n=73)	p value
Age, mean $\pm$ SD	68.7 $\pm$ 15.4	67.3 $\pm$ 14.9	69.9 $\pm$ 15.9	0.331
Female sex, n (%)	61 (46.2)	25 (42.4)	36 (49.3)	0.484
ICU admission, n (%)	94 (71.2)	26 (44.1)	68 (93.2)	<0.001
Fluconazole non-susceptible, n (%)	59 (44.7)	18 (30.5)	41 (56.2)	0.005
Amphotericin B resistant, n (%)	27 (20.5)	6 (10.2)	21 (28.8)	0.009
Antifungal initiation within ≤ 24 h, n (%)	128 (97.0)	59 (100.0)	69 (94.5)	0.128
Positive signal on day 1-2, n (%)	126 (95.5)	58 (98.3)	68 (93.2)	0.224

ICU: Intensive care unit, SD: Standard deviation

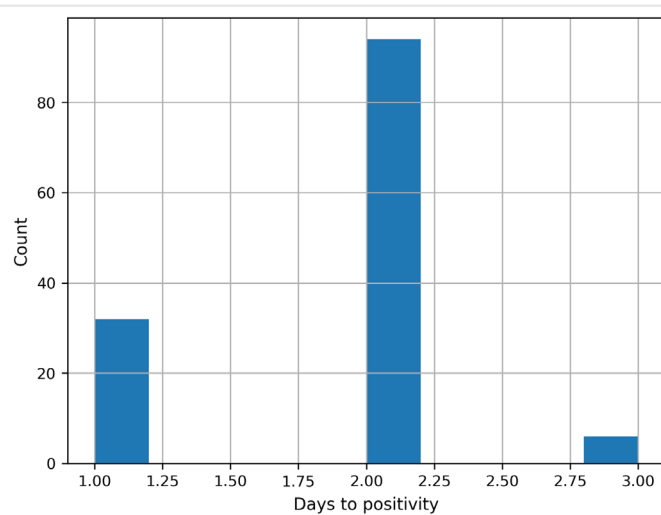


Figure 1. Time to blood culture positivity

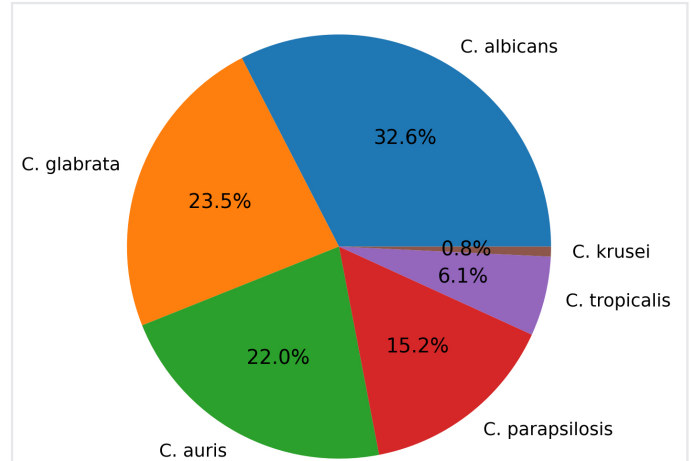


Figure 2. Species distribution of *Candida* isolates from blood cultures

Table 2. Species distribution and mortality

Species	Overall, n (%)	Alive, n (%)	Died, n (%)	Mortality, %
<i>C. albicans</i>	43 (32.6)	26 (44.1)	17 (23.3)	39.5
<i>C. glabrata</i>	31 (23.5)	14 (23.7)	17 (23.3)	54.8
<i>C. auris</i>	29 (22.0)	8 (13.6)	21 (28.8)	72.4
<i>C. parapsilosis</i>	20 (15.2)	7 (11.9)	13 (17.8)	65.0
<i>C. tropicalis</i>	8 (6.1)	4 (6.8)	4 (5.5)	50.0
<i>C. krusei</i>	1 (0.8)	0 (0.0)	1 (1.4)	100.0

Overall p value = 0.093. Mortality (%) was calculated as the proportion of deaths among patients with each *Candida* species. *C. albicans*: *Candida albicans*, *C. glabrata*: *Candida glabrata*, *C. auris*: *Candida auris*, *C. parapsilosis*: *Candida parapsilosis*, *C. tropicalis*: *Candida tropicalis*, *C. krusei*: *Candida krusei*

Table 3. Univariable and multivariable logistic regression analyses of factors associated with 30-day mortality

Variable	Univariable		Multivariable	
	OR (95% CI)	p value	aOR (95% CI)	p value
ICU admission	17.26 (6.08-49.01)	<0.001	15.52 (5.36-44.96)	<0.001
<i>C. auris</i> infection	2.57 (1.05-6.34)	0.056	–	–
Fluconazole non-susceptible	2.92 (1.42-6.01)	0.005	1.87 (0.76-4.63)	0.175
Amphotericin B resistant	3.57 (1.33-9.55)	0.009	2.24 (0.66-7.62)	0.196
Antifungal initiation >24 h	6.84 (0.35-132.06)	0.128	–	–
Blood culture positivity ≥3 days	4.26 (0.48-37.55)	0.224	–	–

Variables with a p value <0.05 in the univariable analysis were entered into the multivariable logistic regression model. OR: Odds ratio, CI: Confidence interval, aOR: Adjusted odds ratio, ICU: Intensive care unit, *C. auris*: *Candida auris*

predictor of mortality (aOR: 15.29, 95% CI: 5.27-44.42; $p<0.001$) (Table 3).

Discussion

In this study, the 30-day mortality rate in patients with candidemia was 55.3%. A single-center study from Türkiye published in 2024 reported a mortality rate of 59.3%, while another study published in 2025 reported a rate of 64% (2,5). Similarly, recent regional and population-based analyses indicate that mortality remains high across different healthcare systems and may vary depending on patients' clinical status, ICU burden, and the distribution of causative species. In this context, the mortality rate observed in our study appears to be consistent with the upper range of contemporary candidemia series (3,6).

When species distribution was evaluated, *C. albicans* was the most frequently identified pathogen in our study, followed by *C. glabrata* and *C. auris*. The identification of *C. auris* as the third most common species suggests that this pathogen has gained clinical significance at Haydarpaşa Numune Training and Research Hospital, which may be partially attributable to the high proportion of ICU patients. This distribution is consistent with the current literature reporting that *C. albicans* remains predominant, while non-*albicans Candida* species are increasingly encountered (1,2,7). In our study, although *C. auris* was not identified as an independent predictor of mortality, the highest mortality rate was observed in this species (72.4%) when species-specific mortality rates were evaluated. When considered together with its association with ICU settings and antifungal resistance characteristics, this finding suggests that *C. auris* retains its clinical significance and underscores the need for surveillance and infection control measures.

In our study, antifungal susceptibility patterns differed markedly among species. All *C. auris* isolates were susceptible to echinocandins, whereas fluconazole resistance was notably high at 82.8%, which is consistent with data reported in the literature. It is well established that fluconazole resistance in *C. auris* isolates exceeds 85% in most series (1,3). In contrast, a notable finding in our study was the remarkably high rate of amphotericin B resistance (89.7%, $n=26$). Recent studies have reported that amphotericin B resistance in *Candida auris* isolates generally ranges between 10% and 40% (8-10). In addition, differences in antifungal susceptibility testing methodologies, in interpretive criteria, and in the predominance of specific *C. auris* clades across geographic

regions may have contributed to the variability in reported amphotericin B resistance rates. In this context, the high resistance rate observed in our study may be related to local epidemiological characteristics and the predominance of ICU patients. In addition, in vitro studies have demonstrated that the activity of antifungal agents against *Candida* species may vary (11). The resistance pattern observed in our center suggests that use of amphotericin B may be limited, particularly in patient populations with a high prevalence of *C. auris*; therefore, echinocandins emerge as a more appropriate option for severe candidemia and for ICU patients. Nevertheless, recent reports of emerging echinocandin-resistant *C. auris* isolates associated with mutations in the *FKS1* gene underscore the importance of ongoing antifungal susceptibility surveillance, even in centers where echinocandin susceptibility remains universal (12). Furthermore, the association between fluconazole non-susceptible isolates and mortality supports the clinical significance of azole resistance.

Our finding that all *C. albicans* isolates were susceptible to fluconazole and echinocandins indicates a clear distinction in antifungal susceptibility among species. However, no significant difference in mortality was observed between *C. auris* and other *Candida* species. This may be attributable to the susceptibility of isolates from both groups to echinocandins and the prompt initiation of empirical anidulafungin therapy following detection of yeast on Gram staining of blood cultures at our center.

The identification of ICU admission as an independent predictor of mortality represents one of the most consistent findings of our study. This observation is strongly aligned with current evidence. Recent studies from Türkiye and Kuwait have identified ICU stay as one of the strongest predictors of poor prognosis in candidemia. This association may be explained by the coexistence of broad-spectrum combination-antibiotic use, critical illness, invasive procedures, prolonged hospitalization, total parenteral nutrition, and multiple comorbidities. Our findings support that candidemia in ICU patients should be considered not only a microbiological event but also a marker of significant clinical vulnerability (1,2,13-15).

In our study, no significant association was observed between the initiation of empirical antifungal therapy within the first 24 hours after yeast detection in blood cultures and a later initiation, with respect to mortality. This finding may be explained by the close daily monitoring of ICU patients at our center and the prompt initiation of antifungal

therapy in the majority of cases (128/132) following the detection of yeast on blood culture Gram staining, which may have limited the variability in the analysis.

This study has several strengths. First, it includes a contemporary cohort and evaluates the species distribution and antifungal susceptibility patterns, along with clinically relevant 30-day mortality. In addition, the inclusion of *C. auris* in the cohort enhances the value of the findings within the current epidemiological context.

Study Limitations

As this investigation was conducted retrospectively at a single institution, the applicability of the results to other healthcare settings may be limited. In addition, some clinically relevant variables that may influence candidemia prognosis, including comorbidity burden, catheter removal, source control, septic shock status, and total duration of antifungal therapy, were not included in the analysis. Antifungal exposure before the onset of candidemia was not evaluated and may have influenced the observed antifungal resistance patterns. Similar limitations have been reported in recent single-center candidemia studies.

Conclusion

Our study demonstrates that candidemia remains a significant infection and is associated with high mortality. While *C. albicans* continues to be the predominant species, the clinical importance of non-*albicans* *Candida* species, particularly *C. auris*, is increasing. The finding that *C. auris* isolates were fully susceptible to echinocandins but highly resistant to amphotericin B indicates a notable susceptibility profile with important implications for treatment management. ICU admission is a major determinant of mortality. Our findings underscore the importance of local epidemiology and susceptibility patterns in guiding empirical treatment strategies.

Ethics

Ethics Committee Approval: The study protocol received institutional ethical approval from the Ethics Committee of Haydarpaşa Numune Training and Research Hospital (decision number: 2026/33, date: February 17, 2026).

Informed Consent: Given the retrospective design of the study and the use of anonymized patient data, the requirement for obtaining individual informed consent was waived by the ethics committee.

Footnotes

Authorship Contributions: Concept - V.A.S., D.T., S.A., R.B., S.Ş., A.İ., S.E., N.C.; Design - V.A.S., D.T., S.A., R.B., S.Ş., A.İ., S.E., N.C.; Data Collection or Processing - V.A.S., D.T., S.A., R.B., S.Ş., A.İ., S.E., N.C.; Analysis or Interpretation - V.A.S., D.T., S.A., R.B., S.Ş., A.İ., S.E., N.C.; Literature Search - V.A.S., D.T., S.A., S.E., N.C.; Writing - V.A.S., D.T., S.A., R.B., S.Ş., A.İ., S.E., N.C.

Conflict of Interest: No conflict of interest was declared by the authors.

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