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Epidemiology, Clinical Features and Predictors of Mortality in Patients with Candidemia in a Tertiary Care Hospital in Turkiye: A Single-Center Retrospective Study

Türkiye'de Üçüncü Basamak Bir Hastanede Kandidemili Hastalarda Epidemiyoloji, Klinik Özellikler ve Mortalite Belirteçleri: Tek Merkezli Retrospektif Bir Çalişma

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ABSTRACT

Objective: *We aimed to evaluate the epidemiology of candidemia among hospitalized patients and identify risk factors associated with mortality.*

Materials and methods: *The medical data of 81 adult patients with candidemia who were hospitalized between May 1, 2015 and May 1, 2016 constituted the study. We recorded vital signs, clinical characteristics, ward or intensive care unit (ICU) interventions, comorbidities, and biochemistry findings. To identify factors independently associated with 30-day mortality, a forward conditional inclusion model was used in multivariable logistic regression.*

Results: *The annual incidence of candidemia was 23 cases per 10000 individuals (0.23%). The three most frequently detected species were C. albicans (46.91%), C. parapsilosis (29.63%) and C. glabrata (8.64%). The 30-day mortality rate was 59.26% (n=48). Multivariable logistic regression showed that older age (OR: 1.037, 95% CI: 1.006 - 1.070, p=0.018), ICU admission (OR: 3.325, 95% CI: 1.132 - 9.766, p=0.029) and acute renal failure (OR: 3.383, 95% CI: 1.024 - 11.173, p=0.046) were independently associated with mortality.*

Conclusion: *We revealed an annual candidemia incidence of 0.23% and a notably high 30-day mortality rate at our center. Older patients, individuals admitted to the ICU, and those with renal dysfunction may face an elevated risk of mortality, underscoring the importance of close monitoring in these populations.*

ÖZET

Amaç: *Bu çalışmada hastanede yatan hastalarda kandidemi epidemiyolojisini değerlendirmeyi ve mortalite ile ilişkili risk faktörlerini belirlemeyi amaçladık.*

Gereç ve yöntem: *Bu çalışmada 1 Mayıs 2015 ile 1 Mayıs 2016 tarihleri arasında hastaneye yatırılan kandidemili 81 yetişkin hastanın tıbbi verileri kullanıldı. Vital bulguları, klinik özellikleri, servis veya yoğun bakım ünitesi (YBÜ) yatışı, komorbiditeleri ve biyokimya bulgularını kaydettik. 30 günlük mortaliteyle bağımsız olarak ilişkili faktörleri tanımlamak için çok değişkenli lojistik regresyonda ileri koşullu dahil etme modeli kullanıldı.*

Bulgular: *Yıllık kandidemi insidansı 10.000 kişi başına 23 vakaydı (%0.23). En sık tespit edilen üç tür ise C. albicans (%46,91), C. parapsilosis (%29,63) ve C. glabrata (%8,64) oldu. 30 günlük mortalite oranı %59,26 (n=48) olarak bulundu. Çok değişkenli lojistik regresyon ile, ileri yaşın (OR: 1.037, 95% CI: 1.006 - 1.070, p=0.018), yoğun bakım ünitesine yatışın (OR: 3.325, 95% CI: 1.132 - 9.766, p=0.029) ve akut böbrek yetmezliğinin (OR: 3.383, 95% CI: 1.024 - 11.173, p=0.046) bağımsız olarak mortaliteyle ilişkili olduğu gösterildi.*

Sonuç: *Merkezimizde yıllık kandidemi insidansının %0,23 olduğunu ve 30 günlük mortalite oranının oldukça yüksek olduğunu ortaya çıkardık. Yaşlı hastalar, yoğun bakım ünitesine kabul edilen kişiler ve böbrek fonksiyon bozukluğu olan kişiler artmış mortalite riskiyle karşı karşıya kalabilir; bu popülasyonlarda yakından izlem önemlidir.*

Keywords:
Candidemia mortality
Candidemia epidemiology
Candidemia clinical feature

Anahtar Kelimeler:
Kandidemi mortalite
Kandidemi epidemiyoloji
Kandidemi klinik bulgu

INTRODUCTION

Invasive candida infection is the most common fungal infection that is detected among hospitalized patients (1), and according to the international EPIC II study (Extended Prevalence of Infection in Intensive Care) candida infections rank third among all agents (2) –with *Candida albicans* being the most common type (3). The burden of candida is well known, but major studies have shown a decreasing trend in the frequency of *C. albicans* from 57.4% 25 years ago to 46.4% in the last 5 years (4). This shift is important since non-albicans candida strains may be less susceptible to azoles (5).

Prior studies have established a number of risk factors associated with candida infection among in-patients, including catheter use, heart disease, occurrence of systemic life-threatening events, renal dysfunction, and exposure to substances (aminoglycoside, nitroimidazole, glycopeptide) (6,7). The gold standard diagnostic approach is culture obtained from blood, peritoneal fluid and pleural fluid. Therefore, molecular diagnostic tests

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that circumvent the need for culture can potentially reduce morbidity and mortality (8).

Resistant fungal infections, including infections caused by Candida spp. (9), are becoming more common (3) and these data illustrate the need for risk stratification in order to create meaningful treatment strategies against resistant fungal infections (10). In a study comparing the COVID-19 pre-pandemic and pandemic period, a slight increase in candidemia periods was detected (11).

Despite advances in management and therapeutics, candidemia can still cause mortality rates as high as 40–60% (6,10). In order to reduce the morbidity and mortality associated with candidemia, a better understanding of candida epidemiology and risk factors is necessary. As such, we aimed to retrospectively examine candidemia cases arising in hospitalized adults during a one-year period and to evaluate risk factors associated with 30-day mortality.

MATERIALS AND METHODS

In this study, cases in which candida species were isolated in blood culture were accepted as candidemia (12). The dataset for this study comprised medical records from 81 patients aged 18 years and above, all diagnosed with candidemia and treated as inpatients at Trakya University Medical Faculty Hospital during the period from May 1, 2015, to May 1, 2016. Throughout this timeframe, a total of 35066 patients had undergone inpatient care for various medical conditions at our hospital.

All patients with candidemia were evaluated for vital signs, clinical characteristics, ward or intensive care unit (ICU) interventions, comorbidities, complete blood counts, biochemistry findings including liver and kidney function tests, inflammation-related parameters, and specific parameters associated with candidemia, such as hospitalization duration, therapy duration, therapeutic agents administered before and after antibiograms, and diagnosis (based on site of infection). In the mortality evaluation, the 30-day period beginning at positive blood culture signal was evaluated. Any treatment that was administered to patients was continued for at least 14 days after the first negative blood culture result (9); however, evidently, treatment duration was cut short in some patients who died before normal termination of therapy.

Sample Collection, Isolation and Identification of Microorganisms

Samples were collected utilizing aseptic procedures and subjected to analysis employing an automated blood culture system (Bactallert 460, bioMérieux, France). Cultures with a positive signal in this automated system underwent Gram staining. Subsequently, dilution sowing was performed (blood agar medium) and incubated at 37°C for 24-48 hours. Specimens with pure growth were verified and these underwent the germ tube test. Yeast isolates demonstrating germ tube formation were identified as *C. albicans*. Those lacking germ tube formation were designated as non-albicans candida, and typing procedures were initiated. Typing methodologies included the conventional, Cornmeal Agar, and the Analytical Profile Index (API) 20 C System (bioMérieux). Yeast isolates were cultured on various media including Sabouraud dextrose agar Antibiograms were performed on most of the samples with VITEK-2 Compact (bioMérieux, France), except for 15 isolates. Antibiograms for fluconazole, micafungin, and voriconazole were assessed, and minimum inhibitory concentration (MIC) values were computed. The procedures outlined by the manufacturer's standard operating protocols were strictly adhered to. The obtained results were appraised in accordance with the recommendations set forth by the Clinical and Laboratory Standards Institute (CLSI).

Candida Score

In determining the Candida score, an objective scoring system devised by Leon et al. was employed to assess the risk of candidemia in critically-ill patients. The scoring system assigned points for a history of major surgical intervention (1 point), severe sepsis (2 points), multiple colonization (1 point), and the use of total parenteral nutrition (1 point). This scoring methodology allowed for the prediction of the risk of invasive candidiasis based on the cumulative score derived from these clinical factors (13).

Statistical Analysis

Two-tailed p-values less than 0.05 were considered statistically significant. All analyses were conducted using IBM SPSS, version 25.0 (IBM Corp., Armonk, NY, USA). The normal distribution of variables was assessed using the Shapiro-Wilk test. Descriptive statistics included presentation of mean ± standard deviation for normally distributed continuous variables or median (25th percentile - 75th percentile) for non-normally distributed continuous variables. We used frequency (n) and relative frequency (%) to describe categorical data distributions and analyzed these via chi-square tests with specific use of Spearman chi-square, Yates's correction, Fisher's exact test, or Fisher-Freeman-Halton test. For normally distributed continuous variables, the independent samples t-test was applied. For non-normally distributed continuous variables, the Mann-Whitney U test was employed. To identify factors independently associated with 30-day mortality, a forward conditional inclusion model was used in multivariable logistic regression.

RESULTS

Among the 81 patients included in the analysis, 30 were females, 51 were males and the median age (Minimum-Maximum) was 65 (18-92) years. During the one-year period in which the data were evaluated, the incidence of candidemia among hospitalized patients was calculated as 23 cases per 10000 individuals (0.23%). The three most frequently detected candida species were *C. albicans* (46.91%), *Candida parapsilosis* (29.63%) and *Candida glabrata* (8.64%). The 30-day mortality rate was 59.26% (n=48). The most common comorbidity was hypertension (38.27%) (Table 1).

The most common candida risk factors detected in the study group were previous antibiotic use (95.06%), gastric acid suppression (93.83%) and urethral catheter (85.19%). Fluconazole resistance was found in 8.47%, Amphotericin B resistance in 4.62%, Voriconazole resistance in 3.39%, while no resistance was found to Micafungin. Patients with 30-day mortality had a higher median age (p=0.005), a higher frequency of ICU stay (p=0.008), and a higher frequency of intubation (p=0.028). The mortality group

Table 1: Comorbidities, laboratory tests and the other variables with regard to mortality

		30-days mortality		
	Total (n=81)	**No (n=33)**	**Yes (n=48)**	**p**
Age	65 (54 - 75)	57 (37 - 70)	68 (58 - 80)	0.005
Sex				
Female	30 (37.04%)	10 (30.30%)	20 (41.67%)	0.420
Male	51 (62.96%)	23 (69.70%)	28 (58.33%)	
Comorbidities				
Diabetes mellitus	14 (17.28%)	5 (15.15%)	9 (18.75%)	0.903
Hypertension	31 (38.27%)	12 (36.36%)	19 (39.58%)	0.952
Chronic renal failure	7 (8.64%)	4 (12.12%)	3 (6.25%)	0.435
Malignancy	30 (37.04%)	8 (24.24%)	22 (45.83%)	0.081
Immunodeficiency	6 (7.41%)	3 (9.09%)	3 (6.25%)	0.683
Cerebrovascular disease	22 (27.16%)	11 (33.33%)	11 (22.92%)	0.435
Stay in intensive care unit	54 (66.67%)	16 (48.48%)	38 (79.17%)	0.008
Intubation	45 (55.56%)	13 (39.39%)	32 (66.67%)	0.028
Body temperature	38.2 (37.5 - 38.3)	38.2 (37 - 38.4)	38.2 (38 - 38.3)	0.658
Heart rate	88 (77 - 110)	84 (75 - 92)	95 (84 - 110)	0.010
Systolic blood pressure	110 (100 - 120)	110 (100 - 120)	107.5 (90 - 122.5)	0.195
Diastolic blood pressure	65 (56 - 70)	70 (60 - 70)	60 (52.5 - 70)	0.184
Systemic inflammatory response syndrome	51 (62.96%)	17 (51.52%)	34 (70.83%)	0.125
WBC (x103)	11.72 ± 6.20	12.40 ± 5.88	11.26 ± 6.43	0.420
Hemoglobin	10.11 ± 1.92	10.28 ± 2.35	9.99 ± 1.58	0.512
Platelet (x103)	188 (94 - 307)	203 (124 - 313)	159 (81.5 - 269.5)	0.374
CRP	139 (65 - 195)	113 (58 - 179)	153 (67 - 198)	0.254
Urea	77 (43 - 105)	50 (32 - 96)	83.5 (62 - 119.5)	0.012
Creatinine	0.87 (0.69 - 1.40)	0.76 (0.60 - 1.20)	0.90 (0.70 - 1.56)	0.216
AST	32 (22 - 50)	30 (22 - 41)	35.5 (25 - 63)	0.123
ALT	23 (14 - 39)	24 (16 - 37)	22 (14 - 47)	0.823
Blood culture signal duration				
One day	52 (64.20%)	22 (66.67%)	30 (62.50%)	
Two days	23 (28.40%)	9 (27.27%)	14 (29.17%)	1.000
Three days or above	6 (7.41%)	2 (6.06%)	4 (8.33%)	
Type of Candida, blood culture				
C. albicans	38 (46.91%)	15 (45.45%)	23 (47.92%)	
C. parapsilosis	24 (29.63%)	12 (36.36%)	12 (25.00%)	
C. glabrata	7 (8.64%)	2 (6.06%)	5 (10.42%)	
C. tropicalis	4 (4.94%)	2 (6.06%)	2 (4.17%)	
C. lusitaniae	4 (4.94%)	1 (3.03%)	3 (6.25%)	0.859
C. krusei	1 (1.23%)	0 (0.00%)	1 (2.08%)	
C. dubliniensis	1 (1.23%)	0 (0.00%)	1 (2.08%)	
C. norvegensis	1 (1.23%)	0 (0.00%)	1 (2.08%)	
C. famata	1 (1.23%)	1 (3.03%)	0 (0.00%)	
Fluconazole susceptibility				
Susceptible	53 (89.83%)	24 (92.31%)	29 (87.88%)	
Intermediate	1 (1.69%)	0 (0.00%)	1 (3.03%)	1.000
Resistant	5 (8.47%)	2 (7.69%)	3 (9.09%)	

Continuation of Table 1: Comorbidities, laboratory tests and the other variables with regard to mortality

Amphotericin B susceptibility				
Susceptible	56 (86.15%)	21 (77.78%)	35 (92.11%)	
Intermediate	6 (9.23%)	4 (14.81%)	2 (5.26%)	0.238
Resistant	3 (4.62%)	2 (7.41%)	1 (2.63%)	
Micafungin susceptibility				
Susceptible	65 (98.48%)	27 (100.00%)	38 (97.44%)	
Intermediate	1 (1.52%)	0 (0.00%)	1 (2.56%)	1.000
Resistant	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Voriconazole susceptibility				
Susceptible	56 (94.92%)	25 (96.15%)	31 (93.94%)	
Intermediate	1 (1.69%)	1 (3.85%)	0 (0.00%)	0.331
Resistant	2 (3.39%)	0 (0.00%)	2 (6.06%)	
Other candida positive cultures				
Urine	41 (50.62%)	17 (51.52%)	24 (50.00%)	1.000
Sputum	8 (9.88%)	3 (9.09%)	5 (10.42%)	1.000
Tracheal aspirate	3 (3.70%)	0 (0.00%)	3 (6.25%)	0.267

Descriptive statistics were presented by using mean ± standard deviation for normally distributed continuous variables, median (25th percentile - 75th percentile) for non-normally distributed continuous variables and frequency (percentage) for categorical variables.

again demonstrated higher urea levels (p=0.012), higher frequency of acute renal failure (p=0.003), and higher frequency of severe sepsis (p=0.025). Deceased patients also had higher candida score (p=0.015), shorter treatment duration (p<0.001), and lower frequencies of negative blood culture (p<0.001) (Table 2). Mortality was unassociated with sex, comorbidities, blood pressure, systemic inflammatory response syndrome, CRP (p=0.254), WBC (p=0.420), candida type (p=0.859) and empirical treatment (p=1.000). It was found that the heart rate level was significantly higher in the patients who died within 30 days (p=0.010),

According to multivariable logistic regression, high age (OR: 1.037, 95% CI: 1.006 - 1.070, p=0.018), stay in ICU (OR: 3.325, 95% CI: 1.132 - 9.766, p=0.029) and acute renal failure (OR: 3.383, 95% CI: 1.024 - 11.173, p=0.046) were independently associated with mortality. Other variables included in the analysis, intubation (p=0.797), heart rate (p=0.164), urea (p=0.203), candida score (p=0.146) and severe sepsis (p=0.637) were found to be non-significant (Table 3).

DISCUSSION

Yeast-associated infections are a clinical challenge due to the inherent complexities in antifungal management. Fungal infections extend hospital stays, elevate morbidity and mortality rates, and increase treatment cost. The epidemiology is characterized by dynamic shifts in species distribution and different resistance patterns (14,15). In this retrospective study, we analyzed the epidemiology of candidemia and risk factors for mortality in hospitalized patients. The most frequently identified candidemia risk factor was previous antibiotic use and the most frequently identified candida species was *C. albicans*. The 30-day mortality rate was 59.26% and the three factors that independently increased mortality were advanced age, ICU stay and acute renal failure.

C. albicans, *C. glabrata*, *C. parapsilosis*, *Candida tropicalis* and *Candida krusei* account for more than 90% of all diagnosed candida cases, but relative frequency varies greatly from study to study (16). In a study conducted by Barchiesi et al in Italy, it was reported that although *C. albicans* remained the most frequently isolated species from 2010 to 2014, its frequency decreased from 68% to 48% (17). This proportional decrease may indicate an increase in other species when taken together with the fact that the annual incidence of candidemia has exhibited an upward trend (from 2.96 to 4.20 cases per 100,000). Noteworthy alterations in the prevalence of Candida species were reported in the aforementioned study which examined a period of 15 years, with a significant decrease in *C. albicans* (despite still being the most common with 58%) and notable frequencies for other types: *C. glabrata* (21%), *C. tropicalis* (5%), and *C. parapsilosis* (5%) (18). The frequency of candida infections shows unpredictable variations even in the same center, as evidenced by a study describing a sharp increase in 2016-2018 compared to 2006-2015 and 2006-2008. This variation could be partially explained by the data showing that *C. albicans* was responsible for 62.8% of cases in the 2006-2008 period and 51.2% in the 2016-2018 period (19), again suggesting that there was a surge in non-albicans cases. Other investigations, for instance by Hii et al., support such conclusions by showing an overall increase in candidemia incidence over time accompanied by a decline in the proportion of *C. albicans* (64.8% to 43.6%) and a 20-fold increase in *C. glabrata* prevalence (1.1% to 21.6%) (20). Similarly, retrospective analyses in Helsinki and Uusimaa hospital districts from 2007 to 2016 depicted *C. albicans* as the predominant cause of candidemia (60.4%), followed by *C. glabrata* (21.5%), *C. parapsilosis* (5.2%), and *Candida dubliniensis* (5.2%) (21).

In a meta-analysis evaluating the epidemiology of

Table 2. Risk factors, diagnosis and the other variables with regard to mortality

		30-days mortality		
	Total (n=81)	**No (n=33)**	**Yes (n=48)**	**p**
Candida risk factors				
Acute renal failure	29 (35.80%)	5 (15.15%)	24 (50.00%)	0.003
Urethral catheter	69 (85.19%)	25 (75.76%)	44 (91.67%)	0.061
Inotropic agent use	28 (34.57%)	7 (21.21%)	21 (43.75%)	0.063
Gastric acid suppression	76 (93.83%)	29 (87.88%)	47 (97.92%)	0.153
Previous antifungal use	11 (13.58%)	3 (9.09%)	8 (16.67%)	0.511
Previous antibiotics use	77 (95.06%)	31 (93.94%)	46 (95.83%)	1.000
Intubation history	51 (62.96%)	17 (51.52%)	34 (70.83%)	0.125
IV catheter history	65 (80.25%)	25 (75.76%)	40 (83.33%)	0.577
Transfusion history	61 (75.31%)	24 (72.73%)	37 (77.08%)	0.854
Candida score	2 (2 - 3)	2 (2 - 3)	2.5 (2 - 4)	0.015
>2.5	32 (40.51%)	9 (27.27%)	23 (50.00%)	0.072
Severe sepsis	44 (55.70%)	13 (39.39%)	31 (67.39%)	0.025
Total parenteral nutrition	51 (64.56%)	19 (57.58%)	32 (69.57%)	0.390
Initial surgery	36 (45.57%)	16 (48.48%)	20 (43.48%)	0.832
Multifocal candida colonization	8 (10.13%)	2 (6.06%)	6 (13.04%)	0.457
Empiric therapy	75 (92.59%)	32 (96.97%)	43 (89.58%)	0.393
Fluconazole	65 (86.67%)	29 (90.63%)	36 (83.72%)	
Amphotericin B	1 (1.33%)	0 (0.00%)	1 (2.33%)	
Caspofungin	0 (0.00%)	0 (0.00%)	0 (0.00%)	1.000
Anidulafungin	8 (10.67%)	3 (9.38%)	5 (11.63%)	
Voriconazole	1 (1.33%)	0 (0.00%)	1 (2.33%)	
Length of stay at therapy onset, days	15 (10 - 24)	13 (8 - 21)	18 (12 - 27)	0.069
Duration of therapy, days	15 (5 - 19)	18 (16 - 23)	7 (3 - 15)	<0.001
Negative blood culture	51 (62.96%)	29 (87.88%)	22 (45.83%)	<0.001
Diagnosis				
Catheter infection	44 (54.32%)	18 (54.55%)	26 (54.17%)	
Intra-abdominal infection	2 (2.47%)	1 (3.03%)	1 (2.08%)	
Lung infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0.889
Urinary tract infection	1 (1.23%)	0 (0.00%)	1 (2.08%)	
Endocarditis	1 (1.23%)	1 (3.03%)	0 (0.00%)	
Unknown	33 (40.74%)	13 (39.39%)	20 (41.67%)	
Length of stay in hospital, days	35 (25 - 50)	39 (27 - 60)	34.5 (20 - 48)	0.093

Descriptive statistics were presented by using mean ± standard deviation for normally distributed continuous variables, median (25th percentile - 75th percentile) for non-normally distributed continuous variables and frequency (percentage) for categorical variables.

candidemia in Europe with population-based studies, it was reported that the overall pooled incidence rate between 2000 and 2019 was 3.88 per 100,000 people (22). Meyahnwi et al. documented the cumulative incidence of candidemia at 5.9 cases per 100,000 in a US population, from 2017 to 2020. Notably, the predominant Candida species identified in their study were *C. glabrata* (38.0%) and *C. albicans* (33.2%), diverging from the trends observed in other investigations (23). Conversely, a study conducted in China reported an annual candidemia incidence ranging between 0.71 and 0.85 per 1000 people from 2009 to 2011, with *C. tropicalis* (28.6%), *C. albicans* (23.3%), and *C. parapsilosis* (19.5%) being the most prevalent Candida species (24). In Brazil, the prevalence of Candida species also demonstrated distinct proportions, with *C. albicans* accounting for 34.3%, followed by *C. parapsilosis* (24.1%), *C. tropicalis* (15.3%), and *C. glabrata* (10.2%) (25). For Turkiye, a prospective observational study assessing data from 2009 and 2010 reported that the incidence of candidemia was 0.94 per 1000 persons, with *C. albicans* isolated in 52.1% of cases, followed by *C. parapsilosis* and *C. tropicalis* (26). In agreement with international literature, Ulu Kılıç et al reported a noteworthy increase in the annual incidence of candidemia in Turkiye, rising from 0.10 to 0.30 cases per 1000 patient days from 2010 to 2016. The predominant

Table 3: Significant factors independently associated with 30-day mortality, multivariable logistic regression analysis

	β coefficient	Standard error	p	Exp(β)	95% CI for Exp(β)
Age	0.037	0.016	0.018	1.037	1.006 1.070
Stay in intensive care unit	1.202	0.550	0.029	3.325	1.132 9.766
Acute renal failure	1.219	0.610	0.046	3.383	1.024 11.173
Constant	-3.029	1.065	0.004	0.048	

CI: Confidence interval, Nagelkerke R2=0.322

candida species in this study were *C. albicans* (48.1%), *C. parapsilosis* (25.1%), and *C. glabrata* (11.7%) (27). In the present study from Turkiye, we found the incidence of candidemia to be 23 per 10000 individuals (0.23%).

In a retrospective analysis of candidemia cases, Aydın et al. reported prevalent risk factors observed between 2013 and 2019. The commonly identified contributors to candidemia included antibiotic use (71.3%), urinary catheterization (56.3%), placement of central venous catheters (50.3%), total parenteral nutrition (47.9%), the presence of solid organ malignancy (46%), surgical procedures (48.6%), chemotherapy (37%), and steroid treatment (25.5%) (15). These results were largely similar to other reports from Turkiye. For instance, Mirza et al found the risk factors for candidemia in their cohort were antibiotic use (94.4%), recent (within the prior month) hospitalization (93%), ICU admission (74.6%), and the utilization of central venous catheters (70.4%) (26). Ulu Kılıç et al. reported that the presence of central venous catheters was a risk factor for non-albicans candidemia, highlighting an interesting relationship (27). In the present study, the most common risk factors for candidemia were antibiotic use (95.06%), gastric acid suppression (93.83%) and urethral catheter use (85.19%). It was thought that revision of infection control policies in the prevention and follow-up of infections in hospitalized patients and the use of current guidelines in the application of antibiotherapy may reduce candida infections.

Epidemiological surveillance studies play a pivotal role in monitoring antifungal resistance profiles and informing updates to guidelines for antifungal therapy (18). Better therapeutic management and creation of new guidelines are needed to reduce anti-fungal resistance, especially in countries with a concerning growth in resistance that may be a result of incautious use of therapeutics (28).

In the study conducted by Koehler et al. spanning from 2000 to 2019, the estimated incidence of candidemia in Europe was approximately 79 cases per day. Among these cases, 29 were projected to result in fatalities within 30 days, yielding a 30-day mortality rate estimated at 37% (22), which is consistent with real-world data showing a death rate of 30.7% in a 10-year period (21). Nonetheless, better management and close follow-up of at-risk individuals appears to result in improved outcomes. For instance, a study evaluating cases between 2014 and 2018 at Nice University Hospital and Antoine Lacassagne Oncology Center found that the 30-day mortality rate decreased to less than half from 2014 (46%) to 2018 (18%) (29). In Schroeder et al.'s retrospective analysis of candidemia cases over a decade in a single center, the reported mortality rate after 28 days was 47% (14). Despite reports of high resistance, a study collecting data from tertiary healthcare institutions during a 3-year period (2009-2010) in China reported a 30-day mortality rate of 26.0% (24). In Italy, the 30-day mortality rate in candidemia cases between 2010 and 2014 was reported as 35% (17). These data demonstrate the extreme variability in candida-attributed mortality, but it is necessary to conduct detailed analysis of studies to understand potential pitfalls and biases in the results. In the present study, 30-day mortality rate (59.26%) is considerably higher compared to the majority of research. This is likely due to differences in the study populations and specific patient characteristics, such as the fact that 66.67% of the patients included in our study had been admitted to the ICU and the study was conducted in a tertiary care institution receiving referral of relatively severe patients.

The elevated mortality observed in patients with candidemia is linked to specific risk factors, including advanced age, high APACHE score, immunosuppression, renal failure, and prior exposure to triazoles. Conversely, initiating antifungal therapy promptly and effectively managing the source of infection early on may serve to mitigate mortality in patients afflicted with candidemia (9). In the present study, factors that independently predicted improved 30-day morale were higher age, ICU stay and having acute renal failure. Our result is consistent with the results of other studies reporting that the risk of mortality increases with age (14,17,21,23,28,30), ICU stay (17,23) and acute renal failure (6, 17). In the study of Medeiros et al., it was reported that older age was associated with a higher risk of mortality (28). Such results concerning age-related risks have been circulated widely in the literature (17,21,30). Many other risk factors reported in prior literature are also worthy of mention. In the current study, contrary to what has been reported in other studies, we did not find a relationship between mortality and a number of these risk factors, including central venous catheter use (19,24), sepsis (6,14,17,28), candida score (14), mechanical ventilation (28,30), intubation (30), and parenteral nutrition (20). According to previous studies, the fact that catheter use was not one of the factors affecting mortality may be related to improved aseptic approaches and catheter care practices. In hospitalized patients, candidemia cases with characteristics such as advanced age, ICU stay and acute renal injury should be treated with broader spectrum antifungals and closely monitored to prevent mortality. The fact that infectious diseases consultation leads to reduced mortality and higher compliance with the guidelines in patients with

candidemia (19) should be taken into consideration and it would be useful to seek the opinion of infectious disease specialists in the follow-up of infection in candidemia cases followed in every unit of the hospital.

One of the limitations of the study is that we may have missed useful information regarding the management of patients with candidemia as a result of some uncontrollable variables that may not have been included in this retrospective data collection approach. Another limitation is that antibiogram testing could not be performed on 15 of the isolates. Despite these, this study has important implications for characterizing the epidemiology of candidemia which may be utilized to create new guidelines and practices.

In conclusion, the findings of this study revealed that *C. albicans* was the predominant causative agent in hospitalized candidemia cases, and that 30-day mortality rate was 59.26% –likely due to the high proportion of patients admitted to the ICU. Notably, advanced age, ICU stay, and acute renal injury emerged as independent factors associated with an increased risk of mortality. It is evident from the data and the limitations of this study that extensive population-based studies are necessary to better understand the local characteristics of candidemia and make recommendations for improved management, thereby enabling more effective preventive and therapeutic interventions.

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