Original Investigation / *Özgün Araştırma*

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Comparative Analysis of Candida Species and Mortality in Pediatric and Adult Intensive Care Unit Patients

Pediyatrik ve Yetişkin Yoğun Bakım Hastalarında Kandida Türleri ve Mortalite: Karşılaştırmalı Bir Analiz

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Abstract

Objective: This study aimed to retrospectively investigate the risk factors affecting mortality in pediatric and adult patients with candidemia followed in the pediatric and adult intensive care units of Ankara Bilkent City Hospital.

Material and Methods: The medical records of 101 pediatric (1 month-18 years) and 75 adult (≥18 years) patients diagnosed with candidemia between 2018 and 2023 were reviewed. Demographic data, Candida species distribution, antifungal treatment strategies, and mortality outcomes were evaluated.

Results: In our study, the number of pediatric patients was 101 (57.4%), while the number of adult patients was 75 (42.6%). In both pediatric and adult groups, non-albicans Candida species were the most frequently isolated pathogens, with rates of 56.4% and 54.7%, respectively. The seven-day and 30-day mortality rates were significantly higher in adult patients compared with pediatric patients (seven-day mortality: 37% vs. 8.9%; 30-day mortality: 14% vs. 7.6%; p< 0.001). In univariate analysis, catheter retention, mechanical ventilation, thrombocytopenia, and corticosteroid use were associated with seven-day mortality in both groups. In the adult group, the absence of antifungal therapy was additionally identified as an independent risk factor. In multivariate analysis, mechanical ventilation and thrombocytopenia were independently associated with seven-day mortality among the pediatric patients, while corticosteroid use was significantly associated with 30-day mortality. Failure to remove the catheter increased the risk of mortality by 48.6-fold in children (p< 0.001) and by 5.2-fold in adults (p= 0.015). Intubation increased mortality risk by 13.1-fold in pediatric patients (p= 0.004) and by 3.3-fold in adults (p= 0.022). The absence

Öz

Giriş: Bu çalışma, Ankara Bilkent Şehir Hastanesi çocuk ve erişkin yoğun bakım ünitelerinde takip edilen pediyatrik ve yetişkin kandidemi hastalarında mortaliteyi etkileyen risk faktörlerini retrospektif olarak incelemeyi amaçlamaktadır.

Gereç ve Yöntemler: 2018-2023 yılları arasında kandidemi tanısı konulan 101 pediyatrik (1 ay-18 yaş) ve 75 yetişkin (18 yaş ve üzeri) hastanın tıbbi kayıtları incelenmiştir. Hastaların demografik verileri, kandida türleri, uygulanan antifungal tedavi yaklaşımları ve mortalite sonuçları değerlendirilmiştir.

Bulgular: Çalışmamızda pediyatrik hasta sayısı 101 (%57.4), erişkin hasta sayısı ise 75 (%42.6) idi. Hem pediyatrik hem de erişkin hastalarda en sık izole edilen tür non-albicans Candida olup oranlar sırasıyla %56.4 ve %54.7 olarak bulundu. Yedi ve 30 günlük mortalite oranları erişkin hastalarda pediyatrik hastalara göre belirgin olarak yüksekti (yedi günlük mortalite: %37'ye karşı %8.9; 30 günlük mortalite: %14'e karşı %7.6; p< 0.001). Tek değişkenli analizde her iki grupta da kateterin çıkarılmaması, mekanik ventilasyon gereksinimi, trombositopeni ve steroid kullanımı yedi günlük mortalite ile ilişkili bulundu. Erişkin hasta grubunda ek olarak antifungal tedavi almamış olmak bağımsız bir risk faktörü olarak belirlendi. Çok değişkenli analizde pediyatrik hastalarda mekanik ventilasyon gereksinimi ve trombositopeni yedi günlük mortaliteyle ilişkili bulunurken steroid kullanımı 30 günlük mortaliteyle anlamlı ilişki gösterdi. Kateterin çekilmemesi çocuklarda 48.6 kat (p< 0.001), erişkinlerde 5.2 kat (p= 0.015); entübasyon çocuklarda 13.1 kat (p= 0.004), erişkinlerde 3.3 kat (p= 0.022); antifungal tedavi eksikliği erişkinlerde 43.5 kat (p< 0.001) mortalite riskini artırdı.

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of antifungal therapy increased the mortality risk by 43.5-fold in adults (p< 0.001).

Conclusion: Mortality rates were significantly higher in adult patients compared to pediatric patients. In both age groups, mechanical ventilation and steroid use emerged as major risk factors for increased mortality. These findings suggest that early initiation of empirical antifungal therapy, especially in high-risk patients, may help reduce mortality. Furthermore, timely catheter removal and closer monitoring of the patients requiring mechanical ventilation or steroid therapy may contribute to improved outcomes by reducing adverse consequences of candidemia.

Keywords: Candida, intensive care unit, pediatric, adult, mortality

Sonuç: Yetişkin hastalarda mortalite oranları, pediyatrik hastalara kıyasla belirgin olarak daha yüksek bulunmuştur. Her iki yaş grubunda da entübasyon (mekanik ventilasyon) ve steroid kullanımı, mortaliteyi artıran ortak risk faktörleri olarak öne çıkmaktadır. Bu bulgular doğrultusunda, özellikle risk faktörleri taşıyan hastalarda, ampirik antifungal tedavinin erken dönemde başlatılmasının mortalite oranlarını azaltabileceği düşünülmektedir. Ayrıca, kateterlerin uygun zamanda ve erken dönemde çıkarılması, mekanik ventilasyon ve steroid kullanımı gibi yüksek riskli durumlarda hastaların daha yakından izlenmesi ve önleyici yaklaşımların benimsenmesi, kandidemiye bağlı olumsuz sonuçların azaltılmasına katkı sağlayabilir.

Anahtar Kelimeler: Kandida, yoğun bakım, pediyatrik, erişkin, mortalite

Introduction

Candidemia is the most prominent form of invasive candidiasis and has become an increasingly important healthcare problem, particularly in tertiary care hospitals (1). It is associated with high morbidity and mortality rates, especially among critically ill patients, immunocompromised individuals, and those with complex medical conditions (2). In the United States, candidemia accounts for approximately 22% of bloodstream infections, making it one of the leading causes; however, bacterial pathogens remain more common (3).

The global incidence of candidemia has increased significantly in recent years, largely attributed to the widespread use of immunosuppressive therapies and broad-spectrum antibiotics. Although *Candida albicans* remains an important pathogen, a shift from *C. albicans* predominance toward non-albicans Candida (NAC) species has been reported in many countries (4,5). This study aims to compare the clinical characteristics of candidemia in pediatric and adult patients admitted to intensive care units and to evaluate risk factors affecting mortality.

Materials and Methods

This study was conducted among adult patients admitted to Ankara Bilkent City Hospital adult intensive care units (ICUs) and pediatric patients admitted to Pediatric ICUs of the Children's Hospital. Adult patients aged 18 years and older who developed candidemia at least 48 hours after ICU admission were included in the study. Epidemiological and clinical data of the included patients were recorded retrospectively.

The following parameters were recorded: Age, sex, presence of a central venous catheter, presence of a urinary catheter, intubation status, use of total parenteral nutrition, underlying diseases (diabetes mellitus, solid organ malignancies, hematological malignancies, solid organ transplantation, chronic obstructive pulmonary disease, acute/chronic renal failure, etc.), chemotherapy/radiotherapy within the last month, antibiotic use within the last month, immunosuppressive therapy within the last month, steroid use within the last month, presence of neutropenia within the last month, recent abdominal/extra-abdominal surgical procedures within the last month, antifungal prophylaxis status prior to candidemia, hemodialysis status, Candida species causing candidemia, antifungal susceptibility of the isolated species, and early mortality (within seven days) and late mortality (8-30 days) following candidemia.

Laboratory procedures included a comprehensive approach consisting of automated blood culture incubation, Gram staining, colony subculture, germ tube testing, evaluation with commercial identification kits, and E-test susceptibility testing, following the guidelines of the Clinical and Laboratory Standards Institute and the European Committee on Antimicrobial Susceptibility Testing. Antifungal susceptibility testing was interpreted according to EUCAST v12.0 (2024) criteria. For fluconazole, *C. albicans*, *Candida parapsilosis*, and *Candida tropicalis* were considered susceptible at ≤2 mg/L and resistant at >4 mg/L; *Candida krusei* was considered intrinsically resistant to fluconazole. For echinocandins, a susceptibility breakpoint of ≤0.03 mg/L was used for *C. albicans* and *Candida glabrata* (6).

Ethics approval for this study was obtained from the Ankara Bilkent City Hospital Clinical Research Ethics Committee No. 2 (Decision no: E2.Kurul-E2-21-69).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 22. The normality of the parameters was assessed using the Kolmogorov-Smirnov test, which indicated that the data were not normally distributed. In addition to descriptive statistical methods [median, interquartile range (IQR), and frequency], the Mann-Whitney U test was used to compare quantitative data between two groups. For the comparison of qualitative data, the chi-square test, Fisher's exact chi-square test, Fisher-Freeman-Halton exact test, and continuity (Yates) correction were applied. Multivariate analysis was performed using logistic regression with the backward stepwise method. Statistical significance was set at p< 0.05.

Results

This study aimed to compare the clinical characteristics of candidemia and the risk factors affecting mortality in pediatric and adult patients admitted to ICUs. The findings revealed significant differences between pediatric and adult patients. A total of 101 pediatric (57%) and 75 adult (42.6%) patients were included in the study. The age of pediatric patients ranged from

1 month to 18 years (mean: 6.4 ± 4.2 years), while adult patients ranged from 19 to 85 years (mean: 58.7 ± 14.9 years) (Table 1).

In adults, underlying diseases (p= 0.032), hypotension (p= 0.014), steroid use (p= 0.001), urinary catheter use (p= 0.010), and intubation rates (p= 0.002) were significantly higher. In contrast, pediatric patients had higher rates of hospitalization within the past year (p= 0.008), fever (p= 0.021), surgical history (p= 0.016), and longer total hospital stays (p= 0.005) (Table 2).

Table 1. Comparison of demographic characteristics of pediatric and adult patients with candidemia

Parameters*	Pediatric	Adult	p
Number of patients	101	75	
Sex, male	51 (50.5%)	30 (40%)	[1]0.167
Days of hospitalization before candidemia (median, IQR)	20 (12-36.5)	23 (13-45)	[2]0.092
Underlying disease	81 (80.2%)	75 (100%)	**[3]<0.001**
Hospitalization within the last year	70 (69.3%)	29 (38.7%)	**[1]<0.001**
History of surgery within the last year	39 (38.6%)	12 (16%)	**[3]0.002**
Presence of hypotension during candidemia	48 (47.5%)	54 (73%)	**[1]0.001**
Presence of fever during candidemia	87 (86.1%)	35 (46.7%)	**[3]<0.001**
Steroid use	27 (26.7%)	31 (41.3%)	**[1]0.042**
Duration of steroid use (median, IQR)	5 (3-11)	9 (5-18)	**[2]0.014**
TPN use	18 (17.8%)	16 (21.3%)	[3]0.696
Urinary catheter	77 (76.2%)	71 (94.7%)	**[3]0.002**
Tracheostomy	12 (11.9%)	12 (16%)	[3]0.572
Intubation	47 (46.5%)	57 (76%)	**[3]<0.001**
Total length of hospital stay (median, IQR)	57 (36-103)	41 (21-67)	**[2]0.008**

*Data are presented as n (%) unless otherwise stated.
[1]Chi-square test, [2]Mann Whitney U test, [3]Continuity (yates) correction.
IQR: Interquartile range, TPN: Total parenteral nutrition.

Table 2. Candida species, site of isolation, and prior antifungal use in pediatric and adult patients

	Pediatric Patient	Adult Patient	p
Candida type			
• Albicans	44 (43.6%)	34 (45.3%)	[1]0.815
• Non-albicans	57 (56.4%)	41 (54.7%)	
Candida species			
• *Candida albicans*	44 (43.6%)	34 (45.3%)	
• *Candida parapsilosis*	36 (35.6%)	18 (24%)	
• *Candida tropicalis*	5 (5%)	4 (5.3%)	
• *Candida lusitania*	5 (5%)	2 (2.7%)	[2]0.158
• *Candida glabrata*	3 (3%)	11 (14.7)	
• *Candida kefyr*	4 (4%)	3 (4%)	
• *Candida krusei*	1 (1%)	1 (1.3%)	
• *Candida guilliermondii*	1 (1%)	0	
• *Candida dubliniensis*	2 (2%)	2 (2.7%)	
Site of growth			
• Cathether+peripheral blood culture	61 (60.4%)	24 (32%)	**[1]<0.001**
• Peripheral blood culture	40 (39.6%)	51 (68%)	
Culture negativity after treatment	93 (92.1%)	41 (45.3%)	**[3]<0.001**
Antifungal use in the last three months before candidemia			
• None	85 (84.2%)	61 (81.3%)	**[1]<0.001**
• Yes/Prophylaxis	16 (15.8%)	0 (0%)	
• Yes/Empirical treatment	0 (0%)	14 (18.7%)	

*All data given as (%).
[1]Chi-square test, [2]Fisher Freeman Halton Exact test, [3]Continuity (yates) correction.
DTA: Deep tracheal aspirate.

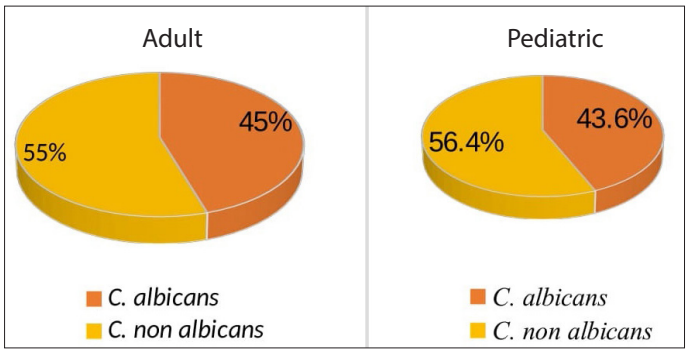

Figure 1. Distribution of *C. albicans* and non-albicans candida in pediatric and adult patients.

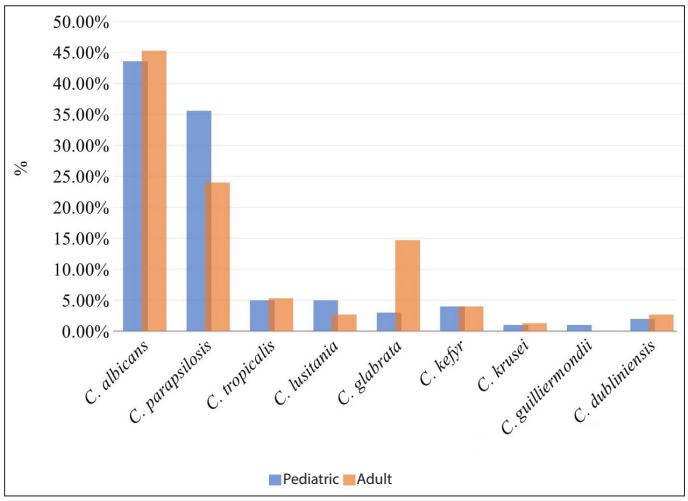

Figure 2. Graphic showing the distribution of candida species in pediatric and adult patients.

In both pediatric and adult patients, *C. albicans* was the most frequently isolated species (Figure 1). In adults, the rate of *C. glabrata* infection was significantly higher (14.7%, p= 0.007), whereas it was detected in 3% of pediatric patients. NAC species were isolated at rates of 56.4% in children and 54.7% in adults (Table 2, Figure 2). Regarding treatment, fluconazole and caspofungin were more commonly used in pediatric patients, whereas echinocandin group antifungals were preferred in adults. Fluconazole use was significantly more common in pediatric patients compared to adults (p< 0.001) (Table 3, Figure 3).

Both seven-day and 30-day mortality rates were significantly higher in adult patients compared to pediatric patients (p< 0.001 for both) (Table 4). Factors associated with increased seven-day mortality included failure to remove the catheter, intubation, and thrombocytopenia. Failure to remove the catheter increased mortality risk by 48.6-fold in children (p= 0.001) and 5.2-fold in adults (p= 0.015); intubation increased mortality risk by 13.1-fold in children (p= 0.004) and 3.3-fold in adults (p= 0.022); and thrombocytopenia increased mortality risk by 7.7-fold in children (p= 0.009) and 11.4-fold in adults (p= 0.002) (Table 5).

For 30-day mortality, failure to remove the catheter, steroid use, lack of antifungal therapy, and leukocytosis were identified as significant risk factors. Failure to remove the catheter increased mortality risk by 11.2-fold in children (p= 0.001) and 4.1-fold in adults (p= 0.018); steroid use increased mortality risk by 6.6-fold in children (p= 0.001); lack of antifungal therapy increased mortality risk by 43.5-fold in adults (p= 0.001); and leukocytosis was associated with a 2.5-fold increased mortality risk in adults (p= 0.040) (Table 4,5).

In logistic regression analysis, the strongest predictors of mortality in pediatric patients were intubation [Odds ratio (OR): 13.1, confidence interval (CI): 5.2-28.3, p= 0.003], thrombocytopenia (OR: 7.7, CI: 2.8-19.4, p= 0.007), and failure to remove the catheter (OR: 48.6, CI: 12.1-109.3, p< 0.001).

Table 3. Antifungal treatments and system involvement in pediatric and adult patients

	Pediatric Patient	Adult Patient	p
Antifungal treatment			
• Fluconazole	55 (54.5%)	10 (13.3%)	
• Voriconazole	1 (1%)	1 (1.3%)	
• Caspofungin	24 (24)	1 (1.3%)	
• Micafungin	1 (1%)	15 (20%)	**[1]<0.001**
• Anidulafungin	0	24 (32%)	
• Liposomal amphotericin B	8 (7.9%)	3 (3%)	
• No antifungal treatment	12 (11.9%)	21 (28%)	
System involvement			
• None	97 (96%)	21 (28%)	
• Liver	4 (4%)	0	**[1]<0.001**
• Eye	0	2 (2.7%)	
• Not investigated	0	52 (69.3%)	
Treatment duration, day (median, IQR)	18 (IQR 14-24)	14 (IQR 7-21)	**[2]0.015**

Data are presented as n (%) unless otherwise stated.
[1]Fisher Freeman Halton exact test, [2]Mann Whitney U test.
IQR: Interquartile range.

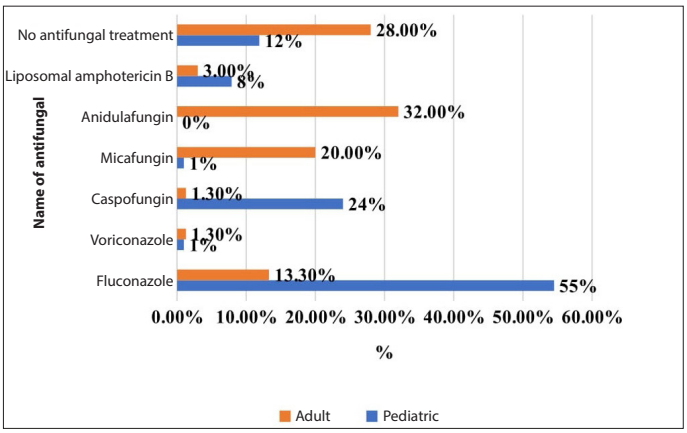

Figure 3. Graphic demonstrating antifungal treatments in pediatric and adult patients.

In adult patients, the most important predictors of mortality were lack of antifungal therapy (OR: 43.5, CI: 18.2-96.7, p< 0.001), leukocytosis (OR: 2.5, CI: 1.2-5.8, p= 0.035), and failure to remove the catheter (OR: 4.1, CI: 1.7-9.4, p= 0.012) (Table 6,7).

Discussion

Candidemia is a complex infection associated with high mortality rates, particularly among intensive care unit patients, and poses significant challenges in treatment management. In our study, risk factors affecting candidemia-related mortality were evaluated in detail in both pediatric and adult patients. Our findings indicate that mortality determinants are associated with different clinical dynamics in these two age groups.

Table 4. Univariate analysis of risk factors affecting seven-day mortality in pediatric patients

		Seven-Day Mortality			OR
Pediatric Patient		**None (n= 92)**	**Present (n= 9)**	**p**	**(95% CI)**
Age (month) Median (IQR)		87.9 (29.4-340.7)	292.8 (12.5-456.6)	[1]0.528	
Age (year) Median (IQR)		2.9 (0.97-11.19)	9.6 (0.41-15)	[1]0.528	
Length of hospital stay 61 (39-108.5)			16 (11-34.5)	[1]0.001*	0.9 (0.9-0.99)
Predisposing factors					
Surgery		35 (38%)	4 (44.4%)	[2]0.7	
Steroid use		21 (22.8%)	6 (66.7%)	[2]0.010*	6.76 (1.5-29.3)
Duration of steroid treatment Median (IQR)		5 (3-10)	4 (2.7-12.7)	[1]0.796	
Chemotherapy		14 (15.2%)	0 (0%)	[2]0.354	
Radiotherapy		3 (3.3%)	0 (0%)	[2]1.000	
Empirical antifungal before candidemia		14 (15.2%)	2 (22.2%)	[2]0.631	
Antibiotics before candidemia		82 (89.1%)	9 (100%)	[2]0.593	
TPN		17 (18.5%)	1 (11.1%)	[2]1.000	
Invasive procedures					
Urethral catheter		68 (73.9%)	9 (100%)	[2]0.110	
Intubation		39 (42.4%)	8 (88.9%)	[2]0.011*	10.8 (1.3-90.3)
PEG		10 (10.9%)	1 (11.1%)	[2]1.000	
Tracheostomy		11 (12%)	1 (11.1%)	[2]1.000	
CVC		80 (87%)	9 (100%)	[2]0.594	
Catheter status after candidemia	Removed	66 (71.7%)	1 (11.1%)	[3]0.001*	
	Not removed	13 (14.1%)	8 (88.9%)		48.61 (5.6-421.5)
	Lock therapy	1 (1.1%)	0 (0%)		
	No catheter	12 (13%)	0 (0%)		
Laboratory parameters					
Platelet	Normal	49 (53.3%)	2 (22.2%)	[3]0.004*	
	Low	22 (23.9%)	7 (77.8%)		7.79 (1.497-40.591)
	High	21 (22.8%)	0 (0%)		

Table 4. Univariate analysis of risk factors affecting seven-day mortality in pediatric patients (continue)

		Seven-Day Mortality			OR
Pediatric Patient		**None (n= 92)**	**Present (n= 9)**	**p**	**(95% CI)**
CRP	Normal	6 (6.5%)	0 (0%)	[2]1.000	
	High	86 (93.5%)	9 (100%)		
Leucocyte	Normal	40 (43.5%)	3 (33.3%)	[3]0.830	
	High	47 (51.1%)	6 (66.7%)		
	Low	5 (5.4%)	0 (0%)		
Lymphocyte	Normal	40 (43.5%)	2 (22.2%)	[3]0.359	
	High	1 (1.1%)	0 (0%)		
	Low	51 (55.4%)	7 (77.8%)		
PMNL	Normal	56 (60.9%)	4 (44.4%)	[3]0.352	
	High	29 (31.5%)	5 (55.6%)		
	Low	7 (7.6%)	0 (0%)		
Candida type that grew	*C. albicans*	41 (44.6%)	3 (33.3%)	[2]0.728	
	Non-albicans	51 (55.4%)	6 (66.7%)		
Antifungal given	No Antifungal treatment	10 (10.9%)	2 (22.2%)	[3]0.356	
	Fluconazole	52 (56.5%)	3 (33.3%)		
	Voriconazole	1 (1.1%)	0 (0%)		
	Caspofungin	20 (21.7%)	4 (44.4%)		
	Micafungin	1 (1.1%)	0 (0%)		
	Amphotericin B	8 (8.7%)	0 (0%)		

[1]Mann Whitney U test, [2]Fisher's exact test, [3]Fisher Freeman Halton exact test, *p< 0.05.
TPN: Total parenteral nutrition, PEG: Percutaneous endoscopic gastrostomy, CVC: Central venous catheter, PMNL: Polymorphonuclear leucocyte, CRP: C-reactive protein, CI: Confidence interval.

Table 5. Univariate analysis of risk factors affecting seven-day mortality in adult patients

		Seven-Day Mortality			OR
Adult Patients		**None (n= 38)**	**Present (n= 37)**	**p**	**(%95 CI)**
Age (year) $_{Median(IQR)}$		72.2 (59.8-81.8)	75.7 (69.7-84.2)	[1]0.227	
Length of stay		65.5 (45.2-100.75)	23 (15.5-35.5)	[1]0.001*	0.939 (0.912-0.967)
Predisposing factors					
Surgery		10 (26.3%)	2 (5.4%)	[2]0.031*	6.250 (1.265-30.877)
Steroid use		13 (34.2%)	18 (48.6%)	[2]0.301	
Duration of steroid treatment $_{Median(IQR)}$		13 (7.5-98.5)	7 (5-14.5)	[1]0.035*	0.939 (0.852-1.036)
Chemotherapy		4 (10.5%)	2 (5.4%)	[3]0.674	
Radiotherapy		2 (5.3%)	1 (2.7%)	[3]1.000	
Empirical antifungal before candidemia		9 (23.7%)	5 (13.5%)	[2]0.404	
Antibiotics before candidemia		37 (97.4%)	37 (100%)	[3]1.000	
TPN		9 (23.7%)	7 (18.9%)	[2]0.825	
Invasive procedures					
Urethral catheter		37 (97.4%)	34 (91.9%)	[3]0.358	

Table 5. Univariate analysis of risk factors affecting seven-day mortality in adult patients (continue)

		Seven-Day Mortality			OR
Adult patients		**None (n= 38)**	**Present (n= 37)**	**p**	**(%95 CI)**
PEG		11 (28.9%)	2 (5.4%)	[2]0.017*	7.130 (1.457-34.895)
Tracheostomy		10 (26.3%)	2 (5.4%)	[2]0.031*	6.250 (1.265-30.877)
Catheter presence		31 (81.6%)	28 (75.7%)	[2]0.732	
Catheter status after candidemia	Removed	15 (39.5%)	4 (10.8%)	[5]0.002*	
	Not removed	7 (18.4%)	20 (54.1%)		5.210 (1.833-14.805)
	No catheter	7 (18.4%)	9 (24.3%)		
	Changed	9 (23.7%)	4 (10.8%)		
Laboratory parameters					
Platelet	Normal	32 (84.2%)	21 (56.8%)	[4]0.001*	
	Low	2 (5.3%)	15 (40.5%)		11.429 (2.366-55.194)
	High	4 (10.5%)	1 (2.7%)		
CRP	Normal	1 (2.6%)	2 (5.4%)	[3]0.615	
	High	37 (97.4%)	35 (94.6%)		
Leucocyte	Normal	19 (50%)	12 (32.4%)	[4]0.066	
	High	17 (44.7%)	25 (67.6%)		
	Low	2 (5.3%)	0 (0%)		
Lymphocyte	Normal	17 (44.7%)	12 (32.4%)	[4]0.345	
	High	0 (0%)	1 (2.7%)		
	Low	21 (55.3%)	24 (64.9%)		
PMNL	Normal	21 (55.3%)	13 (35.1%)	[2]0.129	
	High	17 (44.7%)	24 (64.9%)		
Candida type that grew	*C. albicans*	16 (42.1%)	18 (48.6%)	[2]0.736	
	Non-albicans	22 (57.9%)	19 (51.4%)		
Antifungal given	No antifungal treatment	1 (2.6%)	20 (54.1%)	[4]0.001*	43.529 (5.390-351.53)
	Fluconazole	7 (18.4%)	3 (8.1%)		
	Voriconazole	0 (0%)	1 (2.7%)		
	Caspofungin	1 (2.6%)	0 (0%)		
	Micafungin	10 (26.3%)	5 (13.5%)		
	Anidulafungin	17 (44.7%)	7 (18.9%)		
	Liposomal amphotericin	2 (5.3%)	1 (2.7%)		

[1]Mann Whitney U test, [2]Continuity (yates) correction, [3]Fisher's exact test, [4]Fisher Freeman Halton exact test, [5]Chi-square test, *p< 0.05.
TPN: Total parenteral nutrition, PEG: Percutaneous endoscopic gastrostomy, PMNL: Polymorphonuclear leucocyte, CRP: C-reactive protein, CI: Confidence interval.

Table 6. Logistic regression analysis of parameters affecting seven-day mortality in pediatric patients

		95% CI for OR		
Pediatric Patient	**OR**	**Lower**	**Upper**	**p**
Intubation	13.132	1.293	133.411	0.029*
Thrombocytopenia	6.595	1.045	41.609	0.045*

CI: Confidence interval, OR: Odds ratio.

Table 7. Logistic regression analysis of parameters affecting 30-day mortality in adults and children

		95% CI for OR		
Adult Patients	**OR**	**Lower**	**Upper**	**p**
Failure to remove catheter	4.395	1.277	15.1123	0.019*
Leucocytosis	2.572	0.908	7.286	0.075
		95% CI for OR		
Pediatric Patients	**OR**	**Lower**	**Upper**	**p**
Steroid use	9.282	1.614	53.387	0.013*
Intubation	4.321	0.752	24.834	0.101
Catheter status	24.56	3.122	193.201	0.002*
Thrombocytopenia	8.879	1.436	54.918	0.019*

CI: Confidence interval, OR: Odds ratio.

In adult patients, lack of antifungal therapy, failure to remove the catheter, mechanical ventilation, thrombocytopenia, and steroid use were significantly associated with mortality. These findings highlight the critical importance of early initiation of antifungal therapy and strict control of invasive interventions for improving survival. Consistent with the literature, delayed initiation of antifungal treatment has been reported to significantly increase mortality (7,8).

In pediatric patients, failure to remove the catheter, requirement for mechanical ventilation, thrombocytopenia, and steroid use were associated with mortality; in multivariate analysis, intubation and thrombocytopenia were identified as independent predictors of early mortality. These findings may be explained by the suppression of the immune response and the increased difficulty in infection control due to invasive procedures. Similarly, Zaoutis et al. reported that mechanical ventilation and hematological malignancy were strongly associated with mortality in pediatric candidemia (9).

In our study, failure to remove the catheter increased mortality by 48.6-fold in pediatric patients, compared to 5.2-fold in adults. This difference may be attributed to the greater difficulty of vascular access management and limited alternative access options in children. Large cohort studies by Nucci et al. and Puig-Asensio et al. also reported a strong association between failure to remove the catheter and increased mortality (10,11).

In the adult group, absence of antifungal therapy increased the risk of mortality by 43.5-fold ($p< 0.001$). In a multicenter analysis conducted by Arendrup et al., initiation of antifungal therapy within the first 24 hours was shown to double survival rates (12). This finding supports the life-saving importance of timely initiation of appropriate treatment.

Thrombocytopenia was significantly associated with mortality in both pediatric and adult patients. A multicenter prospective study conducted in Türkiye similarly identified thrombocytopenia as an independent risk factor for candidemia-related mortality, with significantly lower 30-day survival rates observed in patients with low platelet counts (13). This underscores the importance of considering hematological parameters in the pathophysiology of invasive fungal infections.

Steroid use was particularly associated with 30-day mortality in the pediatric group. Systematic reviews on invasive fungal diseases have demonstrated that steroid therapy may increase mortality (14). There is also well-established evidence that glucocorticoids can worsen both the risk and outcomes of invasive fungal infections (15).

Although mortality analysis based on species distribution did not show a significant difference in our study, the literature suggests that *C. krusei* and *C. tropicalis* infections are generally associated with higher mortality, whereas *C. parapsilosis* is associated with lower mortality (16).

The higher mortality rates observed in adult patients compared to pediatric patients may have several explanations. Adult patients often have a higher burden of comorbidities (such as diabetes mellitus, chronic renal failure, malignancy, and organ failure), which complicates infection control and negatively affects response to antifungal therapy (7,8). In addition, sepsis, septic shock, and multiorgan dysfunction occur more frequently in adults, representing key factors contributing to early mortality (16). Another important factor is the delay in initiating antifungal therapy in adults, often due to waiting for diagnostic confirmation and culture results, whereas empirical therapy is typically initiated earlier in pediatric patients (12). This is consistent with our finding that lack of antifungal therapy increased mortality risk by 43.5-fold in adults.

In conclusion, the most significant factors increasing mortality in our study were failure to remove the catheter and mechanical ventilation in pediatric patients, and lack of antifungal therapy and failure to remove the catheter in adult patients. These findings emphasize that early initiation of antifungal treatment, appropriate catheter management, and

limitation of invasive interventions are critical for improving survival.

Ethics Committe Approval: This study was approved by the Ethics Committee for Clinical Research No. 2 at Ankara Bilkent City Hospital (Decision no.: E2-21-69, Date: 24.03.2021).

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