Research Article / Araştırma Makalesi

Evaluation of Clinical and Epidemiologic Characteristics, Risk Factors, and Treatment Regimens of Invasive Candida Infections in Children

Çocuklarda İnvaziv Kandida Enfeksiyonlarının Klinik ve Epidemiyolojik Özelliklerinin Risk Faktörlerinin ve Tedavi Rejimlerinin Değerlendirilmesi

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Abstract: Invasive candida infections are one of the most common healthcare-associated infections. In this study, we have aimed both to determine the risk factors for invasive fungal infections and to evaluate clinical and epidemiologic characteristics of the cases. Pediatric cases who were followed up due to invasive fungal infection in Eskisehir Osmangazi University Hospital Pediatrics Clinic between January 2015 and March 2023 were included in the study. The study included 41 pediatric cases consisting of 23 (56%) males with an overall average age of 38 months. The most common candida species were Candida albicans (54%), Candida parapsilosis (27%), and Candida glabrata. The most common risk factors were prior antibiotherapy (100%), hospitalization (100%), intensive care unit stay (88%), central catheterization (88%), and total parenteral nutrition (TPN). C.albicans strains were resistant to fluconazole in 5%, caspofungin, and micafungin in 10% of the cases. C. parapicillosis strains were resistant to fluconazole in 37%, caspofungin in 45% micafungin in 55%, and amphotericin-B in only 9% of the cases. TPN use and mortality rates were higher in the C. albicans-infected group, negative blood culture persisted for a longer period in the non-albicans candida group.Invasive fungal infections are among the most important healthcare-associated infectious agents and the most important risk factors include the use of broad-spectrum antibiotics, prolonged hospital and intensive care unit stays, central catheterization, mechanical ventilation, TPN use, increased prophylactic antifungal and steroid use. Although C. albicans is still the most common candida species, C parapsilosis is being identified at an increasing rate.
Keywords: candida infections, children, risk factors

Özet: İnvazif kandida enfeksiyonları sağlık bakımı ilişkili enfeksiyonlar arasında en yaygın olanlardan biridir. Bu çalışmada, invaziv mantar enfeksiyonlarının risk faktörlerini, klinik ve epidemiyolojik özelliklerini değerlendirmeyi amaçladık. Çalışmaya Ocak 2015 ile Mart 2023 tarihleri arasında Eskişehir Osmangazi Üniversitesi Hastanesi Çocuk Sağlığı ve Hastalıkları Kliniğinde invaziv mantar enfeksiyonu nedeniyle takip edilen pediatrik olgular dahil edildi. Çalışmaya dahil edilen olguların, yaş ortalaması 38 aydı ve 23'ü (%56) erkekti. En sık saptanan kandida türleri Candida albicans (%54), Candida parapsilosis (%27) ve Candida glabrata idi. En sık görülen risk faktörleri; antibiyotik kullanımı (%100), hastaneye yatış (%100), yoğun bakımda kalış (%88), santral kateterizasyon (%88) ve total parenteral beslenme (TPN) idi. C.albicans suşlarının flukonazole %5 oranında, kaspofungin ve mikafungine ise %10 oranında dirençli olduğu belirlendi. C. parapisillosis suşlarının flukonazole %37 oranında, kaspofungine %45 oranında mikafungine %55 oranında ve amfoterisin-B'ye ise sadece %9 oranında dirençli olduğu görüldü. C. albicans ile enfekte grupta TPN kullanımı ve mortalite oranları daha yüksek iken, albicans dışı kandida grubunda kan kültürü negatifliği daha uzun süre devam etti. Risk faktörler arasında geniş spektrumlu antibiyotik kullanımı, hastanede ve yoğun bakımda uzun süreli kalış süresi, santral kateterizasyon, mekanik ventilasyon, TPN kullanımı, profilaktik antifungal ve steroid kullanımının artması yer almaktadır. C. albicans halen en yaygın kandida türü olmasına rağmen, C parapsilosis giderek artan oranda tanımlanmaktadır.
Anahtar Kelimeler: candida enfeksiyonları, çocuk, risk faktörler

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1. Introduction

Candida species are one of the most important causative pathogens of invasive fungal infections in hospitalized patients. The incidence of invasive fungal infections has increased recently with the increase in the frequency of invasive surgical interventions, widespread use of pediatric intensive care units, increased use of broad-spectrum antibiotics, and prolonged hospitalizations. Candida spp. ranks third among the agents causing healthcare-associated bloodstream infections (1).

Although Candida albicans (C. albicans) is the most frequently isolated fungal species in invasive fungal infections and healthcare-associated fungal infections, there is an increase in non-albicans Candida spp. and resistant strains with the increase in prophylactic azole-derived antifungal use (2-4). Risk factors such as broad-spectrum antibiotic use, catheterization, mechanical ventilation, prolonged hospitalization, and intensive care unit stay predispose to the development of invasive fungal infections (5-6).

It is of vital importance to document the risk factors for fungal infections, the most frequently isolated Candida spp., antifungal resistance, and susceptibility characteristics of each center for both early diagnosis and initiation of appropriate empirical antifungal therapy. In this study, we have aimed both to determine the risk factors for invasive fungal infections and to evaluate treatment regimens, clinical and epidemiologic characteristics of the cases.

2. Materials and Method

Among children between the ages of 1 month and 18 years who were followed up as inpatients in the Pediatrics Clinic Eskişehir Osmangazi University Faculty of Medicine Hospital between January 2015 and March 2023 those with identified growth of candida spp. in their sterile body fluids (blood, tracheal aspirate, abscess, pleural-peritoneal fluid) and central catheter tips were included in the study. Clinical and epidemiologic characteristics, risk factors, and treatment regimens were retrospectively recorded from the hospital automation system. Cases with growth of Candida spp. without any evidence of active infection based on the results of clinical and laboratory tests and cases considered as colonization or contamination were not included in the study.

The presence of chronic disease, history of hospitalization, antibiotic use, intensive care unit stay, presence of a central catheter, mechanical ventilation, total parenteral nutrition (TPN) support, prophylactic antifungal use, steroid use, immunosuppression, neutropenia, and lymphopenia were considered as risk factors for systemic fungal infections. Candidemia was defined as the growth of Candida spp. in blood and/or catheter tip cultures. In patients with central venous catheters (CVC), isolation of Candida spp. from any blood sample or catheter tip culture was considered catheter-associated candidemia.

Blood samples were taken under sterile conditions from patients with suspected candidemia. The samples sent to the microbiology laboratory were placed in BacT/Alert medium bottles and incubated in a BacT/Alert 3D system (BioMérieux, France) for 7 days. Samples found as yeast at the end of the Gram staining were inoculated on Sabouraud dextrose agar (SDA) and 5% sheep blood agar plates. At the end of the incubation period, the germ tube test, Tween 80 agar inoculation, CHROMagar inoculation, and identification with the API ID 32C (BioMérieux, France) were conducted on the colonies. One to two colonies that grew on the plates were suspended in saline (NaCl, 0.85%), and the turbidity was adjusted to 0.5 McFarland standard. RPMI 1640 medium supplemented with 2% glucose and with the pH adjusted to 7.0 and morpholinepropanesulfonic acid (MOPS) buffer were used for susceptibility tests. Yeast suspension was evenly spread onto the surface of the medium. Petri plates were allowed to dry for 10 to 15 min before the Etest (BioMérieux, France) strips were applied. The Etest procedure was performed according to the manufacturer's directions using

fluconazole, voriconazole, itraconazole, posaconazole, amphotericin B, and anidulafungin test strips. MIC values were recorded after 24 to 48 h of incubation at 35°C. Fluconazole, voriconazole, itraconazole, anidulafungin, posaconazole, and amphotericin B were evaluated according to and he Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint values.

Leukocytosis was defined as leukocyte count ≥10,000/mm³, lymphopenia as lymphocyte counts <3000/mm³ for 0-1 age, ≤1,500/mm³ for >1 age, while neutropenia was defined as absolute neutrophil counts (ANC) less than 1500/mm³ (7). The patient's prognosis was evaluated in consideration of their survival within 30 days after isolation of Candida spp. from sterile body fluids. Deaths within 30 days after candidemia were considered candidemia-related mortality regardless of the cause of death. The study was initiated after obtaining the approval of the ethics committee of Eskisehir Osmangazi University (no:612 date: 02.05. 2023).

Statistical Analysis

SPSS version 18.0 program was used in the analysis of the data. The conformity of the variables to normal distribution was checked with the Kolmogorov-Smirnov test. Mean, standard deviation and median values were used when presenting descriptive analyses. Categorical variables were compared with Pearson's chi-square and Fisher's exact tests. The Mann-Whitney U test was used to comparatively evaluate non-normally distributed (non-parametric) variables between groups. The level of statistical significance was set at a p-value below 0.05.

3. Results

The study included 56 patients with growth of Candida spp. identified in the culture media of sterile body fluids and central catheter tips. Fifteen cases were excluded from the study due to colonization and contamination. The remaining 41 cases consisted of 23 (56%) male and 18 female patients with an overall average age of 38 months. Comorbid diseases were present in 40 (97%) cases and the most common comorbidities were neurologic (36%), gastrointestinal (31%) and cardiac (10%) diseases. Growth of Candida spp. most frequently detected in blood (70%), catheter tip (10%), and tracheal aspirate (10%) samples, while the most common candida species were Candida albicans (54%), Candida parapsilosis (C. parapsilosis) (27%) and Candida glabrata (C. glabrata) (14%) in order of decreasing frequency (Table 1). The most common risk factors were prior antibiotherapy (100%), hospitalization (100%), intensive care unit stay (88%), central catheterization (88%), surgery (68%), total parenteral nutrition (TPN) (68%), mechanical ventilation (54%) and urinary catheterization (32%) (Table 1).

C. albicans strains were resistant to fluconazole in 5%, caspofungin, and micafungin in 10% of the cases, while resistance to amphotericin B was not detected. C. parapsilosis strains were resistant to fluconazole in 37%, caspofungin in 45% micafungin in 55%, and amphotericin B in only 9% of the cases (Table 2). The most commonly used antifungal agents in empirical treatment were caspofungin, fluconazole, and amphotericin B, while the most commonly used antifungal agents in targeted treatment were amphotericin B, caspofungin and fluconazole in order of decreasing frequency. While 43.9% of the patients received sequential antifungal treatment, only 1 patient received combined antifungal treatment. The mean duration of antifungal use was 19 days, while any fungal agent could not be identified in blood cultures for a mean duration of 13 days (Table 3).

Total parenteral nutrition (TPN) use and mortality rates were higher in the C. albicans - infected group (p:0.04, p:0.05), while negative blood culture persisted for a longer period in the non-albicans candida group (p:0.05) (Table 4). Longer duration of antifungal use and blood culture negativity was observed in the C. parapsilosis group compared to the C. albicans group (p:0.02, p:0.01), while mechanical ventilation was used more frequently and mortality rates were higher in the C. albicans group (p:0008, p:0.01) (Table

5). We have also observed that prolonged TPN use and mechanical ventilation increased mortality rates (p:0.007, p:0.001) (Table 6). When candida species were analyzed according to the annual incidence rates of candidiasis, it was observed that cases of candidiasis caused by C. albicans were frequently detected almost every year, while the incidence of C. parapsilosis gradually increased within the last 3 years (Figure 1).

Table 1. Demographic and clinical characteristics of the patients

	n:41 (%)
Age (mos)	38 (2-192)
Gender	
Male	23 (56)
Female	18 (44)
Underlying diseases	40 (97)
Neurologic diseases	15 (36)
Gastrointestinal diseases	13 (31)
Congenital heart disease	4 (10)
Hemato-oncological diseases	3 (7)
Renal diseases	2 (5)
Metabolic diseases	2 (5)
Rheumatologic diseases	1 (2)
Pediatric Intensive Care Unit	28 (68)
Pediatric Service	6 (14)
Pediatric Surgery	5 (12)
Pediatric Hemato-Oncology	2 (5)
Blood	29 (70)
Catheter	4 (10)
Tracheal Aspirates	4 (10)
Abscess	3 (7)
Peritoneum	1 (3)
Candida albicans	19 (46)
Non-albicans candida	22 (54)
C. parapsilosis	11 (27)
C. glabrata	6 (14)
C. tropicalis	4 (10)
C. guillermondii	1 (2)
Leukocyte counts	11.000 /mm^3 (1.000-35.700/mm^3)
Leukocytosis	14 (34)
Neutropenia	8 (20)
Lymphopenia	10 (25)
Thrombocytopenia	15 (36)
C-reactive Protein	37 (11-170 mg/L)
Procalcitonin	15 (0.1-100 ng/mL)
Hospital stay (days)	39 (11-87)
Duration of antifungal therapy (days)	19 (8-61)
Duration of culture negativity (days)	13 (5-41)
Exitus	11 (27)
Risk factors	
Hospitalization	41 (100)
Antibiotics used	41 (100)
Carbapenems	34 (83)
Glycopeptides	34 (83)
Cephalosporins	32 (78)
Aminoglycosides	17 (42)
Chronic diseases	40 (97)
Intensive care unit stay	36 (88)
Central catheterization	36 (88)
Surgery	28 (68)
Total parenteral nutrition	28 (68)
Empirical antifungal therapy	24 (58)
Mechanical ventilation	22 (54)

Urinary catheterization	13 (32)
Steroıd Use	13 (32)
Lymphopenia	10 (25)
Neutropenia	8 (20)
Tracheostomy	4 (5)
Immunosuppressive drug use	4 (10)
Hemato-oncologic malignancy	3 (7)
Prophylactic antifungal therapy	3 (7)
Immunodeficiency	2 (5)
Hemodialysis	2 (5)

Table 2. Antifungal resistance patterns of the cases

		Fluconazole		**Caspofungin**		**Amphotericin B**		**Micafungin**		**Voriconazole**	
	n	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**
C. albicans	19	18 (95)	1 (5)	17 (90)	2 (10)	19 (100)	-	17 (90)	2 (10)	18 (95)	1 (5)
C. parapsilozis	11	7 (63)	4 (37)	6 (55)	5 (45)	10 (91)	1 (9)	5 (45)	6 (55)	10 (91)	1 (9)
C. glabrata	6	3 (50)	3 (50)	5 (83)	1 (17)	6 (100)	-	5 (83)	1 (17)	6 (100)	-
C. tropicalis	4	4 (100)	-	4 (100)	-	4 (100)	-	4 (100)	-	4 (100)	-
C. guillenmondii	1	1 (100)	-	1 (100)	-	-	1 (100)	-	1 (100)	1 (100)	-

S: sensitive; R: resistant

Table 3. Antifungal treatment regimens

	n:41
Targeted treatment regimens:	
Amphotericin B	20 (48)
Caspofungin	14 (34)
Fluconazole	4 (9.8)
Voriconazole	2 (4.9)
Micafungin	1 (2.4)
Empirical treatment regimens:	24 (58.5)
Caspofungin	11 (42.3)
Fluconazole	7 (17)
Amphotericin B	4 (9.7)
Micafungin	2 (4.9)
Prophylactic treatment regimens:	3 (7.3)
Fluconazole	2 (4.8)
Voriconazole	1 (2.1)
Sequential treatment regimens:	18 (43.9)
Caspofungin→Amphotericin-B	7 (17)
Fluconazole→Caspofungin	5 (12.1)
Fluconazole→ Amfotericin B	2 (4.9)
Mıcafungin→ Amfotericin B	2 (4.9)
Voriconazole → Amfotericin B	2 (4.9
Combination treatment	1 (2.5)
Amfotericin-B+fluconazole	4 (9.8)
Duration of antifungal treatment (days)	19 (8-61)
Duration of culture negativity (days)	13 (5-41)

Table 4. *Comparative evaluation of cases infected with C. albicans and non-albicans Candida spp.*

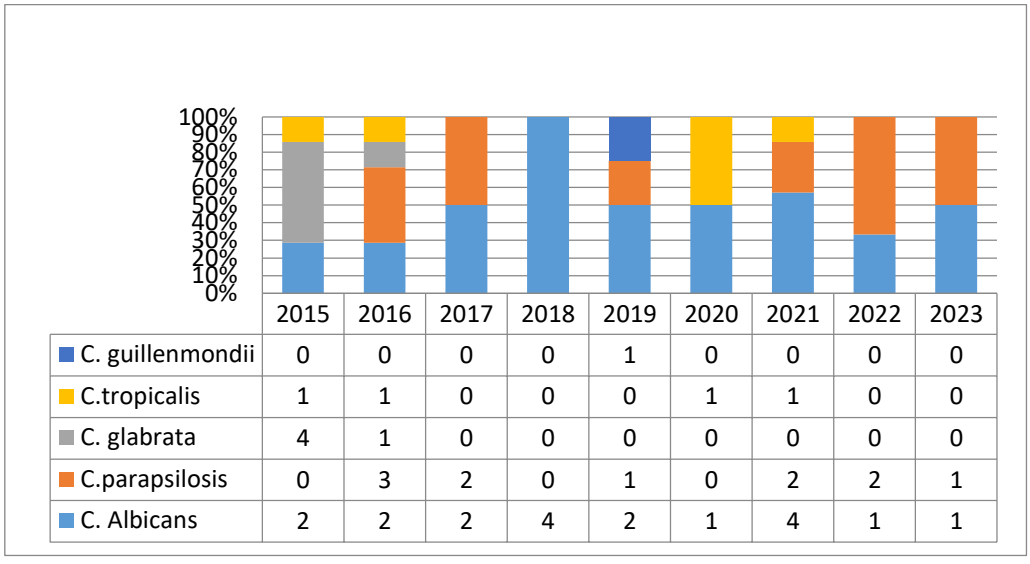
	C. albicans **Total n: 19** **n (%)**	**non-albicans C.** **Total n:22** **n (%)**	**p**
Hospitalization	19 (100)	22 (100)	-
Antibiotic use	19 (100)	22 (100)	-
Carbapenems	17 (90)	17 (77)	0.2
Glycopeptides	16 (84)	18 (82)	0.5
Cephalosporins	15 (79)	17 (77)	0.6
Aminoglycosides	5 (26)	12 (55)	0.06
Chronic diseases	18 (95)	22 (100)	0.1
Intensive care unit stay	17 (909	19 (86)	0.5
Central catheterization	18 (95)	18 (82)	0.2
Surgery	14 (74)	14 (64)	0.3
TPN	16 (84)	12 (55)	**0.04**
Prophylactic antifungal therapy	1 (5)	2 (9)	0.5
Mechanical ventilation	15 (79)	7 (32)	**0.03**
Urinary catheterization	8 (42)	5 (23)	0.1
Steroıd use	8 (42)	5 (23)	0.1
Lymphopenia	7 (37)	3 (14)	0.08
Neutropenia	4 (21)	4 (18)	0.5
Tracheostomy	2 (10)	2 (9)	0.6
Immunosuppressive therapy	3 (16)	1 (5)	0.2
Hemato-oncologic malignancies	2 (10)	1 (5)	0.4
Hemodialysis	1 (5)	2 (9)	0.5
Duration of hospitalization (days)	38 (11-61)	40 (15-87)	0.4
Duration of antifungal therapy (days)	17 (8-42)	20 (9-61)	0.3
Duration of culture negativity (days)	10 (5-32)	16 (6-41)	**0.05**
Exitus	9 (47)	2 (9)	**0.03**

Tablo-5. *Comparative evaluation of cases infected with C. albicans and C. parapsilosis*

	C. albicans **Total n: 19** **n (%)**	***C. parapsilosis*** **Total n:11** **n (%)**	**p**
Hospitalization	19 (100)	11 (100)	-
Antibiotic use	19 (100)	11 (100)	-
Carbapenems	17 (90)	7 (64)	0.1
Glycopeptides	16 (84)	9 (82)	0.6
Cephalosporins	15 (79)	9 (82)	0.6
Aminoglycosides	5 (26)	6 (55)	0.1
Chronic diseases	18 (95)	11 (100)	0.1
Intensive care unit stay	17 (909	9 (82)	0.4
Central catheterization	18 (95)	9 (82)	0.2
Surgery	14 (74)	6 (55)	0.2
Total parenteral nutrition	16 (84)	6 (55)	0.09
Prophylactic antifungal therapy	1 (5)	2 (18)	0.2
Mechanical ventilation	15 (79)	3 (27)	**0.008**
Urinary catheterization	8 (42)	1 (9)	0.06
Steroıd use	8 (42)	4 (36)	0.5
Lymphopenia	7 (37)	1 (9)	0.1
Neutropenia	4 (21)	1 (9)	0.3
Immunosuppressive therapy	3 (16)	1 (9)	0.5
Hemato-oncologic malignancies	2 (10)	1 (9)	0.7
Hemodialysis	38 (11-61)	39 (10-87)	0.5
Duration of hospitalization (days)	17 (8-42)	24 (9-61)	**0.02**
Duration of antifungal therapy (days)	10 (5-32)	18 (6-41)	**0.01**
Duration of culture negativity (days)	9 (47)	1 (9)	**0.01**

Table 6. ***Comparative evaluation of survived, and non-survived cases***

	Survived (n:30)(%)	Excitus (n:11)(%)	Total n:41	p
Pediatric intensive care unit	18 (60)	10 (91)	28	
Pediatric ward	6 (20)	-	6	
Pediatric surgery ward	4 (13)	1 (9)	5	0.2
Pediatric hemato-oncology	2 (7)	-	2	
Blood	22 (73)	7 (64)	29	
Catheter tips	4 (13)	-	4	
Tracheal Aspirates	1 (3.3)	3 (27)	4	0.1
Abscess	2 (6.6)	1 (9)	3	
Peritoneum	1 (3.3)	-	1	
Candida albicans	10 (33)	9 (82)	19	**0.007**
Non-albicans candida	20 (66)	2 (18)	22	
Candida parapsilosis	10 (33)	1 (9)	11	**0.03**
Antibiotic use	30 (100)	11 (100)	41	-
Carbapenems	25 (83)	9 (82)	34	0.6
Glycopeptides	24 (80)	10 (91)	34	0.3
Cephalosporins	23 (76)	9 (82)	32	0.5
Aminoglycosides	12 (40)	5 (45)	17	0.5
Chronic Disease	29 (98)	11 (100)	40	0.6
Intensive care unit stay	26 (87)	10 (91)	36	0.5
Central catheterization	25 (83)	11 (100)	35	0.1
Surgery	19(63)	9 (82)	28	0.2
Total parenteral nutrition	17 (57)	11 (100)	28	**0.007**
Prophylactic antifungal therapy	3 (10)	-	3	0.3
Mechanical ventilation	11 (37)	11 (100)	22	**0.001**
Urinary catheterization	7 (23)	6 (55)	13	0.06
Steroıd use	8 (26)	5 (50)	13	0.2
Lymphopenia	5 (50)	5 (50)	10	0.07
Neutropenia	6 (75)	2 (25)	8	0.6
Immunosuppressive therapy	2 (6.6)	2 (18)	4	0.2
Hemato-oncologic malignancies	2 (6.6)	1 (9)	3	0.6
Duration of hospitalization (days)	39 (15-87)	38 (11-61)	39 (11-87)	0.3
Duration of antifungal therapy (days)	19 (8-61)	19 (9-42)	19 (8-61)	0.2
Duration of culture negativity (days)	12 (5-35)	15 (5-41)	13 (5-41)	0.4



	2015	2016	2017	2018	2019	2020	2021	2022	2023
C. guillenmondii	0	0	0	0	1	0	0	0	0
C.tropicalis	1	1	0	0	0	1	1	0	0
C. glabrata	4	1	0	0	0	0	0	0	0
C.parapsilosis	0	3	2	0	1	0	2	2	1
C. Albicans	2	2	2	4	2	1	4	1	1

Figure 1. Annual distribution of strains of Candida species

4. Discussion

In our study, the most common risk factors for invasive fungal infections were broad-spectrum antibiotic use, history of hospitalization, presence of chronic disease, intensive care unit stay, central catheterization, TPN use, prophylactic antifungal use, and mechanical ventilation. Similarly, Bektaş et al. reported that the most common risk factors for invasive fungal infections were the presence of chronic disease, antibiotherapy, urinary and central catheterization, TPN use, and mechanical ventilation in order of decreasing frequency (2). Similarly, Yılmaz-Çiftdoğan et al. reported that the most important risk factors were central catheterization, TPN use, and antibiotherapy (3). In many pediatric and adult studies conducted worldwide, the presence of chronic disease, long-term hospitalization, TPN use, and central venous catheterization have been reported as important risk factors for invasive fungal infections (5,6). In our study, the risk factors were similar to those cited in the national, and international medical literature, but previous surgery was a more frequently encountered risk factor compared to the relevant literature data which may be explained by the greater number of patients who underwent gastrointestinal surgery in our study.

In our study, the most prevalent candida species was C. albicans, followed by C. parapsilosis. Although C. albicans infection is seen almost every year, the incidence of C. parapsilosis infection has increased in recent years. In many regional and international studies of children and adults, the most common invasive fungal infectious agent differs greatly. Dutta et al, Roilidies et al. and Bektaş et al. reported that the most common invasive fungal infectious agent was C. albicans (2,8,9). On the contrary, Yılmaz-Çiftdoğan et al, Devrim et al, Peman et al and Neu et al emphasized that the most common causative agent of candidiasis was C. parapsilosis (3,10-12). Similarly, in our study, C. albicans was the most commonly identified strain of candida followed by C. parapsilosis. The increase in the frequency of C. parapsilosis infection in both our study and other studies may be explained by the higher rates of biofilm formation by this fungus compared to other fungal agents increasing the risk of catheter-associated candidemia and colonization among healthcare workers.

C. parapsilosis and C. glabrata were more frequently resistant to fluconazole when compared with C. albicans. Similarly, C. parapsilosis and C. glabrata were more often resistant to caspofungin and micafungin rather than C. albicans. Kazak et al. also reported fluconazole resistance as 1.4% for C. albicans and 18.2% for C. parapsilosis (13). In their multicenter study, Lortholary et al. reported an increase in echinocandin resistance for C. parapsilosis strains (14). Belet et al. reported that fluconazole resistance was higher in non-albicans candida compared to C. albicans (15). Many studies have emphasized that non-albicans candidae have higher resistance to both azole antifungals and echinocandins compared to C. albicans, while resistance to amphotericin B is at a lower level in both groups (16-22). This fact may be explained by the increase in resistant candida strains with the increase in empirical and prophylactic antifungal use.

In our study, the mortality rate was 27%, which was higher in the C. albicans group compared to the non-albicans candida group. Similarly, Celebi et al. and Cisterna et al. emphasized that C. albicans infections had both a more aggressive and mortal course compared to non-albicans candida infections (23,24). While TPN use, mechanical ventilation, and mortality rates were higher in the C. albicans group, both the antifungal use and blood culture negativity persisted longer in the C. parapsilosis group. In their study, Bektaş et al. associated TPN and broad-spectrum antibiotic use with C. albicans, while C. parapsilosis was associated with urinary and central catheterization (2). In our study, the ability of C. parapsilosis to form a biofilm resulted in prolongation of treatment and delayed elimination of this fungal agent from the systemic circulation in catheterized cases. At the same time, the higher antifungal resistance in C. parapsilosis compared to C.

albicans infections can be explained by the prolonged duration of treatment and the delay in achieving a negative blood culture.

Conduction of our study in a single center with a limited number of cases, using retrospective study design constituted the main limitations of our study

In conclusion, invasive fungal infections are among the most important healthcare-associated infectious agents and the most important risk factors include the use of broad-spectrum antibiotics, prolonged hospital and intensive care unit stays, central catheterization, mechanical ventilation, TPN use, increased prophylactic antifungal and steroid use. Although C. albicans is still the most common candida species, C parapsilosis is being identified at an increasing rate. Both fluconazole and echinocandin resistance rates are increasing in parallel with the increase in the incidence of infections caused by non-albicans candida species. Invasive fungal infections should be kept in mind in patients with these risk factors, and possible pathogenic candida species and antifungal resistance patterns should be taken into consideration when prescribing empirical antifungal therapy.

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Ethics

Ethics Committee Approval: The study was approved by Eskişehir Osmangazi University Noninterventional Clinical Research Ethical Committee (Decision no: 612, Date: 02.05.2023).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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