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A retrospective study between 2012-2019: Epidemiology of *Candida* infections in intensive care units

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Abstract

Candida, the most common causative agent among fungal infections, is associated with high mortality, morbidity, and increased costs. Early diagnosis and effective treatment planning are crucial for patient prognosis. This study aimed to retrospectively evaluate *candida* infections in adult intensive care units (ICU). Between January 2012 and May 2019, 373 patients with clinical and laboratory diagnoses of *Candida* infection who were hospitalized in the adult ICUs of Kahramanmaraş Sütçü İmam Faculty of Medicine University were included in our study. In this retrospective study, data of patients related to age, gender, hospitalization clinic, length of hospitalization, comorbidities, invasive and non-invasive procedures were recorded. Of the patients included in the study, 52.8% (197) were female and 47.2% (176) were male, with a mean age of 68.7±17.4 years. Of the isolated samples, 200 (53.6%) were *Candida albicans* and 173 (46.4%) were *non-albicans Candida* (NAC). There were significant differences between *C. albicans* and NAC groups in the presence of urinary catheter (p=.046), central venous catheter (p=.028), enteral nutrition (p=.026), and length of hospitalization (p=.047). The mean *Candida* score was 2.34±0.06 and patients with higher *candida* scores had a higher mortality rate (p<.001). The mortality rate was 68.1%. The advanced age, duration of hospitalization, use of total parenteral nutrition, presence of a central venous catheter, and sepsis/septic shock were found to be independent risk factors for mortality. *Candida* infections have high mortality and morbidity. Data on *Candida* epidemiology vary regionally and the initiation of effective empirical treatment in these infections directly affects the prognosis. Therefore, data on species distribution and antifungal resistance rates in each hospital will guide physicians in terms of patient management.

Keywords: *Candida*, risk factors, mortality, intensive care units

Introduction

Among fungal infections, *Candida* species are the most common opportunistic pathogens that can cause a wide range of diseases from superficial candidiasis to invasive candidiasis (IC), especially in immunocompromised patients [1].

The most common causative agents of IC infections: *C. albicans*, *C. glabrata* (*Nakaseomyces glabrata*), *C. tropicalis*, *C. parapsilosis* and *C.krusei* (*Pichia kudriavzevii*) [2]. Although *C. albicans* remains the most prevalent *Candida* species in the general population, there have been changes in species distribution over the last few decades [1]. The decrease in the rate of *C. albicans* and the increase in the rates of C.parapsilosis and *C. glabrata* are significant. Furthermore, the increasing prevalence of antifungal-resistant *C. albicans* and the emergence of multidrug-resistant *non-albicans Candida* (NAC) species such as *Candida auris* are causing health concerns worldwide [3].

Invasive candidiasis has a mortality ranging from 20% to 50% despite the current use of effective antifungal therapy. It can prolong hospitalization from approximately 2 weeks to 2 months, depending on the underlying causes influenced by the underlying conditions [4]. Today, invasive *candida* infections are common in hematology clinics and intensive care units (ICU). High acute physiology and chronic health evaluation II (APACHE II) score, renal failure, presence of diabetes mellitus (DM), previous major abdominal surgeries, long-term use of broad-spectrum antibiotics, use of central catheters, total parenteral nutrition (TPN) administration and immunosuppressive therapies are

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high-risk factors of fungal infection in ICU [5]. The other important risk factor is *Candida* colonization. Studies have shown that colonization increases rapidly on the eighth day of hospitalization and the incidence of IC reaches its highest level on the tenth day [6,7].

Early diagnosis and initiation of treatment in *candida* infections are of great importance in terms of reducing mortality and morbidity. Although conventional diagnostic methods are still used as the gold standard despite their low sensitivity, the use of advanced serologic and molecular diagnostic methods provides information in terms of early diagnosis, prognosis follow-up, and treatment monitoring and is used in routine practice [8]. Delays and difficulties in microbiologic diagnosis have necessitated the development of predictive models for empirical treatment initiation. For this purpose, *candida* colonization index (CCI) and *Candida* score (CS) are used [9].

This study aimed to retrospectively evaluate the epidemiology and risk factors of *candida* infections in adult ICUs between January 2012 and May 2019.

Material and Methods

In this study, patients hospitalized in the adult ICUs of Kahramanmaraş Sütçü İmam University Faculty of Medicine Hospital between January 2012 and May 2019 were retrospectively evaluated. A local ethics committee decision dated 19.06.2019 (Decision no: 22) was received from Kahramanmaraş Sütçü İmam University.

Patients aged 18 years and older, with *Candida spp.* growth in cultures during ICU hospitalization were included in the study. Age, gender, hospitalization clinic, duration of hospitalization, comorbidity, risk factors for *Candida* infection, presence of central venous catheter (CVC), history of surgery, presence of mechanical ventilator, TPN intake, and broad-spectrum antibiotic use were recorded. Species isolated from the cultures, C-reactive protein (CRP), procalcitonin, white blood cell results, and information about the patient's prognosis (discharge or exclusion) were obtained. "Statistical Package for Social Sciences (SPSS) for Windows 21" program was used to record patient information.

Culture results were evaluated by infection physicians. Patients considered to be contaminated and patients under 18 years of age were excluded from the study.

Culture samples were first obtained pure culture according to the 'standard identification procedure for yeast isolates' and cultured on chloramphenicol SDA (Oxoid, England) with or without cycloheximide to determine the morphological characteristics. For the identification of *Candida* species, the color and colony morphology were evaluated in a chromogenic medium (HiChrome™ *Candida* Differential Agar, India) with a germ tube test. BD Phoenix automatized identification system was used to identify the isolates at the species level.

Statistical Analysis

The "Statistical Package for Social Sciences for Windows 21" program was used for data analysis. Data were expressed as mean±standard deviation and percentage. Kolmogorov-Simirnov and Shapiro-Wilk tests were used to determine whether the variables were normally distributed. Numerical variables with normal distribution were compared using the Student t-test and variables without normal distribution were compared using the Mann Whitney-U test. The chi-square test or Fisher exact test was used for the comparison of categorical variables. Multivariable regression analysis was used to determine independent risk factors. Power analysis was performed and $p<.05$ was accepted as significant in statistical analyses.

Results

The study included 373 patients, 197 females (52.8%) and 176 males (47.2%). The mean age of the patients was 68.7±17.1 years, the mean age of women was 68.3±18.1 years, and the mean age of men was 69.2±16 years. The mean age was 70.3±1.1 years in the *Candida albicans* group and 66.8±1.4 years in the NAC group. No significant difference was found between the groups in terms of gender and age distribution (p=.61).

The mean duration of hospitalization was 36.9±34.4 days (min-max: 2-320). There was no significant correlation between the day of culture positivity and length of hospitalization (p=.609). When the groups in which *Candida albicans* and NAC were isolated were compared in terms of length of hospitalization and the clinical distribution of the patients with culture positivity was examined, it was found that patients were followed up in the internal medicine ICU, anesthesia ICU, and other ICUs of our hospital (such as pulmonary diseases ICU, general surgery ICU, coronary ICU, neurology ICU, cardiovascular surgery ICU), 127 (34.1%), 118 (31.6%), 128 (34.3%), respectively.

When the patients were evaluated in terms of underlying diseases, it was determined that 46 (12.3%) of the patients had no known comorbidity and the others had at least one known comorbidity. DM was found to be present in 98 patients (26.3%) and malignancy in 93 patients (24.9%). Renal failure was detected in 52 patients (13.9%). When the distribution of comorbidities by gender was analyzed, it was found that DM and rheumatologic diseases such as systemic lupus erythematosus and rheumatoid arthritis were more common in female patients (DM, p=.052 and rheumatologic diseases, p=.012). The distribution of underlying diseases according to gender is presented in Table 1.

To determine the risk factors of the patients, factors such as state of consciousness, surgical history, presence of mechanical ventilation, TPN, use of antibiotics or immunosuppressive agents, and presence of catheter were evaluated. It was determined that 352 (94.4%) of the patients

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had hospitalization for more than one week, 332 (89%) had urinary catheter use, 237 (63.5%) had sepsis/septic shock, and 225 (60.3%) had TPN use, and no significant difference was found in the comparison of these risk factors by gender. Antibiotic use was determined in 347 (93%) and CVC was used in 182 (48.8%) of the patients and the presence of these risk factors was significant in female patients compared to male patients (antibiotic use p=.032, CVC p=.004).

Table 1. Distribution of comorbidities by gender

Additional disease	Female n=197	Male n=176	Total n=373	p*
DM	60 (30.5%)	38 (21.6%)	98 (26.2%)	0.052
Hypertension	34 (17.3%)	24 (15.5%)	58 (15.5%)	0.335
CAD	36 (18.3%)	26 (14.8%)	62 (16.6%)	0.365
Asthma/COPD	7 (3.6%)	8 (4.5%)	15 (4.0%)	0.626
Kidney failure	33 (16.8%)	19 (10.8%)	52 (13.9%)	0.097
Malignancy	46 (23.4%)	47 (26.7%)	93 (24.9%)	0.455
Neurological disease	7 (3.6%)	8 (4.5%)	15 (4.0%)	0.626
Rheumatologic disease	7 (3.6%)	0 (0%)	7 (1.8%)	**0.012**
Liver failure	2 (1%)	4 (2.3%)	6 (1.6%)	0.335
CVD	15 (7.6%)	15 (8.5%)	30 (8.0%)	0.747
Thyroid disease	2 (1%)	2 (1.1%)	4 (1.0%)	0.910
IBD	0 (0%)	1 (0.6%)	1 (0.2%)	0.289

*The Chi-square ($\chi 2$) test was used to compare the groups; $p<0.05$ was considered statistically significant; DM: diabetes mellitus, CVD: cerebrovascular disease, COPD: chronic obstructive pulmonary disease, IBD: inflammatory bowel disease, CAD: coronary artery disease

When the culture results of the patients were evaluated, *Candida* typing was not performed in 59 (15.8%) cases, and 200 (53.6%) of the cases were isolated as *C. albicans* and 173 (46.4%) as NAC. Among NAC, the most common species was *C. tropicalis* with a rate of 12.3%. It was followed by *C. glabrata* with 8%, *C. parapsilosis*, and *C. krusei* with 3.5%. The distribution of *Candida* species is shown in Table 2.

Table 2. Distribution of *Candida* species

***Candida* species**	**N**	**%**
C. albicans	200	53.6
C. tropicalis	46	12.3
C. glabrata	30	8.0
C. parapsilosis	13	3.5
C. kefyr	8	2.1
C. krusei	13	3.5
C. dubliniens	2	0.5
C. lusitaniae	2	0.5
Candida spp.	59	15.8
Total	**373**	**100**

There was no statistically significant difference in species distribution according to years (p=.064). Accordingly, the distribution of *Candida* species according to years is given in Figure 1.

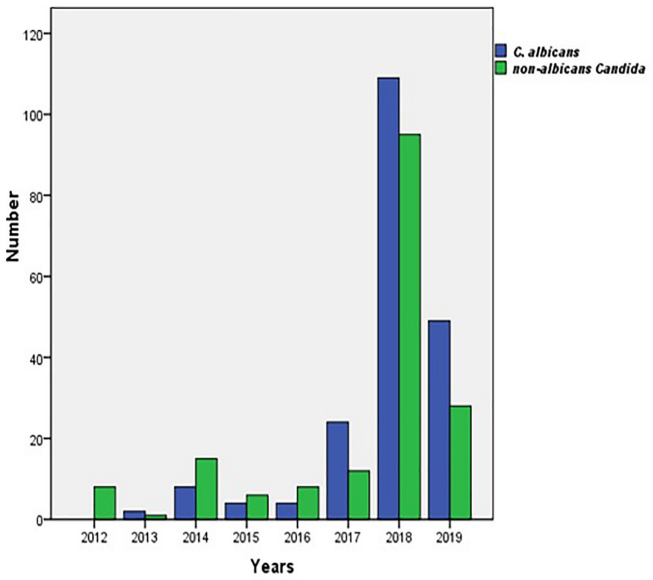

Figure 1. Distribution of *Candida* species according to years

When we looked at the risk factors for *C. albicans* and NAC isolated groups, a significant difference was found in terms of long-term hospitalization, enteral nutrition, presence of urinary catheter and CVC (Table 3).

Of the samples, 209 (56%) were urine, 99 (26.5%) blood, 50 (13.4%) tracheal aspirate, and the others were wound, vaginal and sputum cultures. *Candida glabrata* and *C. parapsilosis* were

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most frequently isolated from blood samples, while other species were more frequently isolated from urine samples.

CRP, procalcitonin, and white blood cell values were recorded on the days of culture positivity. The mean CRP value was 137.8±85.7 mg/L (normal value: 0-5 mg/L), the mean procalcitonin value was 11.7±26.07 ug/ml (normal value: 0-0.1ug/L) and the mean white blood cell value was 15.9±41.4 109/L. There was no significant difference in CRP, procalcitonin, and white blood cell values between *C. albicans* and NAC groups.

Table 3. Distribution of risk factors by species

Risk factors	C.albicans, n (%)	NAC, n (%)	Total, n (%)	p*
Age	70.32±15.78	66.88±18.46	68.73±17.147	0.054
Unconsciousness	83 (48.8)	87 (51.2)	170 (45.5)	0.089
Urinary catheter	172 (51.8)	160 (48.2)	332 (89.0)	**0.046**
PEG	14 (56.0)	11 (44.0)	25 (6.7)	0.805
Endotracheal intubation	93 (51.7)	87 (48.3)	180 (48.2)	0.465
Mechanic ventilation	112 (51.4)	106 (48.6)	218 (58.4)	0.303
Peripheral venous catheter	118 (57.0)	89 (43.0)	207 (55.4)	0.143
Peripheral arterial catheter	69 (53.5)	60 (46.5)	129 (34.5)	0.971
Central venous catheter	87 (47.8)	95 (52.2)	182 (48.7)	**0.028**
TPN	125 (55.6)	100 (44.4)	225 (60.3)	0.355
Hemodialysis	26 (46.4)	30 (53.6)	56 (15.0)	0.242
Surgical drainage tube	17 (60.7)	11 (39.3)	28 (7.5)	0.434
Use of immunosuppressive agents	25 (58.1)	18 (41.9)	43 (11.5)	0.527
Bronchoscopy	1 (16.7)	5 (83.3)	6 (1.6)	0.067
Thoracentesis	2 (50.0)	2 (50.0)	4 (1.0)	0.884
Respiratory failure	44 (50.0)	44 (50.0)	88 (23.5)	0.436
Tracheostomy	15 (44.1)	19 (55.9)	34 (9.1)	0.244
Transfusion of blood and its products	30 (46.9)	34 (53.1)	64 (17.1)	0.235
Enteral nutrition	71 (46.7)	81 (53.3)	152 (40.7)	**0.026**
Colostomy	7 (77.8)	2 (22.2)	9 (2.4)	0.141
Length of hospitalization**	200 (53.6)	173 (46.4)	373 (100.0)	**0.047**
Nasogastric tube	22 (53.7)	19 (46.3)	41 (10.9)	0.996
Paracentesis	1 (33.3)	2 (66.7)	3 (0.8)	0.479
Use of broad-spectrum antibiotics	188 (54.2)	159 (45.8)	347 (93.0)	0.429
Surgery	65 (53.7)	56 (46.3)	121 (32.4)	0.979
Candida colonization	33 (56.9)	25 (43.1)	58 (15.5)	0.586
Sepsis/Septic shock	125 (52.7)	112 (47.3)	237 (63.5)	0.654

*Chi-square ($\chi 2$) test was used to compare the groups; **Independent sample t test was used to compare the cases with a hospitalization duration of >7 days; $p<0.05$ was considered statistically significant; PEG: percutaneous endoscopic gastrostomy, TPN: total parenteral nutrition

When the prognosis of patients with *Candida* infection was evaluated, 119 (31.9%) of the patients survived, while 254 (68.1%) were excluded. There was no significant difference between the mortality rates of patients with *Candida albicans* and NAC infections (p=.983) (Table 4). When the risk factors were evaluated, the age, state of consciousness, prolonged hospitalization, presence of a urinary catheter, CVC, TPN, broad-spectrum antibiotic use, respiratory failure, mechanical ventilation, and sepsis/septic shock were found to be statistically significant for mortality (Table 5).

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Table 4. Association of *C. albicans* and non-albicans species with mortality

	Survival		Excitus		Total		p*
	N	%	n	%	n	%	
C. albicans	63	52.9	137	53.9	200	53.6	
NAC	56	47.1	117	46.1	114	46.4	0.983
Total	119	100	254	100	373	100	

*The Chi-square ($\chi 2$) test was used to compare the groups. $p<0.05$ was considered statistically significant; n: number; NAC: *non-albicans Candida*

Table 5. Comparison of risk factors between the survival and the exitus groups

Risk factors	Survival (n=119)	Excitus (n=254)	Total (n=373)	p*
Age	50.01±1.219	78.62±0.515	68.73±17.147	**0.006**
Gender (female)	55 (46.2%)	142 (55.9%)	197 (52.8%)	0.081
Unconsciousness	34 (28.6%)	136 (53.5%)	170 (45.6%)	**<0.001**
Urinary catheter	99 (83.2%)	233 (91.7%)	332 (89.0%)	**0.014**
PEG	11 (9.2%)	14 (5.5%)	25 (6.7%)	0.179
Endotracheal intubation	35 (29.4%)	145 (57.1%)	180 (48.3%)	**<0.001**
Mechanic ventilation	46 (38.7%)	172 (67.7%)	218 (58.4%)	**<0.001**
Peripheral venous catheter	70 (58.8%)	137 (53.9%)	207 (55.5%)	0.376
Peripheral arterial catheter	45 (37.8%)	84 (33.1%)	129 (34.6%)	0.369
Central venous catheter	47 (39.5%)	135 (53.1%)	182 (48.8%)	**0.014**
TPN	61 (51.3%)	164 (64.6%)	225 (60.3%)	**0.014**
Hemodialysis	22 (18.5%)	34 (13.4%)	56 (15.0%)	0.199
Surgical drainage tube	8 (6.7%)	20 (7.9%)	28 (7.5%)	0.694
Use of immunosuppressive agents	10 (8.4%)	33 (13.0%)	43 (11.5%)	0.196
Bronchoscopy	3 (2.5%)	3 (1.2%)	6 (1.6%)	0.338
Thoracentesis	1 (0.8%)	3 (1.2%)	4 (1.1%)	0.766
Respiratory failure	19 (16.0%)	69 (27.2%)	88 (23.6%)	**0.018**
Tracheostomy	11 (9.2%)	23 (9.1%)	34 (9.1%)	0.953
Transfusion of blood and its products	17 (14.3%)	47 (18.5%)	64 (17.2%)	0.314
Enteral nutrition	43 (36.1%)	109 (42.9%)	152 (40.8%)	0.214
Colostomy	4 (3.4%)	5 (2.0%)	9 (2.4%)	0.414
Length of hospitalization*	119 (31.9%)	254 (68.1%)	373 (100%)	**0.006**
Nasogastric tube	12 (10.1%)	29 (11.4%)	41 (11.0%)	0.701
Paracentesis	0 (0.0%)	3 (1.2%)	3 (0.8%)	0.234
Use of broad-spectrum antibiotics	104 (87.4%)	243 (95.7%)	347 (93.0%)	**0.003**
Surgery	42 (35.3%)	79 (31.1%)	121 (32.4%)	0.420
Candida colonization	17 (14.3%)	41 (16.1%)	58 (15.5%)	0.645
Sepsis/Septic shock	53 (44.5%)	184 (72.4%)	237 (63.5%)	**<0.001**

*Chi-square ($\chi 2$) test was used to compare the groups; **Independent sample t test was used to compare the cases with a hospitalization duration of >7 days; $p<0.05$ was considered statistically significant; PEG: percutaneous endoscopic gastrostomy, TPN: total parenteral nutrition

Risk factors with p<.05 on univariate analysis were re-evaluated by Binary regression logistic analysis. Advanced age (p<.001), length of hospitalization (p<.001), TPN use (p=0.025), presence of CVC (p=0.010), and sepsis/septic shock (p=0.018) were found to be significantly associated with mortality (Table 6).

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Table 6. Effect of risk factors on mortality binary regression logistic analysis results

Risk factors	B	Exp(B)	95% confidence interval	P
Advanced age	0.036	1.036	1.020-1.053	**<0.001**
Duration of hospitalization	0.025	0.976	0.964-0.988	**<0.001**
Antibiotic use	0.463	1.589	0.581-4.346	0.367
Total parenteral nutrition	0.607	1.834	1.078-3.121	**0.025**
Sepsis/septic shock	0.665	1.944	1.119-3.377	**0.018**
Central venous catheter	0.716	2.046	1.184-3.533	**0.010**
Mechanical ventilation	0.640	1.896	0.971-3.704	0.061

The mean CS of the patients was calculated as 2.34±0.065. The mortality rate in the group with CS≥2.5 was significantly higher than in the group with CS<2.5 (p<.001). The table showing the relationship between CS and mortality is given below (Table 7).

Table 7. Association of *Candida* score with mortality

	Survival (n=119)		Excitus (n=254)		Total (n=373)		p*
	N	%	n	%	n	%	
CS<2.5	82	41.4	116	58.6	198	100	**<0.001**
CS≥2.5	37	21.1	138	78.9	175	100	

*The Chi-square ($\chi 2$) test was used to compare the groups; p<0.05 was considered statistically significant; n: number, CS: *candida* score

Discussion

Candida is the most frequently isolated causative agent of fungal infections and may present in various clinical pictures ranging from superficial infections to metastatic organ involvement. The presence of risk factors such as prolonged hospitalization, TPN use, DM, renal failure, hemodialysis, CVC use, broad-spectrum antibiotic use, malignancy, immunosuppression conditions such as transplantation or chemotherapy, and surgery (especially abdominal) facilitates the development of infection [10]. The need for colonization-infection differentiation, the diagnostic difficulty caused by the inability to detect culture positivity at all times, the prolonged hospitalization period of the treatment, and the high mortality and morbidity increase the clinical importance of *candida*.

In studies on IC, it was generally found that there was no difference between male and female genders [11,12]. Although the age range varies regionally, it varies between 58.4 and 75.1 years in the studies evaluated [13-15]. In the study by Al-dorzi et al., 52.5% of the patients were male and the mean age was 58.4 years [15]. The mean age was 56.4 years in the *Candida albicans* group and 60.2 years in the NAC group.

Similarly, no statistically significant difference was found when *Candida* infections were evaluated in terms of age and gender in our study. Unlike these studies, in the study of Pu et al. including 257 patients, the mean age was 59.15 years, 145 of the patients were over 60 years of age and it was reported that advanced age was associated with *C. albicans* infections and was an independent risk factor [13].

In our study, the mean duration of hospitalization was 36.9 days and the mean day of diagnosis was 19.56 days. The mean hospitalization period was 33.50 days in the *C. albicans* group and 40.86 days in the NAC group. Similarly, in the study conducted by Zhang W. et al. in patients with candidemia, the NAC group had a longer hospitalization period [16].

In a prospective multicenter study conducted in the USA, 4276 patients were evaluated and risk factors for the development of IC were found to be acute renal failure, TPN use, and previous surgical history [17]. In a study conducted in the UK, no significant relationship was found between the development of IC and age, gender, DM, and the presence of pancreatitis. However, the study identified high APACHE II scores, abdominal surgery, TPN use, the presence of a surgical drain, and *Candida* colonization as risk factors [18]. Karacaer et al. found to be independent risk factors for prolonged ICU hospitalization, the presence of CVC, hyperglycemia, and co-infection [19]. In a prospective study conducted by Aguilar et al. in surgical ICUs, the most common risk factors were the presence of CVC, urinary catheter, TPN use, ICU stay longer than seven days, and mechanical ventilation [20]. In another study conducted in our country, when 100 colonized and non-colonized patients were evaluated in terms of risk factors, it was shown that TPN use, previous abdominal surgery, and broad-spectrum antibiotic use were independent factors and *Candida* colonization increased 8.8-fold due to antibiotic use and 3.6-fold due to surgery [21]. In our study, the most common comorbidities were DM

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and malignancy. The risk factors identified were, in order of frequency, hospitalization for more than seven days, presence of a urinary catheter, use of broad-spectrum antibiotics, use of TPN, presence of mechanical ventilator, peripheral venous catheter, and CVC. In the evaluation according to species distribution, the difference between C.albicans and NAC isolates in terms of urinary catheter, presence of CVC, enteral nutrition, and length of hospitalization was statistically significant.

Pu et al. evaluted 257 cases of IC, 125 (48.6%) *C. albicans* and 132 (51.4%) NACs were identified [13]. Of the isolated NACs, 45 (17.5%) *C. tropicalis*, 42 (16.3%) *C. parapsilosis*, 33 (12.8%) *C. glabrata*, 4 (1.6%) *C. krusei*, 3 (1.2%) *C. sake*, 2 (0.8%) *C. dubliniensis*, 2 (0.8%) *C. guilliermondii* and 1 (0.4%) *C. intermedia*. Pfaller et al. evaluated 256,882 samples and reported that although there was no continuous downward trend in *C. albicans* isolation rates, *C. glabrata*, *C. parapsilosis* and *C. tropicalis* rates increased annually [22]. Erdem et al. reported that the mean age of the patients was 62.6 years and 56.5% were female. In this study, 116 isolates obtained from 92 patients were examined, 73 of these samples were obtained from urine, 26 from blood, seven from the surgical incision area, four from drains, and four from tracheal aspirates. *C. albicans* and NAC were isolated in 54.4% and 45.6% of the samples, respectively. Urinary tract infection was found in 72.1% of the patients and candidemia in 32.9%. Among patients with urinary tract infections, 66.6% were female, and female gender was found to be significantly higher in terms of infection development [23]. When we evaluated the distribution of *Candida* species, 59 (15.8%) of the patients could not be typed, 200 (53.6%) grew, and 114 (30.6%) grew NAC. *Non-albicans* species were 46 (12.3%) *C. tropicalis*, 30 (8%) *C. glabrata*, 13 (3.5%) *C. parapsilosis*, 13 (3.5%) *C. krusei*, 8 (2.1%) *C. keyfr* and 4 (1%) *C. dubliniens* and *C. lusitaniae*. Of the samples, 209 were obtained from urine, 99 from blood, 50 from tracheal aspirate culture, and 12 from surgical incision sites. 56% of the patients had UTI and 26.5% had candidemia. Of the cases of candiduria, 56.9% were females and 52.5% of candidemia cases were males. Similarly, there are studies in the literature reporting that candiduria develops more frequently in women and candidemia in men [13,23].

In a study by Ghazi et al. evaluating the epidemiology of *Candida* in the Middle East and North Africa, mortality rates were reported as 42.8%-69% [24]. In a study conducted in Europe, the crude mortality rate for IC was found to be 42% and it was shown that age, severe hepatic failure, SOFA score, and presence of septic shock increased mortality [18]. In the study by Karacaer et al., the mortality rate was 77.7%. It was reported that the relationship between age, gender, APACHE II score, antibiotic use, presence of chronic disease, presence of CVC and urinary catheter, and duration of hospitalization and mortality was statistically significant and APACHE II score and presence of CVC were independent risk factors [19]. In the study by Al-Dorzi et al. there was no significant difference in mortality between NAC (48.4%) and *C. albicans* (51.6%) isolated groups and the mortality rate was 58.6% [15]. In the study by Çetin et al., the mortality rate was 70.7% and no significant difference was found between the species in terms of mortality [14]. They reported that mechanical ventilation and TPN use increased mortality. In our study, the mortality rate was 68.1%. There was no significant difference in mortality between *C. albicans* and NAC groups. In terms of risk factors, mortality increases with advanced age. There was a significant correlation between mortality and the use of broad-spectrum antibiotics, presence of a urinary catheter, presence of CVC, prolonged hospitalization, use of TPN, unconsciousness, and sepsis.

Laine et al. found that including 139 candidemia patients, 37% of patients had CS 3 and above and the most common risk factors were sepsis (53%) and multifocal *candida* colonization (62%) [25]. In our study, the *candida* risk score was above 2.5 in 175 patients (46.9%) and the mean CS was 2.34. The most common risk factors that increased the CS were sepsis (63.5%) and TPN use (60.3%). This value was 2.35 in the *C. albicans* isolated group and 2.34 in the NAC isolated group. Of the patients with CS ≥2.5, 138 (78.9%) ended up as excitus. There was a significant correlation between CS and mortality. Similar to the study by Al-Dorzi et al. the mean CS was 1.97 and the CS was higher in the NAC-isolated group than in the *C. albicans* isolated group. The mean CS was found to be 1.74 in survivors and 2.14 in excitus patients and 78 (62.9%) of 124 patients with a CS≥2 resulted in death [15].

Conclusion

In conclusion, the necessity of invasive interventional procedures in ICUs leads to an increase in *candida* infections. Although the frequency of non-albicans *Candida* infections has increased worldwide, *C. albicans* still maintains its first place. The need for colonization/infection differentiation, the fact that culture positivity is not always detected, and the diagnostic difficulties caused by the fact that cultures take 3-7 days to be concluded, as well as the high mortality and morbidity rates increase its clinical importance. Therefore, to initiate effective antifungal treatment, epidemiologic data of the hospitals should be taken into consideration and antifungal susceptibility tests should be performed carefully.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical Approval
Kahramanmaraş Sütçü İmam University Faculty of Medicine Ethics Committee: 19.06.2019, Decision no: 22.

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