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Changing epidemiology and risk factors for candidemia in critically ill patients

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Ethics Committee Approval
Ethics Committee of Bakirkoy Dr. Sadi Konuk Education and Research Hospital, date:14.05.2018 and number:2018/182.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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Abstract

Background/Aim: Candidemia is a common cause of bloodstream infections in critically ill patients, resulting in high mortality and morbidity. This retrospective case-control study was designed to identify epidemiological characteristics and risk factors for candidemia in an intensive care unit.

Methods: A total of 166 patients hospitalized in the intensive care unit between January 2013 and December 2017 were included in this case-control study. Candidemia was defined as at least one positive blood culture for *Candida* spp. with fever or other clinical findings consistent with infection. Patients who acquired candidemia more than 48 hours after admission represented the case group (n=83). Control group (n=83) consisted of case-matching patients who were hospitalized during the same period and did not develop candidemia.

Results: In the candidemia group *Candida albicans* (57.8%) was the most common species, followed by *Candida glabrata* (13.3%) and *Candida parapsilosis* (12%). The rate of *C. albicans* decreased from 69.2% to 50% during the five-year study period. Out of 83 candidemia infections, 36 (43.4%) were associated with central venous catheters. *C. parapsilosis* had an increasing rate in parallel with central venous catheter-associated candidemia rates. When comparing cases and controls, in univariate analysis, Sequential Organ Failure Assessment (SOFA) score, blood transfusion, central venous catheter placement, intubation, gastrointestinal surgery and total parenteral nutrition were significantly more common in the candidemia group ($P<0.05$ for each). The rate of the patients whose C*andida* scores were higher or equal to 3, was significantly higher in candidemia group ($P=0.03$). According to the multivariate analysis, SOFA scores ($P<0.001$, OR:1.25, 95% CI:1.15-1.37), gastrointestinal surgery ($P=0.03$, OR:2.60, 95% CI:1.10-6.12), central venous catheter ($P=0.04$, OR:2.62, 95% CI:1.05-6.57) and total parenteral nutrition ($P=0.02$, OR:2.61, 95% CI:1.12-6.06) were independent risk factors for candidemia, while enteral feeding ($P=0.02$, OR:0.27, 95% CI:0.09-0.80) was protective against.

Conclusion: The result of our study is an evidence of the changing epidemiology of candidemia, which showed a shift towards non-*albicans Candida* spp. over the years. The increasing rate of *C. parapsilosis* and central venous catheter-associated candidemia has highlighted the need for more attention to the central line care and hand hygiene. Our study also revealed that critically ill patients with high SOFA score, gastrointestinal surgery, central venous catheter, and total parenteral nutrition have an elevated risk for developing candidemia. Unless necessary, limitation of total parenteral nutrition, and ensuring the earlier implementation of enteral feeding may be protective from candidemia.

Keywords: Candidemia, Epidemiology, Intensive care unit, Risk factors

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Introduction

Candida species are normally colonized in the oral cavity, skin and intestinal tract of humans and becomes pathogenic due to various risk factors, such as consumption of broad-spectrum antibiotics, exposure to invasive procedures, malignancy, human immunodeficiency virus (HIV) infection, organ transplantation and prolonged hospital stay [1]. Candidemia is one of the most common causes of bloodstream infections (BSIs) in the world. In the United States of America (USA), between 2013–2017, the incidence of candidemia was 9:100.000 individuals with a variety by geographic location and patient population. Centers for Diseases and Prevention (CDC) estimates that approximately 25,000 cases of candidemia occur nationwide each year [2,3]. According to the data of the European Center for Disease Prevention and Control (ECDC), *Candida* spp. was the eighth cause of intensive care unit (ICU)-acquired BSIs in Europe in 2016 and 2017 [4, 5].

While *Candida albicans* is still considered the leading cause of candidemia, increasing rates of non-*albicans Candida* species have been reported to account for almost 50% of all candidemia [6]. Because candidemia is a common cause of BSIs in critically ill patients resulting in high mortality and morbidity, each hospital needs to identify its own candidemia data. This study aims to evaluate the epidemiologic characteristics of candidemia cases, distribution, and comparison of *Candida* isolates, and identify the risk factors for candidemia in our ICU.

Materials and methods

This retrospective case-control study was conducted in our 612-bed tertiary care, university-affiliated hospital, a referral center for several hospitals in the vicinity. Our hospital has a 31-bed Anesthesiology and Reanimation ICU, nine-bed neurology ICU, 16-bed coronary ICU, seven-bed cardiovascular ICU, 26-bed neonatal ICU, and a 16-bed pediatric ICU. This study was performed in Anesthesiology and Reanimation ICU which accepts patients from both internal medicine and surgical wards. The study approval was obtained from the Ethics Committee of Bakirkoy Dr. Sadi Konuk Education and Research Hospital (No: 2018/182 -14/05/2018).

Adult patients (at least 18 years old) hospitalized in the ICU between January 2013 and December 2017 who acquired candidemia more than 48 hours after admission were included in the study and represented the study group. Candidemia was defined as at least one positive blood culture for *Candida* spp. with fever or other clinical findings consistent with infection. In cases with recurrent candidemia, only the first episode was included in the study. Control group consisted of patients who were hospitalized in ICU during the same period and did not develop candidemia. Control patients were selected from the electronic hospital records and matched 1:1 with the cases in terms of age and Acute Physiology and Chronic Health Evaluation (APACHE) II scores. For randomization, among case-matched patients who were hospitalized during the same period, with similar ages and APACHE II scores, those who were admitted earlier in ICU was selected as controls.

The patients under 18 years of age who had candidemia in the first 48 hours of ICU admission or in other wards before ICU admission were excluded from the study.

Demographic characteristics, invasive procedures before candidemia (for cases) or within 2 weeks after admission (for controls), such as a central venous catheter (CVC), urinary catheterization, endotracheal intubation, total parenteral nutrition (TPN), history of surgery up to one month before candidemia (for cases) or before hospitalization (for controls) were recorded. Quantitative variables such as Sequential Organ Failure Assessment (SOFA) scores, APACHE II scores, age, length of stay and duration of antifungal treatment were also recorded. *Candida* scores were calculated by adding 2 points for severe sepsis, 1 point for TPN, 1 point for surgery, and 1 point for multifocal *Candida* colonization. Patients were followed up until discharge from ICU or death. All data were collected from the patients' files and the records of the infection control committee of our hospital.

Conventional mycological methods such as colony morphology, germ tube test, and Phoenix Yeast ID panel (Becton Dickinson Diagnostics, Sparks, ABD) were used for identification of *Candida* species. Antifungal susceptibility tests were performed with broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI) M27-A3 document [7, 8]. The unidentified non-*albicans Candida* isolates were named as "other non-*albicans Candida* spp."

Statistical analysis

Statistical Package for Social Sciences version 25.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Descriptive data were presented as mean (standard deviation), frequency, median, and percentage values. Chi-Square test and Fisher's Exact test were used for comparing categorical variables. The normality of continuous variables was tested with the Kolmogorov Smirnov test. Normally and non-normally distributed continuous variables were compared with Student's t-test and Mann-Whitney U test, respectively. Significant variables in the univariate analysis were evaluated with the multivariate logistic regression analysis to determine independent risk factors. *P*-values less than or equal to 0.05 were considered statistically significant.

Results

A total of 166 cases, including 83 candidemia and 83 non-candidemia patients, were included in the study between January 2013 and December 2017. In the candidemia group, *C. albicans* was the most common species (n=48, 57.8%), followed by *Candida glabrata* (n=11, 13.3%), *Candida parapsilosis* (n=10, 12%), *Candida krusei* (n=7, 8.4%), and *Candida tropicalis* (n=3, 3.6%). In four of 83 patients (4.8%), non-*albicans Candida* isolates could not be identified. During the five year study period, the rate of *C. albicans* was 57.8% (n=48) and the rate of non-*albicans Candida* species was 42.2% (n=35). The distribution of *albicans* and non-*albicans Candida* species among the years was presented in Figures 1 and 2. Candidemia occurred in a median of 14 days (Interquartile range [IQR]: 15-26 days) after admission. Fever was higher than 38 degrees in only 50.6% of candidemia patients at the time of blood culture positivity. Out of 83 candidemia infections, 36 (43.4%) were

CVC associated. Incidence of CVC-associated candidemia patients among the years and the distribution of species was shown in Figures 3 and 4.

Figure 1: Frequency of *Candida albicans* and non-*albicans Candida* spp. from 2013 to 2017

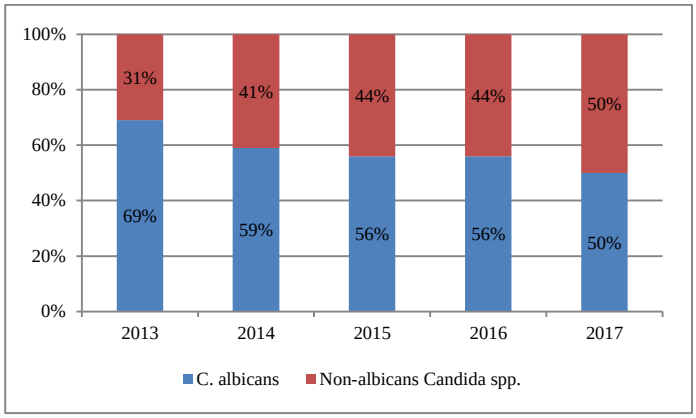


Figure 2: Overall distribution of *Candida* species isolates during the study period

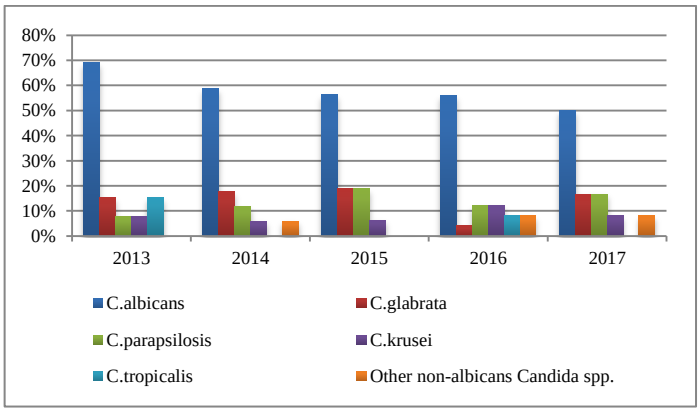


Figure 3: Frequency of CVC associated and non-CVC associated candidemia between 2013 and 2017

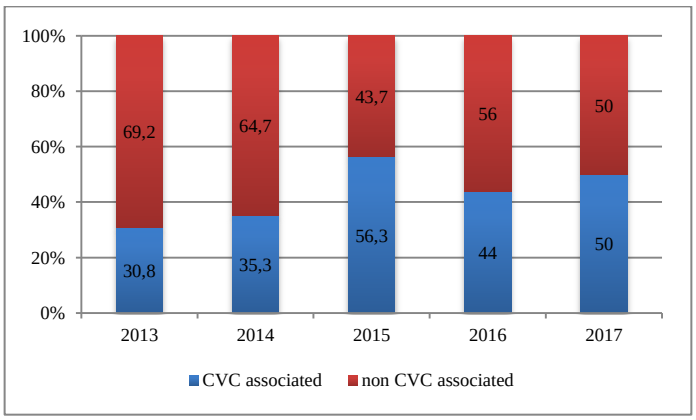
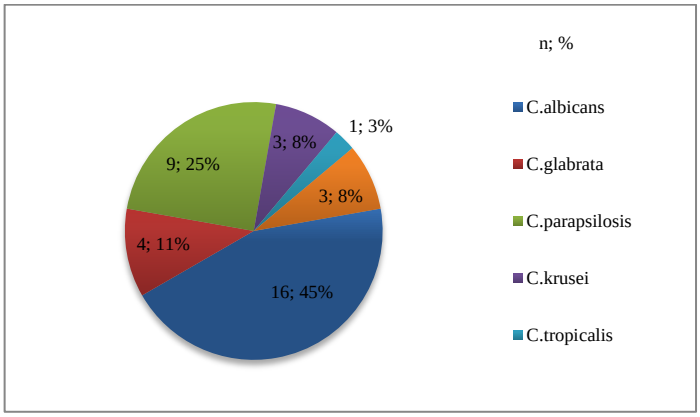


Figure 4: Distribution of *Candida* species in CVC associated candidemia patients



When comparing the cases with *C. albicans* and non-*albicans Candida* in terms of demographic characteristics, underlying diseases, invasive procedures, and mortality, the rate of diabetes mellitus (DM) and percutaneous endoscopic gastrostomy (PEG) were higher in *C. albicans* group (P=0.01, OR: 10.10, 95% CI: 1.23-82.49, P=0.03, OR: 3.96, 95% CI: 1.03-15.18) (Table 1). There was no significant difference between the two groups in terms of APACHE II and SOFA scores, mortality rates, length of stay in ICU, median day of candidemia onset and, duration of antifungal therapy. The rate of antibiotic usage before candidemia was also similar in both groups.

Table 1: Characteristics of *Candida albicans* and non-*albicans* candidemia

	Patients with *Candida albicans* (n=48)	Patients with non-*albicans Candida* spp. (n=35)	*P*-value
Male gender, n (%)	27 (56.3)	20 (57.1)	0.93
Age, year, mean (SD)	57 (16.80)	53.37 (21.18)	0.38
APACHE II, median (IQR)	22 (17-27)	20 (14-23)	0.07
SOFA, median (IQR)	12 (9-18)	13 (11-19)	0.36
Day of candidemia, day, median (IQR)	15 (5-22)	12 (3-27)	0.63
Fever ≥38°C at the time of candidemia, n (%)	22 (55)	20 (64.5)	0.41
Candida spp. isolation at least one site of the body other than blood, n (%)	26 (60.5)	16 (55.2)	0.65
Length of stay, day, median (IQR)	31 (19-47)	27 (20-38)	0.32
Duration of antifungal treatment, mean (SD)	16.52 (7.44)	13.74 (9.60)	0.23
Hypertension, n (%)	9 (18.8)	5 (14,3)	0.59
Congestive heart disease, n (%)	1 (2.1)	0 (0)	1
Diabetes mellitus, n (%)	11 (22.9)	1 (2.9)	0.01*
Chronic renal failure, n (%)	6 (12.5)	3 (8.6)	0.72
Cerebrovascular disease, n (%)	5 (10.4)	0 (0)	0.07
Malignancy, n (%)	10 (20.8)	5 (14.3)	0.44
Chronic obstructive pulmonary disease, n (%)	2 (4.2)	1(2.9)	1
PEG, n (%)	13 (27.1)	3 (8.6)	0.03*
Tracheostomy, n (%)	31 (64.6)	17 (48.6)	0.14
Central venous catheter, n (%)	40 (83.3)	28 (80)	0.69
GIS surgery, n (%)	21 (43.8)	18 (51.4)	0.48
Intubation, n (%)	46 (95.8)	31 (88.6)	0.23
Enteral feeding, n (%)	43 (89.6)	30 (85.7)	0.73
Nasogastric tube, n (%)	46 (95.8)	31 (88.6)	0.23
Total parenteral nutrition, n (%)	33 (68.8)	24 (68.6)	0.98
Hemodialysis/CRRT, n (%)	21 (43.8)	15 (42.9)	0.93
Mortality, n (%)	34 (70.8)	25 (71.4)	0.95

SD: Standard deviation, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment, IQR: interquartile range, PEG: percutaneous endoscopic gastrostomy, GIS: gastrointestinal system, CRRT: continuous renal replacement therapy, * p≤0.05, the difference between two groups is statistically significant.

To identify the risk factors for candidemia, we compared the patients with and without candidemia. The characteristics of these groups and the results of the univariate analysis were shown in Table 2. The ratio of *Candida* spp. isolation in at least one part of the body other than blood, such as urine or endotracheal aspirate, and median SOFA scores were significantly higher in the candidemia group (P=0.02, P=0.001, respectively). Blood transfusion, CVC placement, intubation, gastrointestinal system (GIS) surgery and TPN were significantly more common in the patients with candidemia (P=0.01, P=0.05, P=0.04, P=0.004, P=0.04). The rate of the patients whose *Candida* scores were higher or equal to 3 was significantly higher in candidemia group (P=0.03). Significant variables in univariate analysis were included in multivariate analysis and, logistic regression was used to establish a significant model. According to the results of logistic regression analysis, SOFA score (P<0.001, OR: 1.25, 95% CI: 1.15-1.37), GIS surgery (P=0.03, OR: 2.60, 95% CI: 1.10-6.12), CVC placement (P=0.04, OR: 2.62, 95% CI: 1.05-6.57) and TPN (P=0.02, OR: 2.61, 95% CI: 1.12-6.06) were independent risk factors for candidemia, while enteral feeding (P=0.02, OR: 0.27, 95% CI: 0.09-0.80) was protective (Table 3). Mortality rates were also significantly higher in candidemia patients (P=0.001).

Table 2: Univariate analysis of risk factors for candidemia in ICU

	Patients with candidemia (n=83)	Patients without candidemia (n=83)	*P*-value	OR	95% CI
Male gender, n (%)	47 (56.6)	48 (57.8)	0.87	1.05	0.56-1.94
Age, year, mean (SD)	55.47 (18.74)	55.41 (20.01)	0.98		
APACHE II, median (IQR)	21 (16-25)	19 (16-24)	0.26		
SOFA, median (IQR)	12 (10-18)	8 (6-11)	<0.001×		
Hospitalization before ICU, n (%)	30 (36.1)	29 (34.9)	0.87	1.05	0.55-1.99
Length of stay, day, median (IQR)	31 (18-46)	27 (20-38)	0.32		
Candida score≥3, n (%)	33 (39.8)	20 (24.1)	0.03×	2.07	1.06-4.05
Underlying diseases, n (%)					
Hypertansion	14 (16.9)	19 (22.9)	0.33	0.68	0.31-1.47
Congestive heart disease	1 (1.2)	5 (6)	0.21	0.19	0.02-1.66
Diabetes mellitus	12 (14.5)	16 (19.3)	0.40	0.70	0.31-1.60
Chronic renal failure	9 (10.8)	7 (8.4)	0.59	1.32	0.46-3.73
Cerebrovascular disease	5 (6)	7 (8.4)	0.54	0.69	0.21-2.28
Malignancy	15 (18.1)	18 (21.7)	0.56	0.79	0.37-1.71
Chronic obstructive pulmonary disease	3 (3.6)	5 (6)	0.21	0.58	0.13-2.53
Invasive procedures, n (%)					
PEG	16 (19.3)	12 (14.6)	0.42	1.41	0.62-3.20
Trakeostomy	48 (57.8)	53 (63.9)	0.42	0.77	0.41-1.45
Blood transfusion	57 (68.7)	41 (49.4)	0.01×	2.24	1.19-4.22
Central venous catheter	68 (81.9)	57 (68.7)	0.05×	2.06	1-4.27
Urinary catheter	82 (98.8)	78 (94)	0.21	5.25	0.60-46
Surgery	54 (65.1)	49 (59)	0.42	1.29	0.68-2.42
GIS surgery	39 (47)	21 (25.3)	0.004×	2.61	1.35-5.04
Intubation	77 (92.8)	68 (81.9)	0.04×	2.83	1.04-7.70
Enteral feeding	73 (88)	64 (77.1)	0.07	2.16	0.93-5
Nasogastric tube	77 (92.8)	79 (95.2)	0.51	0.65	0.17-2.39
Total parenteral nutrition	57 (68.7)	44 (53)	0.04×	1.94	1.03-3.66
Hemodialysis/CRRT	36 (43.4)	31 (37.3)	0.42	1.28	0.69-2.39
Drain	47 (56.6)	43 (51.8)	0.53	1.21	0.65-2.23
Mortality, n (%)	59 (71.1)	38 (45.8)	0.001×	2.01	1.53-5.53

ICU: intensive care unit, SD: Standard deviation, PEG: percutaneous endoscopic gastrostomy, GIS: gastrointestinal system, CRRT: continuous renal replacement therapy, IQR: interquartile range, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment, × p≤0.05, the difference between two groups is statistically significant.

Table 3: Multivariate analysis of risk factors for candidemia in ICU

	Patients with candidemia (n=83)	Patients without candidemia (n=83)	*P*-value	OR	95% CI
Candida score≥3, n (%)	33 (39.8)	20 (24.1)	0.26	1.69	0.66-4.29
Blood transfusion, n (%)	57 (68.7)	41 (49.4)	0.44	1.36	0.61-3.03
Central venous catheter, n(%)	68 (81.9)	57 (68.7)	0.04×	2.62	1.05-6.57
GIS surgery, n (%)	39 (47)	21 (25.3)	0.03×	2.60	1.10-6.12
Intubation, n (%)	77 (92.8)	68 (81.9)	0.97	0.97	0.28-3.39
Total parenteral nutrition, n (%)	57 (68.7)	44 (53)	0.02×	2.61	1.12-6.06
Enteral feeding, n (%)	73 (88)	64 (77.1)	0.02×	0.27	0.09-0.80
SOFA, median (IQR)	12 (10-18)	8 (6-11)	<0.001×	1.25	1.15-1.37

OR: odd's ratio, CI: confidence interval, SOFA: sequential organ failure assessment, IQR: interquartile range, × *P*≤0.05, the difference between two groups is statistically significant.

Antifungal susceptibility tests could be performed in only 44.5% (n=37) of the candidemia patients. According to the results, in *C. albicans*, fluconazole resistance was 8%, and no resistance to amphotericin B and echinocandins was observed. In non-*albicans Candida* species, fluconazole resistance was 80% in *C. glabrata*, only one strain among *C. parapsilosis* was resistant to fluconazole. Among candidemia patients, 84.3% (70/83) had antibiotic consumption before the onset of candidemia, carbapenems being the most used.

Discussion

We report the epidemiological data and risk factors for candidemia in the ICU of a tertiary care regional referral center. The candidemia incidence in our ICU was 2.88 per 1000 patient-days with an all-cause mortality rate of 71.1%. In various studies, candidemia incidence in ICU is reported as 0.24-34.3 patients per 1000 admissions [9, 10]. The two large multinational studies, "The Extended Prevalence of Infection in Intensive Care (EPIC II) study" and "European ICU project (EUCANDICU)" reported a prevalence of 6.87 and 5.52 per 1000 admissions, respectively, for candidemia among ICU patients [11, 12]. In comparison to the results of nationwide studies, the incidence of candidemia in our ICU was lower than that in other countries. This result was associated with few numbers of neutropenic patients with hematologic or oncologic malignancy in our study.

Although *C. albicans* is traditionally known as the leading cause of candidemia worldwide, in recent years, a shift towards non-*albicans Candida* spp. has been reported [13-15]. In a multicenter study with 2496 patients from the United States and Canada, in 62.5% of participating sites, non-*albicans Candida* spp. accounted for>50% of all cases of invasive candidiasis [13]. In a recent study conducted in the ICU and surgical wards in China, *C. albicans* was isolated in only 33.8% of candidemia cases [14]. Similarly, the proportion of non-*albicans Candida* spp. exceeded *C. albicans* in another study from the Asia-Pacific region [15]. From different regions of our country, rates of *C. albicans* in candidemia were reported as 75% by Tukenmez Tigen et al, 72% by Yılmaz Karadag et al, 52.4% by Mermutluoglu et al. and 57% by Arslan et al [16-19]. In compliance with these studies, *C. albicans* was the overall leading cause of candidemia in our study, but with a decreasing rate from 69.2% to 50% during the study period. We observed that the species distribution is changing from *C. albicans* towards non-*albicans* spp. in our institution, compatible with the literature. *C. glabrata* and *C. parapsilosis* were the most common non-*albicans Candida* species in our study and, especially the increasing frequency of *C. parapsilosis* over the years was striking. *C. parapsilosis* is known to show a propensity to colonize the catheters by adhering to the surface through a fibrin sheath [20]. As we observed that the distribution of CVC associated candidemia was in parallel with the distribution of *C. parapsilosis*, the upward trend of *C. parapsilosis* was attributed to this finding. Thus, nine (90%) of ten candidemia caused by *C. parapsilosis* were related to the central catheter. Our study also showed that the proportion of CVC associated candidemia was considerable in our institute and it is essential to reduce these rates. Efforts should be made to increase hand hygiene compliance and improve central line care.

Recent studies indicated that the risk factors associated with the increased rates of non-*albicans Candida* spp. were major operations, GIS surgery, TPN, hemodialysis, blood transfusions, malignancy, chemotherapy, and previous use of fluconazole [21-23]. In our study TPN, hemodialysis and CVC rates were similar in both *C. albicans* and non-*albicans Candida* spp. groups. History of GIS surgery was insignificantly more common in the non-*albicans Candida* spp. group. In *the C. albicans* group, rates of DM and PEG were significantly higher than that in the non-*albicans Candida* spp. It is known that patients with DM have an increased susceptibility to infections. In a recent study, Gursoy et al. [24] suggested that there is a higher presence of intestinal *C. albicans* colonization in diabetic patients. Similar to our study, Al Dorzi et al. [25] found that insulin-treated DM rates were higher in *C. albicans* than non-*albicans Candida* spp. in their study conducted at the ICUs of two tertiary care centers.

There are many studies in the literature concerning the risk factors for the development of candidemia. Presence of CVC, TPN, broad-spectrum antibiotic usage, history of surgery, blood transfusion, length of hospitalization, urethral catheterization, and chronic renal failure were the risk factors for candidemia [23, 26, 27]. In our study, the presence of CVC, blood transfusion, intubation, TPN, and GIS surgery were more common in the candidemia group compatible with the literature.

Although the rates of surgical interventions were similar in both groups, GIS surgery was significantly higher in the candidemia group (Table 2). Similar to our study, Das et al. determined that the risk of developing candidemia is higher in the patients with a history of GIS surgery than other types of surgical interventions [27]. The gastrointestinal system is known as the habitat of *Candida* species and from the impaired mucosa barrier of GIS, *Candida* spp. can translocate into the bloodstream, causing candidemia [28].

Colonization with *Candida* species is known as a prerequisite for candidemia. In recent studies, *Candida* colonization rate in the ICU was reported as 50-100% and invasive candidiasis developed in 3-25% of the patients who had *Candida* colonization [29, 30]. In our study, the isolation of *Candida* spp. in the samples other than blood was significantly higher in the candidemia group.

Identifying the patients at high risk of candidiasis is crucial for both early initiation of antifungal treatment and avoiding unnecessary use of antifungal therapy. A score named "*Candida* score" was identified in 2006 by Leon et al. in a multicenter study conducted in ICUs, and in 2009, a significant association between the rate of invasive candidiasis and the increasing values of the "*Candida* score" was demonstrated [31,32], which is calculated as follows: *Candida* score = 0.908 × (total parenteral nutrition) + 0.997 × (surgery) + 1.112 × (multifocal *Candida* species colonization) + 2.038 × (severe sepsis) and a score >2.5 is significant for invasive candidiasis. In 2009, they used a rounded *Candida* score, calculated as follows: 1 × (total parenteral nutrition) + 1 × (surgery) + 1 × (multifocal Candida colonization) + 2 × (severe sepsis) and if score is smaller than 3, invasive candidiasis is highly improbable. Our results were in accordance with Leon's data. In the candidemia group, 40% of the patients had a score ≥3, significantly higher than the non-candidemia group.

In multivariate analysis, CVC, TPN, GIS surgery, and SOFA scores were independent risk factors for candidemia, compatible with the literature. As we know that SOFA scores assess the severity of organ dysfunction in critically ill patients, the result of our study supported the fact that more severely ill patients are at higher risk for *Candida* infections. As a striking result of multivariate analysis, enteral feeding was determined as a protective factor for candidemia (OR: 0.27, 95% CI: 0.09-0.80). This can be explained by the fact that enteral feeding is more physiological than parenteral nutrition and can protect the patient from the catheter-related infections caused by TPN.

Limitations

The retrospective a single-center design of the study are its major limitations. Another limitation is that antifungal susceptibility tests were performed in nearly half of the patients. Because of the small sample size of the strains that had antifungal susceptibility tests, the resistance ratios may not be generalizable. Nevertheless, our study provides important epidemiological findings that can be useful in the management of candidemia.

Conclusion

The result of our study is evidence of the changing epidemiology of candidemia and showed a shift towards non-*albicans Candida* spp. over the years. The most common non-*albicans Candida* species in our ICU were *C. glabrata* and *C. parapsilosis*. Fluconazole resistance in *C. glabrata* should be considered before using azoles in empirical treatment. The increasing rate of *C. parapsilosis* and CVC-associated candidemia has highlighted the need for more attention to central line care and hand hygiene. Also, as another finding of our study, half of the patients had no fever during candidemia, which may lead to delay in diagnosis and treatment. History of GIS surgery, TPN, CVC, and high SOFA scores in ICU patients are independent risk factors for candidemia. Besides, enteral nutrition was a protective factor. Unless necessary, limitation of TPN use and ensuring the earlier implementation of enteral feeding will be effective in preventing candidemia.

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