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# Epidemiological analysis of Nosocomial Candida infections: Experience of a university hospital

## Nozokomiyal Kandida enfeksiyonlarının epidemiyolojik analizi: Bir üniversite hastanesi deneyimi

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**SUMMARY**

**Objective:** A retrospective investigation was made in a university hospital setting of the distribution of Candida infections in terms of species, different clinical features of infections, risk factors for candidemia caused by these fungi and their antifungal susceptibilities.

**Method:** This study was conducted between January 1st, 2014, and December 31st, 2017. Patients included in the study were those diagnosed with candida infection as a result of Candida species, isolated from at least one clinical sample of those taken from hospitalized patients, including blood, urine, and other clinical samples, and who were then administered antifungal therapy. The identification of Candida species was performed using Matrix-Assisted Laser Desorption/Ionization Time-of-Mass Spectrometry (MALDI-TOF MS).

**Results:** During the study period, the candida infection rate was found to be 5.86% in the 2760 episodes of infection, and the incidence of candida infection was found to be 0.35 in 1000 bed days. The most common infection site for candida was the urinary tract (61.1%), followed by the blood-stream (31.5%). In 66% of all candida infections, *Candida albicans* was defined as the causative agent. The distribution of *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, *Candida lusiteniae*, *Candida krusei*, and *Candida kefyr* were determined as 9.9%, 9.3%, 4.9%, 2.5%, 1.9% and 1.2%, respectively. The sensitivity to fluconazole and amphotericin B was determined as 97.2% and 99.1% in the *C. albicans* isolates, respectively. The sensitivity ratios for both fluconazole and amphotericin B were determined as 78.2% in the non-albicans strains. Multivariate logistic regression analysis showed that total parenteral nutrition (TPN) [Odds ratio (OR) 3.69, 95% Confidence interval, 1.595-8.570; p=0.002] was an independent risk factor for candidemia in patients with Candida infection.

**Conclusions:** *C. albicans* was the most encountered species in candida infections in our hospital. TPN was determined as an independent risk factor for the development of candidemia. Determinations of the species distribution of fungal infections and the antifungal sensitivity are important for the selection of effective treatment.

**Keywords**: Candida infection, clinical features, risk factors for candidemia

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**ÖZET**

**Amaç:** Bu çalışmada retrospektif olarak bir üniversite hastanesindeki kandida enfeksiyonlarının etken bazında dağılımı, bu etkenlerin yol açtığı enfeksiyonların farklı klinik özelliklerinin ve kandidemi için risk faktörlerinin belirlenmesi ve etken kandidaların antifungal duyarlılıklarının saptanması amaçlanmıştır.

**Yöntem:** Çalışma 01 Ocak 2014 - 31 Aralık 2017 tarihleri arasında gerçekleştirilmiştir. Hastaneye yatırılarak takip edilen hastalardan alınan kan, idrar ve diğer vücut örneklerinden en az birinde kandida üremesi kandida enfeksiyonu olgusu olarak değerlendirilmiş ve antifungal tedavi verilen olgular değerlendirmeye alınmıştır. İzolatların tanımlanması Matrix-Assisted Laser Desorption/Ionization Time-of-Mass Spectrometry (MALDI-TOF-MS) sistemi kullanılarak yapılmıştır.

**Bulgular:** Çalışma süresi içinde toplam 2760 enfeksiyon epizodunda kandida enfeksiyon hızı %5.86, kandida enfeksiyonu insidans dansitesi ise 1000 yatak gününe 0.35 olarak bulunmuştur. En sık saptanan kandida enfeksiyonu üriner sistem enfeksiyonu olup (%61.1), bunu %31.5 ile kandidemi takip etmiştir. Tüm kandida enfeksiyonlarının %66'sında *Candida albicans* etken olarak tanımlanmıştır. Bunu %9.9 ile *Candida glabrata*, % 9.3 ile *Candida tropicalis*, %4.9 ile *Candida parapsilosis*, %2.5 ile *Candida lusiteniae*, %1.9 ile *Candida krusei* ve %1.2 ile *Candida kefyr* takip etmiştir. Saptanan *C. albicans* izolatlarında flukonazol duyarlılığı %97.2, amphotericin B duyarlılığı ise %99.1 olarak bulunmuştur. Non-albicans kandida suşlarında ise flukonazol ve amfoterisin B duyarlılığı %78.2 olarak saptanmıştır. Çoklu regresyon analizinde total parenteral nütrisyon (TPN) uygulamasının [Odds ratio (OR) 3.69, %95 Güvenlik Aralığı (%95 GA) 1.595-8.570; P=0.002] kandidemi için bağımsız risk faktörü olduğu gözlenmiştir.

**Sonuç:** Hastanemizde ortaya çıkan kandida enfeksiyonlarında *C. albicans* suşları ön plandadır. Kandidemi gelişiminde total parenteral nütrisyon kullanımı bağımsız bir risk faktörü olarak görülmektedir. Hastanelerde fungal enfeksiyon etkenlerinin dağılımlarının ve antifungal duyarlılıklarının bilinmesi effektif tedavi seçiminde önemlidir.

**Anahtar sözcükler:** Kandida enfeksiyonu, klinik özellikler, kandidemi için risk faktörleri

## INTRODUCTION

Candida species, which are fungi morphology that can produce true or false hyphae, can cause diseases ranging from local mucosal infections to invasive fungal infections in humans[1]. Candida species are the most common cause of opportunistic fungal infections and account for approximately 70-90% of invasive fungal infections[2]. The incidence and prevalence of invasive fungal infections have increased since the 1980s, especially in the vast majority of immunocompromised patients and / or in hospitalized patients with severe underlying diseases[3,4].

More than 15 different subtypes of Candida species are known to be etiological agents in human infections. However, more than 90% of invasive infections are caused by *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida krusei*[5]. Over the past two decades, non-albicans species have gained medical importance, and isolation frequency has increased in microbiological specimens[6].

The increase in the frequency of healthcare-related infections associated with Candida species is more commonly involved in patients with immunosuppression and using broad-spectrum antibiotics. Furthermore, the role of hospital staff and the contaminated material used the management of a patient in the emergence of Candida infections in critical patient care units such as intensive care has been demonstrated by molecular methods[7].

The timely administration of appropriate antimicrobial treatment is crucial in patients with specified clinical conditions. Thus, the determination of the distribution of fungal infections and considering the antifungal susceptibility of etiological agents are important. Late diagnosis of candida infections or late initiation of antifungal therapy may lead to high mortality rates in the units where serious cases are treated, such as intensive care units and hematology-oncology units. The aim of this study was to investigate the distribution of nosocomial Candida infections in our hospital and to determine the antifungal sensitivities of these infections.

## MATERIAL AND METHODS

This study was conducted between January 1st, 2014 and December 31st, 2017. Retrospective data were obtained from the patient and laboratory-based surveillance records. Identification of nosocomial infections was performed according to the diagnostic criteria determined by the United States Centers for Diseases Control and Prevention (CDC)[8]. The patients included in the study were those with Candida species, isolated from at least one of clinical samples including blood, urine, abscesses and endoscopic esophageal biopsy specimens taken from hospitalized patients, which was then considered as a case of candida infection and antifungal

therapy was administered. Cases were excluded if Candida growth in clinical samples was evaluated as colonization, and no antifungal treatment was given. The first fungal agent isolated from a patient was included in the study, recurrent isolates of the same patient were not included. Clinical samples other than the blood sample sent from patients were planted on 5% sheep blood agar and Eosin-Methylene-Blue (EMB) agar. Blood samples were cultured in blood culture bottles (Bactec FX-Becton Dickinson®, Maryland / USA) and incubated at 37˚ C in the incubator. Samples of Candida type fungi were also implanted in Sabouraud dextrose agar (SDA) medium. Germ tube tests were conducted on the produced candida strains. Isolates were defined using Matrix-Assisted Laser Desorption/Ionization Time-of-Mass Spectrometry (MALDI-TOF MS) based on the Bruker IVD MALDI Biotyper 2.3 (Bruker Daltonik GmbH, Bremen, Germany) device. The system gives a score of 0-3 according to the measurement results. According to the manufacturer's guide, (Bruker Daltonics, Germany) values <, 1.7 do not pass the reliability level, scores between 1.7-2.0 are reliable definitions of type basis, and scores between 2.0-3.0 are reliable definitions of both type and species basis. In the present study, evaluations were made of the results of fungal definitions of 155 strains (95.7%) identified at the species level, of ≥2.0, 7 isolates (4.3%) were identified at the genus level and 1.7-2.0 reliability scores were obtained. Antifungal sensitivity tests for amphotericin B, fluconazole, and itraconazole were applied using the colorimetric liquid microdilution method (TREK Diagnostic-Sensititre® al Yeastone®, West Sussex, UK). Approval for the study was obtained from the Local Ethics Committee (decision no: 2018-04/36).

***Statistical analysis:***

Data obtained in this descriptive study were analyzed using SPSS version 15.0 (SPSS, Inc, Chicago, IL, USA). Results were shown as the mean ± standard deviation for continuous variables, and the number of cases and percentage (%) for nominal variables. Categorical variables were evaluated using the $\chi 2$ test. Univariate analysis was performed by determining the independent variables for the logistic model formed in order to determine the characteristics that affect the development of candidemia in patients with Candida infection. In this analysis, variables with p-value <0.1 were analyzed using backward logistic regression analysis; the Odds ratio (OR) and 95% confidence interval (95% CI) were determined. A value of p <0.05 was considered statistically significant.

## RESULTS

The study was included a total of 162 patients who developed candida infection during the defined 4-year period. The patients comprised 53.1% females and 46.9% males with a mean age of 66 ± 16 years (range: 18-92 years). Of the total 162 patients with candida infection, 37% were hospitalized in the anesthesiology intensive care unit. The demographic characteristics of the patients are shown in Table 1.

The rate of candida infection was determined to be 5.86%, and the incidence rate of candida infection was 0.35 per 1000 beds in a total of 2760 infection episodes that occurred between 2014 and 2017 years (Table 2).

The most common candida infection in this process was urinary tract infection (UTI) (61.1%), followed by candidemia at 31.5%. The incidence of candidemia was 0.11 per 1000 patient days. The agent was determined to be *C. albicans* in 66%, followed by *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, *C. lusiteniae*, *C. krusei*, and *C. kefyr* at 9.9%, 9.3%, 4.9%, 2.5%, 1.9% and 1.2%, respectively. The remaining 4.3% could not be identified on the basis of type (Table 3).

**Table 1:** Demographic features and concomitant situations

| **Variables** | **N (%)** |
|---|---|
| **Gender** | |
| Female | 86 (53.1) |
| Male | 76 (46.9) |
| **Hospitalized Department** | |
| Anesthesiology and Intensive Care Unit | 60 (37) |
| Hematology-Oncology | 32 (19.8) |
| Internal Medicine | 31 (19.1) |
| General Surgery Intensive Care Unit | 18 (11.1) |
| Neurology | 7 (4.3) |
| Neurosurgery Intensive Care Unit | 4 (2.5) |
| Urology | 4 (2.5) |
| Burn Unit | 2 (1.2) |
| Gynecology and Obstetrics | 1 (0.6) |
| Cardiology | 2 (1.2) |
| Cardiovascular Surgery | 1 (0.6) |
| **Clinical Diagnosis** | |
| Shortness of Breath | 54 (33.3) |
| Malignancy | 36 (22.2) |
| Intraabdominal Disease | 18 (11.1) |
| Cerebrovascular Disease | 11 (6.8) |
| Renal Disease | 11 (6.8) |
| Trauma | 7 (4.3) |
| Sepsis | 6 (3.7) |
| Others * | 19 (11.8) |
| **Concomitant Situations** | |
| Malignancy | 63 (38.9) |
| Hypertension | 44 (27.2) |
| Diabetes Mellitus | 38 (23.5) |
| Chronic Obstructive Pulmonary Disease | 31 (19.1) |
| Cerebrovascular Disease | 26 (16.0) |
| Coronary Artery Disease | 13 (8.0) |
| Heart Failure | 8 (4.9) |
| Chronic Renal Failure | 17 (10.5) |
| Trauma | 5 (3.1) |

*Others (number; %): Pulmonary thromboembolia (2; 1.2%), Gastrointestinal hemorrhage (4; 2.5%), Fournier gangrene (2; 1.2%), Diabetic ketoacidosis (3; 1.9%), Coroner artery disease (2; 1.2%), Burn (2; 1.2%), Aort aneurysm (1; 0.7%), Silicosis (1; % 0.7), Anemia (2; %1,2)

**Table 2:** Candida infection rate and incidence density according to years

| **Year** | **Patient Days** | **Candida Infection Rate*** | **Candida Infection Incidence Density **** |
|---|---|---|---|
| **2014** | 116278 | 3.8 | 0.23 |
| **2015** | 116738 | 7.1 | 0.37 |
| **2016** | 110405 | 8.8 | 0.52 |
| **2017** | 117473 | 4.3 | 0.29 |
| **Total** | **460894** | **5.86** | **0.35** |

*Candida Hospital Infection Rate: Candida infection count/total infections x 100

**Candida Infection Incidence Density: Candida infections count/duration of hospitalization (days) x 1000

**Table 3:** Distribution of Candida species according to years

| Candida species | Years | | | | |
|---|---|---|---|---|---|
| | **2014** | **2015** | **2016** | **2017** | **Total N *(%)*** |
| *Candida albicans* | 21 | 32 | 30 | 24 | 107 (66.0) |
| *Candida tropicalis* | - | 5 | 7 | 3 | 15 (9.3) |
| *Candida krusei* | - | - | 2 | 1 | 3 (1.9) |
| *Candida parapsilosis* | - | - | 8 | - | 8 (4.9) |
| *Candida lusiteniae* | - | 1 | 3 | - | 4 (2.5) |
| *Candida glabrata* | 2 | 2 | 6 | 6 | 16 (9.9) |
| *Candida kefyr* | - | 2 | - | - | 2 (1.2) |
| *Candida spp* | 4 | 1 | 2 | - | 7 (4.3) |
| TOTAL | **27** | **43** | **58** | **34** | **162 (100)** |

The sensitivities to fluconazole and amphotericin B were found as 97.2%, and 99.1% in *C. albicans* isolates, respectively. In the non-albicans candida strains, the sensitivity to both fluconazole and amphotericin B was found to be 78.2%. The antifungal susceptibilities of all factors were shown in Table 4.

**Table 4:** Antifungal susceptibilities of Candida species

| | Antifungal agents | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Fluconasole | | | Itraconasole | | | Amphotericin B | | |
| Species | S | I | R | S | I | R | S | I | R |
| *C.albicans* (n=107)(%) | **104 (97.2)** | **2 (1.9)** | **1 (0.9)** | **84 (78.5)** | **21 (19.6)** | **2 (1.9)** | **106 (99.1)** | **0 (0)** | **1 (0.9)** |
| *Non-albicans Candida (n=55)(%)* | **43 (78.2)** | **5 (9.1)** | **7 (12.7)** | **20 (36.4)** | **24 (43.6)** | **11 (20)** | **43 (78.2)** | **6 (10.9)** | **6 (10.9)** |
| *C.tropicalis* (n=15)(%) | 9 (60) | 4 (26.7) | 2 (13.3) | 4 (26.7) | 6 (40) | 5 (33.3) | 7 (46.7) | 3 (20) | 5 (33.3) |
| *C.glabrata* (n=16)(%) | 13 (81.2) | 1 (6.3) | 2 (12.5) | 6 (37.5) | 8 (50) | 2 (12.5) | 15 (93.7) | 1 (6.3) | 0 (0) |
| *C.parapsilosis* (n=8)(%) | 8 (100) | 0 (0) | 0 (0) | 0 (0) | 7 (87.5) | 1 (12.5) | 7 (87.5) | 1 (12.5) | 0 (0) |
| *C.lusiteniae* (n=4)(%) | 4 (100) | 0 (0) | 0 (0) | 1 (25) | 3 (75) | 0 (0) | 3 (75) | 1 (25) | 0 (0) |
| *C.krusei* (n=3)(%) | 0 (0) | 0 (0) | 3 (100) | 0 (0) | 0 (0) | 3 (100) | 3 (100) | 0 (0) | 0 (0) |
| *C.kefyr* (n=2)(%) | 2 (100) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 1 (50) |
| *Candida spp* (n=7)(%) | 7 (100) | 0 (0) | 0 (0) | 7 (100) | 0 (0) | 0 (0) | 7 (100) | 0 (0) | 0 (0) |
| Total (n=162) (%) | **147 (90.7)** | **7 (4.4)** | **8 (4.9)** | **104 (64.2)** | **45 (27.8)** | **13 (8)** | **149 (91.9)** | **6 (3.7)** | **7 (4.4)** |

S: Sensitive, I: Intermediate, R: Resistant

The use of total parenteral nutrition (TPN), blood transfusion, cerebrovascular disease, heart failure, male gender, presence of surgical drainage tubes, nasogastric tube, intubation, and previous macrolide use were found to be associated with the development of candidemia.

In multivariate logistic regression analysis, the application of TPN [Odds ratio (OR) 3.69, 95% CI (1.5% CI) 1.595-8.570; P = 0.002] was found to be an independent risk factor for the development of candidemia and to increase the risk 3.69-fold. The univariate analysis results for risk factors facilitating the development of candidemia in patients with Candida infection are shown in Table 5, and the multivariate logistic regression analysis results are shown in Table 6.

**Table 5:** Association of risk factors of cases developing candidemia (Univariate analysis results)*

| **Variables** | **Patients Not Developing Candidemia (n=111)** | **Patients Developing Candidemia (n=51)** | **p-value** |
|---|---|---|---|
| **Age** | | | 0.180 |
| <65 years | 42 (37.8) | 25 (49) | |
| ≥65 years | 69 (62.2) | 26 (51) | |
| **Gender** | | | |
| Female | 64 (57.7) | 22 (43.1) | |
| Male | 47 (42.3) | 29 (56.9) | **0.085** |
| **Invasive Device** | | | |
| Drainage Tube | 24 (21.6) | 18 (35.3) | **0.065** |
| Intubation | 54 (48.6) | 17 (33.3) | **0.068** |
| Chest tube | 10 (9.0) | 8 (15.7) | 0.209 |
| Urinary catheter | 97 (87.3) | 40 (78.4) | 0.143 |
| Mechanical ventilation | 54 (48.6) | 18 (35.3) | 0.112 |
| Central venous catheter | 68 (61.3) | 34 (66.7) | 0.508 |
| Nasogastric catheter | 54 (48.6) | 12 (23.5) | **0.003** |
| **Concomitant Diseases** | | | |
| Serebrovascular disease | 23 (20.7) | 3 (5.9) | **0.017** |
| Chronic obstructive pulmonary disease | 23 (20.7) | 8 (15.7) | 0.449 |
| Malignancy | 39 (35.1) | 24 (47) | 0.148 |
| Diabetes mellitus | 26 (23.4) | 12 (23.5) | 0.988 |
| Chronic renal failure | 14 (12.6) | 3 (5.9) | 0.194 |
| Hipertension | 34 (30.6) | 10 (19.6) | 0.143 |
| Coronary artery disease | 10 (9.0) | 3 (5.9) | 0.496 |
| Heart failure | 8 (7.2) | 0 (0) | **0.049** |
| **Previous History of Antibiotic Use** | | | |
| Penicillin | 80 (72.1) | 36 (70.6) | 0.846 |
| Cephalosporin | 13 (11.7) | 8 (15.7) | 0.484 |
| Quinolon | 13 (11.7) | 5 (9.8) | 0.720 |
| Glycopeptid | 39 (35.1) | 22 (43.1) | 0.329 |
| Carbapenem | 50 (45.1) | 23 (45.1) | 0.995 |
| Macrolide | 32 (28.8) | 8 (15.7) | **0.072** |
| **Type of Nutrition** | | | |
| Enteral nutrition | 39 (35.1) | 13 (25.5) | 0.222 |
| Total parenteral nutrition (TPN) | 18 (16.2) | 21 (41.2) | **0.001** |
| **Others** | | | |
| Hemodialisis | 24 (21.6) | 10 (19.6) | 0.770 |
| Use of H2-receptor antagonist | 59 (53.2) | 21 (41.2) | 0.157 |
| Immunesuppression | 18 (16.2) | 12 (23.5) | 0.266 |
| Blood transfusion | 32 (28.8) | 23 (45.1) | **0.042** |

* Values are expressed as n (%).

**Table 6:** Independent risk factors for the development of candidemia in cases with Candida infection (Multivariate logistic regression analysis)

| Variable | p-value | Odds Ratio | %95 CI |
|---|---|---|---|
| Gender | 0.214 | 1.59 | 0.763-3.338 |
| Total parenteral nutrition | **0.002** | **3.69** | **1.595-8.570** |
| Blood transfusion | 0.301 | 1.50 | 0,695-3.236 |
| Nasogastric catheter | 0.044 | 0.42 | 0.182-0.976 |
| Use of macrolides | 0.778 | 0.86 | 0.327-2.308 |
| Drainage tube | 0.172 | 1.78 | 0.777-4.107 |
| Serebrovascular disease | 0.194 | 0.40 | 0.102-1.590 |
| Heart failure | 0.999 | 0.000 | 0.000 |

CI: Confidence Interval

## DISCUSSION

In this study, the characteristics of candida infections, species distribution, and antifungal sensitivities results are presented. In our center, the units with the most common infections caused by Candida species were seen to be the anesthesiology intensive care unit (37%) and the Department of hematology-oncology (19.8%). The increase of candida infections in these units may be correlated with the follow-up of patients with advanced age group and underlying chronic diseases, the concomitance of immune system-suppression, invasive applications, and high usage of broad-spectrum antibiotics.

In this study, the isolated species in 66% of all Candida infections was determined to be *C. albicans*, followed by *C. glabrata* at 9.9%, *C. tropicalis* at 9.3%, *C. parapsilosis* at 4.9%, *C. lusiteniae* at 2.5%, *C .krusei* at 1.9% and *C. kefyr* at 1.2%. The remaining 4.3% could not be identified on the basis of type. In the Artemis Global Antifungal Surveillance Study by Pfaller et al.[9], the incidence of *C. albicans* between 1997-2007 was reported as 65.3%, followed by *C. glabrata* (11.3%), *C. tropicalis* (7.2%) and *C. parapsilosis* (6%), respectively. Cornistein et al.[10] detected *C. albicans* in 43.3%, *C. tropicalis* in 24.6% and *C. glabrata* in 8.1% of 321 clinical samples. Takakura et al.[11] found that the rate of *C. albicans* was 40.7% and *C. parapsilosis*, 23%, respectively. In studies from Turkey, Çiçek et al.[12] reported *C. albicans* at 51.1% and *C. tropicalis* at 15.8%; Temiz et al.[13] isolated *C. albicans* at 71%, *C. tropicalis* and *C. glabrata* at 8.7%; and Turhan et al.[14] isolated *C. albicans* at 41.9% and *C. parapsilosis* at 24.8%. Geographic differences and characteristics of the patient population may result in differences in candida epidemiology, but *C. albicans* remained significant among the Candida species in our center.

Candida-related infections may occur in a broad clinical spectrum. Clinical manifestations may vary due to the type of infection, the respective organ, and the level of immune system suppression[15]. In the study period, the distribution of Candida infections was examined according to systems. UTI was detected in 61.1%, and candidemia was found in 31.5% of the patients. These infection rates were seen to be similar to those in the literature. In a study by Erdem et al.[16], the UTI rate was determined as 72.1%, and candidemia rates at 32.9%. In the study made by Hazırolan[17] reported that the rate of UTI was 56.8%, and the rate of candidemia was 39.4% in infections caused by Candida isolates. Yang et al.[18] reported that the rate of UTI was 54.8%, and the rate of candidemia was 30.6% in 516 fungal infection episodes in intensive care units between 1998 and 2009.

There are difficulties in determining the worldwide rate of candidemia as there is no denominator criterion for the incidence of candidemia. While some countries apply community-based surveillance and use population data as the denominator, other studies have used the duration of disease, discharge, and admission to hospital and intensive care units, resulting in different results of incidence rates of

candidemia[19]. According to the results of studies which have included various European centers, the candidemia incidence was reported as 0.8-2.5/1000 hospitalizations[20], while Kılıç et al.[21] reported that this rate has increased in recent years. In hospital-based surveillance studies, this rate has been found to be 0.23 per 1000 days of disease (0.06-0.39) in Latin-American countries, 0.15 per 1000 days of disease (0.01-1.77) in a study comprising Asian countries and 0.05 (0.01-0.06) per 1000 days of disease in China[22]. In the current study in our center, this rate was 0.11 (0.07-0.19) per 1000 patient days, which was consistent with the literature.

Candidemia is well-defined in specific populations, including hospitalized in surgical departments patients, intensive care unit patients, mechanically ventilated patients, and use of a central venous catheter, indwelling urinary catheter and exposure to total parenteral nutrition[20]. Falcone et al.[23] reported that the presence of severe sepsis or septic shock, a recent history of a *Clostridium difficile* infection, concomitance of diabetes mellitus, total parenteral nutrition, chronic obstructive pulmonary disease, concurrent usage of intravenous glycopeptide treatment, a peripherally inserted central catheter and immunosuppressive treatment are all independent risk factors for the development of candidemia. In Turkey, Yapar et al.[24] reported that a history of taking antibiotics, the use of TPN, blood transfusion, and the presence of urethral catheters were risk factors for the development of candidemia. In the current study, risk factors in patients with candidemia, including TPN, blood transfusion application, the concomitance of cerebrovascular disease, heart failure, male gender, presence of a drainage tube, nasogastric catheter and intubation, and exposure to macrolide group antibiotic were associated with the development of candidemia. According to the multivariate logistic regression analysis, TPN was determined to be statistically significant (p=0.002) and to be an independent risk factor. The using of TPN increased the risk of candidemia development by 3.69-fold.

Sensitivity testing has become important in antifungal treatment, with an increase in alterations in distributions and shifts to more resistant isolates in recent years[25]. In a study by Al-Dorzi et al.[26] investigated the epidemiology and antifungal sensitivity in two different intensive care units in Saudi Arabia, the sensitivity of *C. albicans* species to fluconazole was reported to be 83.3%, and to amphotericin B, 92.9%. In Non-albicans candida strains, it was reported the sensitivity of 67.9% to fluconazole and 98.5% to amphotericin B. In a study made by Posteraro et al.[27], the sensitivity ratio of *C. albicans* to fluconazole was reported as 99.7% and the sensitivity ratio of all Candida isolates to amphotericin B was reported as 97%. For the most common four Candida species isolated by Mohamed et al.[28] in Malaysia the sensitivity to amphotericin B was identified as 100%, while the sensitivity of *C. albicans* to fluconazole was found to be 87.2%. Aydemir et al.[29] reported resistance to fluconazole of *C. albicans* isolates at 1.1% and to amphotericin B at 2.1%, while these rates were reported as 7.7% and 6.4%, respectively for non-albicans Candida strains. Küçükateş et al. [30] reported that all the detected *C.albicans* were sensitive to amphotericin B. However, in the same study, the resistance ratio to fluconazole of *C. albicans* was reported as 47.8%. In the current study, the sensitivity of *C. albicans to* fluconazole and amphotericin B was determined as 97.2% and 99.1%, respectively, and the sensitivity of non-albicans both fluconazole and amphotericin B was determined as 78.2%.

## CONCLUSION

The results of this study demonstrated that *C. albicans* strains are at the forefront of candida infections occurring in our hospital. The application of TPN was seen to be an independent risk factor for the development of candidemia. It is therefore important to determine the distribution of fungal infections in hospitals, especially in ICUs, and to be aware of antifungal sensitivity.

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