

## Original Article

**Increasing spread of *Candida auris* and investigation of risk factors for invasive infections in colonized patients**Tuğba Arslan Gülen<sup>1</sup>, Nida Akar<sup>2</sup>, Ebru Oruç<sup>1</sup>, Tuba Turunç<sup>1</sup>, Koray Daş<sup>3</sup>, Nurdan Ünlü<sup>4</sup>, Aygün Uğurbekler<sup>5</sup><sup>1</sup> Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences, Adana City Training and Research Hospital, Adana, Türkiye<sup>2</sup> Department of Medical Mycology, University of Health Sciences, Adana City Training and Research Hospital, Adana, Türkiye<sup>3</sup> Department of General Surgery, University of Health Sciences, Adana City Training and Research Hospital, Adana, Türkiye<sup>4</sup> Department of Anesthesiology and Intensive Care, University of Health Sciences, Adana City Training and Research Hospital, Adana, Türkiye<sup>5</sup> Hospital Infection Control Committee, Adana City Training and Research Hospital, Adana, Türkiye**Abstract**

**Introduction:** *Candida auris* is a yeast that has a high mortality rate in critically ill patients and is resistant to many antifungal agents enhancing its clinical importance. Our study identifies the risk factors for *C. auris* invasive infection, antifungal susceptibility, and outcomes.

**Methodology:** A total of 100 adults with *C. auris* isolated in any clinical specimen between 07.01.2022 and 31.12.2023 were enrolled in this retrospective cohort study. Data were obtained via retrospective screening of patient files. *C. auris* identification was performed by MALDI-TOF MS. Antifungal susceptibility was carried out by VITEK 2 and CDC methodology. Colonized and infected patients were compared to assess the risk factors for and outcomes of invasive infection.

**Results:** Twenty (20%) patients developed invasive infections, with 16 (80%) having candidemia. Age, *Candida* score, prior antifungal agent use, number of previously used antibiotics  $\geq 3$ , presence of central venous catheter or nasogastric catheter, and being monitored out of burn unit were the risk factors, and *Candida* score was identified as an independent risk factor for invasive infection development. Of the isolates, 55% were resistant to fluconazole and 100% were resistant to amphotericin B. No micafungin resistance was detected. The overall mortality rate in patients with invasive infection was 75%.

**Conclusions:** Knowing the risk factors for invasive infection will help early initiation of empirical antifungal therapy by ensuring early identification of high-risk patients, and *Candida* score appears to be an effective method for this. Revealing antifungal susceptibility will also guide the selection of appropriate empirical treatment.

**Key words:** *Candida auris*; *Candida* colonization; infection; risk factors; surveillance; antifungal resistance.

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**Introduction**

*Candida auris* is a multidrug-resistant yeast with high mortality rates among hospitalized patients [1]. Although it was first identified in 2009 in Japan, a retrospective epidemiological study from South Korea re-identified a *Candida* strain found in 1996 as *C. auris* [2].

It is known to spread and cause outbreaks in hospital settings because it can survive and persist for weeks in dry, nonporous surfaces outside the host [3-5]. It colonizes the skin and leads to invasive infections in healthcare settings due to rapid contamination [6]. Another clinical implication is the high mortality rate due to resistance to many antifungal drugs and the

probability of delayed effective treatment [7]. According to the literature, the mortality rate related to invasive *C. auris* infections ranges from 30% to 72% [8]. Worldwide, more than 90% of *C. auris* isolates are resistant to fluconazole and resistance to amphotericin B shows variations [9-11]. For this reason, antifungal treatment options for *C. auris* are limited, and treatment must be tailored according to the results of antifungal susceptibility testing. A study reported that cumulative candidemia incidence in patients colonized with *C. auris* reached the level of 25% on day 60 [12]. Therefore, identifying colonized patients and monitoring them in terms of invasive infection comes to the forefront to prevent spread in the setting of an

outbreak.

After the isolation of *C. auris* in the urine specimen of a patient followed in the Burn Unit of Adana City Training and Research Hospital on 07 January 2022, the patient was subjected to strict contact isolation, and infection control protocol was implemented to prevent and control the spread. Daily supervision and visits were performed by the infection control committee to monitor protocol compliance. This protocol includes:

- a) Implementation of strict contact isolation measures; establishing patient and healthcare worker cohorts; ensuring the cleaning and disinfection of patient rooms three times a day and providing disinfection after mechanical cleaning in case of getting dirty; in case the patients are referred to another department for imaging, tests, etc. procedures ensuring coordination and arrangement by informing the infection control committee in advance.
- b) Environmental intervention package to reduce *C. auris* burden; subjecting patient rooms to cleaning-disinfection-pulverization processes after the operation and discharge of patients, and opening the room for new patient admission if there is no growth in environmental samples taken;
- c) Screening the patients who have been followed in the same clinic as the patients colonized with *C. auris* for skin colonization through weekly surveillance cultures; and
- d) Placing a warning message via automation in the files of colonized patients after hospital discharge to ensure strict contact isolation.

Despite the interventions within this protocol, the number of patients with *C. auris* isolation in the burn unit and other intensive care units of our hospital has increased in time. Therefore, the present study aimed to reveal the risk factors to predict the invasive infections caused by *C. auris* in risky units and to evaluate susceptibility to antifungal drugs.

## Methodology

### *Study design and setting*

The study was designed as a retrospective and observational cohort study and adult patients ( $\geq 18$  years) with *C. auris* isolated from any clinical specimen between 07.01.2022 and 31.12.2023 were included in the study. Patients' demographic, clinical, laboratory, and microbiological data were accessed by retrospectively screening the patient files through infection control committee data and automation. Patients' comorbid conditions, history of past surgeries, history of total parenteral nutrition, presence of a

central venous catheter, and previously used antimicrobial therapies were recorded. Antifungal susceptibility profiles, antifungal therapies used, and control blood culture-negativity day were assessed in patients with invasive *C. auris* infection. Patients with candidemia were evaluated in terms of complications such as infective endocarditis and fungal endophthalmitis and the results were recorded. The overall mortality rate was calculated in patients who developed invasive infections. The *Candida* score is a scoring system created by Leon *et al.* by evaluating 4 independent risk factors; sepsis was determined as 2 points, abdominal surgery 1 point, total parenteral nutrition 1 point and multifocal candida colonization 1 point, and a value of  $\geq 3$  was accepted as a cut-off [13]. *Candida* score was calculated using the following formula: *Candida* score = 1 x (total parenteral nutrition) + 1 x (past surgery) + 1 x (multifocal colonization) + 2 x (sepsis). The Sequential Organ Failure Assessment (SOFA) recommended by the Third International Consensus Definitions of Sepsis and Septic Shock (Sepsis-3) was used to define sepsis [14]. The SOFA score of the patients was calculated using forms integrated into the hospital automation system. Colonized and infected patients were compared to identify the risk factors for invasive infection.

### *Definitions*

*C. auris* colonization: isolation of *C. auris* from at least one non-sterile region (specimens from skin and/or respiratory tract) in the absence of clinical signs and symptoms of infection;

Multi-site colonization: isolation of *C. auris* from more than one non-sterile region;

Candidemia: isolation of *C. auris* from at least one blood culture in the presence of signs and symptoms of infection;

Invasive candida infection: isolation of *C. auris* from sterile regions of the body;

Urinary system infection: clinical signs and symptoms of urinary infection without another focus of infection and the growth of *C. auris* in the urine culture;

Control blood culture negativity: absence of growth in control cultures obtained every other day after the 72nd day of treatment.

### *Microbiological identification and antifungal susceptibility*

Blood samples taken from the patients until 25.10.2023 were analyzed using BD Bactec FX (Becton-Dickinson, US) device, whereas those obtained after 25.10.2023 were analyzed using

Bact/Alert 3D 480 (BioMérieux, France) device. The specimens, where yeast cells are detected in gram staining of the blood cultures with positive signaling, were further cultivated in the Sabouraud dextrose agar (RTA, Türkiye). Urine samples were cultivated in the 5% sheep blood agar (RTA, Türkiye) and Eosin Methylene Blue agar (RTA, Türkiye) and incubated at 37 °C. The yeast colonies grown were identified using the method of matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, US). Antifungal

susceptibility was analyzed in a VITEK 2 (BioMérieux, France) device with an AST-YS08 card, and the minimum inhibitor concentration (MIC) values were interpreted according to the temporary clinical threshold values recommended by the Centers for Disease and Control (CDC).

### Statistical analysis

The data were analyzed using SPSS Statistics version 22.0 software (IBM Corp, Armonk, NY, USA). Continuous variables were evaluated for normal distribution using the Shapiro-Wilk test. Categorical variables were expressed as frequency (n) and percentage (%), continuous variables that met the assumptions for parametric tests were presented as mean and standard deviation (SD), and those that did not were presented as median, minimum, and maximum values. Chi-square and Fisher's exact significance tests were used to analyze categorical variables. Pairwise comparisons of group means were done using Student's t-test if parametric test assumptions were met and Mann-Whitney U test if parametric test assumptions were not met. Logistic regression analysis was performed to identify independent risk factors associated with mortality.

### Ethics statement

Ethics committee approval was received from the Adana City Training and Research Hospital Ethics Committee (No: 21.12.2023-142/3025). This study was conducted by the principles of the Declaration of Helsinki.

### Results

*C. auris* was isolated from a total of 149 patients, of whom 49 were excluded from the study as they were under the age of 18 years; accordingly, 100 patients were included in the analyses. Colonization was detected in 96 (96%) patients, with 16 (16%) having colonization before infection, whereas 4 patients developed invasive infection without prior colonization. Candidemia was detected in 16 patients (isolation also from the peritoneal fluid culture in one patient), and four patients were diagnosed with urinary system infections. The rate of developing invasive infections among colonized patients was 16.7%. While the number of patients from whom *C. auris* was isolated from clinical samples was 46 in 2022, it was 103 in 2023. Table 1 demonstrates the demographic and clinical characteristics of the patients. The median age of patients was 43.5 years, and 64 (64%) were from the burn unit. Of the patients, 54 (54%) had co-infections,

**Table 1.** Demographical and clinical characteristics of patients.

Variables	Total (n = 100)
<b>Gender, n (%)</b>	
Male	73 (73)
Female	27 (27)
Age, median (minimum-maximum)	43.5 (18-84)
Clinic, n (%)	
Burn Unit	64 (64)
Intensive care units (Outside of the burn unit)	36 (36)
<b>Comorbid conditions, n (%)</b>	
Diabetes mellitus	15 (15)
Hypertension	15 (15)
Coronary artery disease	12 (12)
Chronic pulmonary disease	7 (7)
Cardiac failure	5 (5)
Reumatological disease	1 (1)
Time from hospital admission to culture positivity (day), median (minimum-maximum)	14 (0-85)
Total hospitalization time (day), median (minimum-maximum)	40 (6-344)
History of surgical operation, n (%)	58 (58)
Previously used antibiotic count, median (minimum-maximum)	2 (0-7)
Number of patients with multiple site colonization, n (%)	38 (39.6)
<b>* Site of body colonization, n (%)</b>	
Inguinal	36 (37.5)
Inguinal + Axillary	26 (27.1)
Axillary	19 (19.8)
Inguinal + Urinary	5 (5.2)
Inguinal + Ear + Axillary	3 (3.1)
Urinary	3 (3.1)
Inguinal + Ear	2 (2.1)
Axillary + Ear	1 (1.04)
Inguinal + Axillary + Ear + Urinary	1 (1.04)
Candida score, median (minimum-maximum)	1 (0-4)
Number of patients with invasive <i>Candida auris</i> infection, n (%)	20 (20)
Number of patients treated for invasive <i>Candida auris</i> infection, n (%)	16 (80)
<b>Antifungal agents used for invasive <i>Candida auris</i> infection, n (%)</b>	
Micafungin	7 (43.8)
Micafungin + Fluconazole	3 (18.8)
Fluconazole	2 (12.5)
Anidulafungin	2 (12.5)
Anidulafungin + Fluconazole	1 (6.3)
Micafungin + Liposomal Amphotericin B	1 (6.3)
Appropriateness of initial antifungal treatment, n (%)	12 (100)
The timing of the antifungal treatment (day), median (minimum-maximum)	3 (0 – 6)
Total duration of antifungal therapy (day), median (minimum-maximum)	20 (1-56)
Blood culture negativity day	6 (3-20)

\*Number of colonized patients = 96.

**Table 2.** Risk factors for the development of invasive *Candida auris* infection.

Variables	Colonized patients n = 80	Infected patients n = 20	p
<b>Sex, n (%)</b>			
Male	61 (76.3)	12 (60)	0.143
Female	19 (23.7)	8 (40)	
Age, median (minimum-maximum)	41 (18-84)	51 (28-78)	<b>0.027</b>
History of surgical operation, n (%)	46 (57.5)	12 (60)	0.839
Multiple site colonization, n (%)	29 (36)	12 (60)	0.053
Time from hospital admission to culture positivity (day), median (minimum-maximum)	13 (0-82)	20.5 (0-85)	0.078
Candida score, median (minimum-maximum)	1 (0-3)	3 (1-4)	<b>&lt; 0.001</b>
<b>Comorbid conditions, n (%)</b>			
Diabetes mellitus	10 (12.5)	5 (25)	0.173
Hypertension	11 (13.8)	4 (20)	0.493
Coronary artery disease	7 (8.8)	5 (25)	0.06
Chronic pulmonary disease	7 (8.8)	0	0.339
Cardiac failure	4 (5)	1 (5)	1
<b>Invasive interventions, n (%)</b>			
Urinary catheter	50 (62.5)	19 (95)	0.005
Central venous catheter	31 (38.8)	18 (90)	<b>&lt; 0.001</b>
Mechanical ventilation	18 (22.5)	7 (35)	0.248
Nasogastric tube	13 (16.3)	9 (45)	<b>0.013</b>
Total parenteral nutrition	2 (2.5)	2 (10)	0.178
<b>Previously used antibiotic count, n (%)</b>			
< 3	54 (67.5)	3 (15)	<b>&lt; 0.001</b>
≥ 3	26 (32.5)	17 (85)	
Antifungal usage before <i>Candida auris</i> isolation, n (%)	8 (10)	7 (35)	<b>0.011</b>
<b>Clinic, n (%)</b>			
Burn unit	56 (70)	8 (40)	<b>0.012</b>
Intensive care units (Outside of the burn unit)	74 (30)	12 (60)	

with healthcare-associated pneumonia (n = 19, 19%) and bloodstream infections caused by other agents (n = 11, 11%) being the most common co-infections. Echocardiographic and ophthalmological examinations were performed on only eight patients with candidemia, and none of them had pathological findings.

*Candida* score was statistically significantly higher in infected patients than in colonized patients ( $p < 0.001$ ). The presence of a central venous catheter (SVC) and nasogastric tube (N/G), and previous use of antifungal agents and at least three different antibiotics were higher in infected patients as compared to colonized patients ( $p < 0.05$ ). The number of patients with invasive infection was statistically significantly higher among those who were monitored outside the burn unit ( $p = 0.012$ ). The groups were comparable in terms of the rate of underlying disease (Table 2).

Univariate analysis revealed that age (Odds ratio (OR): 1.032; 95% confidence interval (CI): 1.002-1.062;  $p = 0.034$ ), *Candida* score (OR: 9.127; 95% CI:

3.398-24.512;  $p < 0.001$ ), previous use of antifungal agents (OR: 4.846; 95% CI: 1.498-15.674;  $p = 0.008$ ), number of previously used antibiotics  $\geq 3$  (OR: 11.769; 95% CI: 3.164-43.773;  $p < 0.001$ ), presence of SVC (OR: 14.226; 95% CI: 3.085-65.602;  $p = 0.001$ ) and N/G (OR: 4.217; 95% CI: 1.457-12.202;  $p = 0.008$ ), and being monitored outside the burn unit (OR: 3.500; 95% CI: 1.269-9.652;  $p = 0.015$ ) are the risk factors for invasive *C. auris* infection. A high *Candida* score was found as an independent risk factor (OR: 9.127; 95% CI: 3.398-24.512;  $p < 0.001$ ) (Table 3).

Regarding antifungal susceptibility patterns, 55% of the isolates were resistant to fluconazole, and 100% were resistant to amphotericin B. While none of the isolates was resistant to micafungin, one isolate (5%) was resistant to caspofungin. MIC value for voriconazole was 0.5 in 60% of the isolates, whereas it was 2 in only one isolate (5%) (Table 4).

Of the patients, 14 received echinocandin-based regimens, three received micafungin-fluconazole, and

**Table 3.** Analysis of independent risk factors for the development of invasive *Candida auris* infection.

Variables	Univariate Odds Ratio (95% CI)	p	Multivariate Odds Ratio (95% CI)	p
Age	1.032 (1.002-1.062)	<b>0.034</b>		
<i>Candida</i> score	9.127 (3.398-24.512)	<b>&lt; 0.001</b>	9.127 (3.398-24.512)	<b>&lt; 0.001</b>
*Previously used antibiotic count	11.769 (3.164-43.773)	<b>&lt; 0.001</b>		
**Clinic	3.500 (1.269-9.652)	<b>0.015</b>		
Central venous catheter	14.226 (3.085-65.602)	<b>0.001</b>		
Nazogastric tube	4.217 (1.457-12.202)	<b>0.008</b>		
Previously antifungal usage	4.846 (1.498-15.674)	<b>0.008</b>		

\*< 3 vs  $\geq 3$ , \*\*Burn vs non-burn. CI: Confidence Interval.

**Table 4.** In vitro antifungal susceptibility profile of *Candida auris* isolates and the temporary clinical breakpoints recommended by the CDC.

Antifungal Agent	MIC Range (n = 20)	GM	MIC <sub>50</sub>	MIC <sub>90</sub>	Temporary MIC breakpoints
Fluconazole	8-32	21.1	32	32	≥ 32
Amphotericin B*	8-16	10.32	8	16	≥ 2
Micafungin	0.06 - 0.25	0.08	0.12	0.12	≥ 4
Caspofungin	0.25-8	0.79	0.25	0.25	≥ 2
Voriconazole	0.50-2	1	0.5	1	-
Anidulafungin	-	-	-	-	≥ 4

\* n = 19 for Amphotericin B; MIC: Minimum inhibitory concentration; GM: Geometric mean.

one received micafungin-liposomal amphotericin B combination (Table 1). It was determined that four patients (two with candidemia and two with UTI), who developed mortality before growth in the culture, had not received an antifungal agent. All patients who received treatment were found to have appropriate antifungal treatment regimens based on antifungal susceptibility results. The median day of antifungal treatment initiation was determined as 3 days (minimum: 0, maximum: 6). It was determined that antifungal treatment was started in two patients on the day of culture sample was taken and in two patients on the 6th day. Mortality was detected in 11 (68.8%) of 16 patients who received antifungal therapy. The overall mortality rate was 75% (n = 15) in infected patients.

**Discussion**

*C. auris* poses a serious threat due to misidentification, colonization in human skin and surrounding tissue, and multidrug resistance phenotype [15]. In the present study, we evaluated 100 patients with *C. auris* isolated from the cultures of various specimens, with 20 patients developing invasive infections. Our results indicate that the number of patients with isolated *C. auris* has increased over time. Particularly, periodic increases have been linked to periodical decreases in adherence to infection control measures in the units where the patients with colonization were monitored. In addition, the ability to survive in the environment for a long time and resistance to many disinfectant agents are the contributing factors [16]. The incidence of *C. auris* has increased exponentially, especially in the last 5 years all over the world. While the number of clinical cases reported from the United States between 2019 and 2021 was 3270, it is seen that this number was 2377 in 2022 alone [17,18].

It is known that the risk factors for invasive infections caused by *C. auris* are the same as the risk factors for infections caused by non-auris *Candida* species [19]. Studies in the literature have usually compared *C. auris* and other *Candida* species in terms of risk factors [20-22]. In a single-center cross-sectional study conducted in 2024, only the candidemia patients

caused by *C. auris* were included and 46 patients were evaluated to identify the risk factors, and similar risk factors with other studies were identified [23]. In the literature, there is a limited number of cohort studies investigating the risk factors for invasive infection in patients colonized with *C. auris* as in the present study [12,24,25]. One of these studies investigated the cumulative candidemia incidence and contributing factors in colonized patients and found that 17% of the colonized patients developed candidemia [12]. In our cohort, the rate of developing invasive infection was 16.7%, which is similar to the above-mentioned study. In the same study, continuous renal replacement therapy, respiratory colonization, duration of previous intensive care unit stays, and multisite colonization were higher in the patients with *C. auris* candidemia, with multisite colonization being an independent risk factor for candidemia [12]. According to the results of our study, the rate of multi-site colonization was similar in both groups, and age, prior antifungal use, number of previously used antibiotics being ≥ 3, presence of central venous catheter and nasogastric catheter, and being monitored outside the burn unit were the risk factors for invasive *C. auris* infection, with *Candida* score being an independent risk factor. In the study conducted by Bayona *et al.* with a similar study design, univariate analysis revealed a statistically significantly high *Candida* score. In that study, digestive disease, catheter isolate, and APACHE II score were identified as independent risk factors for candidemia [24]. Garcia-Bustos *et al.* conducted a cohort study and found the rate of developing candidemia in colonized patients to be 18%. They found that total parenteral nutrition, history of surgery, sepsis, prior use of an antifungal agent, presence of SVC and arterial catheter, chronic renal failure, and multifocal colonization are independent risk factors for candidemia [25]. The *Candida* scoring system, which was developed by Leon *et al.*, is being widely used in risky patients monitored in the intensive care units [13]. A linear and significant relationship was identified between increased scores and the incidence of invasive candidiasis. The incidence rate was 2.3, 8.5, 16.8, and 23.6 with scores of < 3, 3, 4, and 5, respectively, and the likelihood of invasive

candidiasis was found to be lower in the patients with *Candida* score < 3.

Patients staying in the burn unit accounted for a great proportion of our study population, and the probability of developing invasive infection was found to be significantly higher among patients following outside the burn unit. We think that strict infection prevention measures implemented due to the outbreak in the burn unit, washing the patients with chlorhexidine although its benefit has not been proven yet, active surveillance to detect colonized patients, and close clinical monitoring might have prevented the development of invasive infection.

Antifungal susceptibility studies revealed that 90% of overall *C. auris* isolates are resistant to fluconazole, 8% are resistant to amphotericin B, and 2% are resistant to echinocandins. According to the data from the CDC, 90% of *C. auris* isolates in the USA are resistant to fluconazole, 30% are resistant to amphotericin B, and < 2% are resistant to echinocandins [26]. Different from the other *Candida* species, *C. auris* shows multidrug resistance (MDR). This was reported by the CDC in 2019 when the CDC listed *C. auris* in the first place among emergency threats for antimicrobial resistance [27].

In the Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, antifungal drugs have no clinical threshold for MIC value specific to *C. auris*. The CDC issued temporary clinical threshold values based on the clinical threshold value specified for *Candida* species that are close relatives of *C. auris* and on the expert opinion. The correlation between microbiological clinical threshold values and clinical outcomes remains unknown [27].

In the present study, 55% of the isolates were resistant to fluconazole and 100% were resistant to amphotericin B. While all isolates were susceptible to micafungin, a single isolate (5%) was resistant to caspofungin. In a study from Türkiye, all the strains were resistant to amphotericin B and susceptible to micafungin, which is similar to the results of the present study [28]. The use of caspofungin is not recommended because, in both CLSI and EUCAST data, there was a high variability in caspofungin MIC values across centers, species, and time, especially when studying *Candida* species. Until this problem is resolved, it is recommended that caspofungin MIC values for *Candida* species should not be studied and reported; instead, micafungin or anidulafungin data should be used [29]. Although there is no clinical threshold for the MIC value of voriconazole, it can be said taking the

clinical thresholds for *C. albicans* as the basis that all isolates are resistant to voriconazole; however, further studies are needed for voriconazole resistance in Türkiye. Using the VITEK 2 automated system as the reference method in detecting antifungal susceptibility of the strains instead of the fluid microdilution method is the limitation of the present study. In addition, a genotypic examination of the strains was not performed and it could not be identified which clade it belonged to or close to. Recent studies suggest that isolates from different geographical clades are mixed in a single location and the isolation area alone may not indicate the clade status of an isolate [30]. Most of the Clade 1 (South Asia) isolates are resistant to fluconazole, with varying resistance to amphotericin B and acquired resistance to echinocandins. Nearly half of the Clade 4 (South America) isolates are resistant to fluconazole but show varying resistance to amphotericin B. Clade 3 (South Africa) isolates are usually resistant to azoles. Clade 2 (East Asia) isolates are susceptible to all antifungal agents, they do not lead to invasive infection or outbreaks, but cause colonization only [31]. Finally, a study published in July 2024 reported that there is a sixth clade and that it is susceptible to all antifungal agents [32]. In the present study, all of the strains were resistant to amphotericin B and more than half were resistant to fluconazole. Although the fluconazole susceptibility profile was similar to that of Clade 4, resistance to amphotericin B was not consistent with any clade. Because of the limited number of strains in our study, multicenter studies with larger sample sizes and detailed genotypic analysis are required to identify the general resistance rates of *C. auris* strains in Türkiye. In addition, the fact that susceptibility profiles of *C. auris* isolates obtained from the patients were quite similar supports the presence of a nosocomial outbreak.

Although *C. auris*-associated mortality rate is similar to that of non-*auris Candida* species in the literature, it is important because it causes outbreaks and leads to mortality in high-risk patients [8,33,34]. In our cohort, while the mortality rate in the patients who developed invasive infection was 75%, it was 68.8% in the patients who received antifungal therapy. Due to late diagnosis, mortality was detected in four patients before treatment. The mortality rate in the present study is higher than previously reported mortality rates. Simon *et al.* reported a 30-day mortality rate of 30.1% in the patients with *C. auris* candidemia and found no difference with non-*auris Candida* species in terms of mortality [33]. When our patient population was evaluated together with antifungal susceptibility results,

it was seen that all patients were started on treatment with appropriate antifungal agents. However, when the time of starting antifungal agents is evaluated, the prolongation of the period up to 6 days is seen as a factor that affects mortality. At the same time, the low rate of echocardiographic and ophthalmological examinations performed for metastatic focus may have affected the detection of septic complications and contributed to the high mortality rate. Also, the presence of concurrent bacterial co-infections in patients and the fact that our patient population consisted of critically ill patients followed in the ICU may have affected mortality.

The limitations of the present study include retrospective design, inability to evaluate treatment response since antifungal therapies were not arranged according to certain standards, and inability to genotypic analysis of the strains.

## Conclusions

*C. auris* is a yeast of critical importance as it leads to nosocomial outbreaks, it is difficult to control the spread of *C. auris* in case of an outbreak, and it is associated with high mortality rates in high-risk patients. In the present study, the mortality rate was 75%, supporting that the mortality is higher than other *Candida* species. Detection of colonized patients and identification of the risk factors for invasive infection in colonized patients would prevent mortality by allowing early initiation of antifungal treatment. Particularly, it seems appropriate to use the *Candida* score for this purpose. The fact that all of the strains were resistant to amphotericin B, which does not match with any clade, indicates the necessity of genotypic analysis. Our results need to be verified in further studies that will be conducted with a larger patient population and include genotyping analysis.

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## Conflict of interests

No conflict of interests is declared.

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