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ORIGINAL RESEARCH

Clinical Characteristics, Antifungal Susceptibility, and Prognosis of *Candidozyma auris* Infections: A Single-Center Retrospective Study*

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ABSTRACT

Candidozyma auris (formerly *Candida auris*) is an emerging multidrug-resistant fungal pathogen associated with healthcare-associated infections and high mortality. This study evaluated the clinical characteristics, antifungal susceptibility profiles, and risk factors for candidemia and mortality in patients with *C. auris* isolation. This retrospective cohort study included patients with at least one clinical specimen positive for *C. auris* between May 2023 and June 2025. Patients were classified as having colonization or infection based on clinical and microbiological criteria. Trend analysis evaluated changes across colonization, non-bloodstream infection, and candidemia, and risk factors for candidemia and mortality were assessed using Firth penalized logistic regression. Forty-nine patients were included (median age, 67 years), of whom 63.3% were in the intensive care unit at the time of isolation. Colonization and infection were identified in 55.1% and 44.9% of patients, respectively, with candidemia being the most common presentation (68.2% of infections). The frequencies of intensive care unit stay, central venous catheter use, and total parenteral nutrition increased significantly from colonization to candidemia (p for trend <0.05). In multivariable analysis, intensive care unit stay (aOR 4.2, p=0.03) and total parenteral nutrition (aOR 6.9, p=0.04) were independently associated with candidemia. All isolates were resistant to fluconazole, echinocandins showed high in vitro activity, and amphotericin B MICs were ≥2 µg/mL in 64.3% of isolates. Overall, in-hospital mortality was 46.9%. Charlson Comorbidity Index, total parenteral nutrition, and clinically significant infection were independently associated with in-hospital mortality.

Key Words: *Candida auris.* Candidemia. Drug resistance. Fungal. Intensive care units. Total parenteral nutrition.

***Candidozyma auris* Enfeksiyonlarının Klinik Özellikleri, Antifungal Duyarlılığı ve Prognozu: Tek Merkezli Retrospektif Çalışma**

ÖZET

Candidozyma auris (eski adıyla *Candida auris*), sağlık hizmetiyle ilişkili enfeksiyonlar ve yüksek mortalite ile ilişkili, çok ilaca dirençli, yeni ortaya çıkan bir fungal patojendir. Bu çalışmada, *C. auris* izole edilen hastalarda klinik özelliklerin, antifungal duyarlılık profillerinin ve kandidemi ile mortalite için risk faktörlerinin değerlendirilmesi amaçlanmıştır. Bu retrospektif kohort çalışmasına, Mayıs 2023 ile Haziran 2025 tarihleri arasında en az bir klinik örneğinde *C. auris* saptanan hastalar dahil edilmiştir. Hastalar, klinik ve mikrobiyolojik kriterlere göre kolonizasyon veya enfeksiyon olarak sınıflandırılmıştır. Kolonizasyon, kan dolaşımı dışı enfeksiyon ve kandidemi arasındaki değişimleri değerlendirmek amacıyla trend analizi ile değerlendirilmiş; kandidemi ve hastane içi mortalite ile ilişkili risk faktörleri Firth cezalandırılmış lojistik regresyon analizi kullanılarak incelenmiştir. Çalışmaya medyan yaşı 67 olan 49 hasta dahil edilmiş olup, izolasyon sırasında hastaların %63,3'ü yoğun bakım ünitesinde izlenmekteydi. Hastaların %55,1'inde kolonizasyon, %44,9'unda ise enfeksiyon saptanmış olup, enfeksiyon tablosu içinde en sık kandidemi (%68,2) saptanmıştır. Yoğun bakım ünitesinde yatış, santral venöz kateter varlığı ve total parenteral nütrisyon kullanım sıklığı kolonizasyondan kandidemiye doğru anlamlı olarak artış göstermiştir (trend için p<0,05). Çok değişkenli analizde, yoğun bakım ünitesinde yatış (düzeltilmiş OR [aOR] 4,2; p=0,03) ve total parenteral nütrisyon (aOR 6,9; p=0,04) kandidemi ile bağımsız olarak ilişkili bulunmuştur. Tüm izolatlar flukonazole dirençli bulunurken, ekinokandinler yüksek in vitro aktivite göstermiş, izolatların %64,3'ünde amfoterisin B için minimum inhibitör konsantrasyonu (MİK) ≥2 µg/mL olarak saptanmıştır. Hastane içi mortalite %46,9 olarak bulunmuştur. Charlson Komorbidite İndeksi, total parenteral nütrisyon ve klinik olarak anlamlı enfeksiyon, hastane içi mortalite ile bağımsız olarak ilişkili bulunmuştur.

Anahtar Sözcükler: *Candida auris.* Kandidemi. Antifungal ilaç direnci. Yoğun bakım ünitesi. Total parenteral beslenme.

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Candidozyma auris (formerly known as *Candida auris*) has increasingly been reported in recent years as an important cause of healthcare-associated infections[1]. Due to its ability to cause hospital outbreaks, persist on skin and environmental surfaces for prolonged periods, and lead to invasive infections, it has become a significant public health concern[2,3]. The fact that colonization does not always result in infection complicates clinical management[2,4]. In addition, its high level of azole resistance and variable resistance patterns to other antifungal agents represent major challenges that limit treatment options[1,5,6].

Similar to global trends, healthcare-associated *C. auris* infections, including outbreaks, have also been reported in our country[2,7,8]. In this study, we aimed to present our clinical experience with *C. auris* and to evaluate the clinical characteristics, infection types, antifungal susceptibility profiles, and clinical outcomes of patients with *C. auris* isolation in our hospital.

Materıals and Methods

This study was designed as a retrospective observational cohort study. Our hospital is a 900-bed tertiary care center serving the South Marmara region and frequently receiving patient referrals from neighboring provinces. In our center, when *C. auris* is detected in any clinical specimen, in accordance with national guideline, screening samples are obtained from body surfaces (inguinal and axillary regions) of the patient and, when necessary, from nearby patients to assess colonization within 24 hours of detection[8].

Patients who were followed in our hospital between May 2023 (index case) and June 2025 and had at least one clinical specimen positive for *C. auris* were included in the study.

When multiple samples from the same patient were positive, isolates from different anatomical sites were included; however, in cases of repeated isolation from the same site, only the first isolate was considered.

When *Candida* growth was detected in clinical samples, isolates were cultured on CHROMagar™ Candida (Becton Dickinson), and colonies were identified using MALDI-TOF MS (Microflex LT/SH, Bruker Daltonics, Bremen, Germany). Antifungal susceptibility testing for fluconazole, amphotericin B, anidulafungin, and micafungin was performed using the CLSI M27-A3 reference broth microdilution method[9].

Demographic characteristics, clinical data, invasive procedures, and treatment information were obtained from the electronic medical record system.

Infection types (candidemia, urinary tract infection, pneumonia, intra-abdominal, and surgical site infections) were defined based on the standard clinical and microbiological criteria of the Centers for Disease Control and Prevention / National Healthcare Safety Network (CDC/NHSN) guidelines[10]. Patients who met these objective criteria and exhibited compatible clinical, laboratory, and, where applicable, radiological findings were classified as having *infection*, whereas the isolation of *C. auris* from surveillance or clinical specimens in the absence of active clinical signs or CDC/NHSN diagnostic criteria for infection was classified as *colonization.* Accordingly, urinary tract infection was diagnosed only when CDC/NHSN criteria were fulfilled in the presence of compatible clinical findings, and pneumonia was diagnosed only when CDC/NHSN pneumonia criteria were met together with compatible clinical and radiological findings.

The primary outcome was defined as in-hospital mortality, and the secondary outcome was 30-day mortality. Information on infection control measures implemented during the study period was obtained from the Infection Control Committee.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous variables were presented as median (interquartile range [IQR]), and categorical variables as frequencies and percentages. Comparisons between two groups were performed using the Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test, as appropriate, for categorical

variables. Comparisons among three independent groups (colonization, non-bloodstream infection, and candidemia) were performed using the Kruskal–Wallis test. The association between colonization and subsequent candidemia was evaluated only among patients who underwent screening, using Fisher's exact test. Trend analysis was performed to evaluate changes across the ordered clinical categories (colonization, non-bloodstream infection, and candidemia). For categorical variables, the chi-square test for trend (linear-by-linear association) was used, and *p* for trend values were calculated. For continuous variables, comparisons among the three clinical groups were performed using the Kruskal–Wallis test. Risk factors for candidemia and in-hospital mortality were first assessed using univariate logistic regression analysis. Variables with a *p*-value <0.10 in the univariate analysis or considered clinically relevant were entered into separate multivariable Firth penalized logistic regression models. Because of the limited number of outcome events, the number of variables included in each multivariable model was restricted to minimize model overfitting. Firth penalized logistic regression was selected to reduce small-sample bias and separation associated with conventional logistic regression. Odds ratios (ORs) and adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs) were reported, as appropriate. All statistical tests were two-sided, and a *p*-value <0.05 was considered statistically significant.

Ethics Approval

Ethical approval was obtained from the Bursa Uludağ University Non-Interventional Clinical Research Ethics Committee (Decision No: 2025/789/14-8). Because of the retrospective nature of the study, the requirement for written informed consent was waived by the Bursa Uludağ University Non-Interventional Clinical Research Ethics Committee.

Results

The first case of *C. auris* in our center was identified in May 2023 from blood culture and conjunctival swab specimens. One week later, another case was detected in blood cultures of a patient hospitalized on a different floor within the same department. Immediately following case identification, infection control measures were implemented, including contact precautions, restriction of healthcare personnel contact, minimizing caregiver changes, informing all consulting departments, and ensuring appropriate environmental cleaning. After routine cleaning with water and detergent, disinfection was performed using a 1000 ppm chlorine solution. Hand hygiene compliance was reinforced through repeated training and increased monitoring. Following these initial cases, no new cases were detected for three months. However, starting from 2024, a rapid increase and clinical clustering of patients with C. *auris* isolation were observed, particularly in intensive care units. Although these findings may reflect possible nosocomial transmission, a definitive outbreak or clonal spread could not be conclusively demonstrated due to the lack of molecular typing.

A total of 49 patients with *C. auris* isolation between May 2023 and June 2025 were included. The median age was 67 years (range: 24–91), and 51% were female. At the time of isolation, 63.3% (n=31) were in intensive care units and 36.7% (n=18) were in general wards. Healthcare-associated risk factors were present in the majority of patients. The most common factors were central venous catheter presence (79.6%), prior antibiotic use (95.9%), and hospitalization within the previous three months (67.3%). Among the 33 patients with a history of hospitalization within the last three months, 14 (42.4%) had been hospitalized in our institution. Immunosuppressive therapy was present in 28.6% of patients. Regarding surgical history, 44.9% had undergone intra-abdominal surgery and 20.4% had a history of surgical debridement for pressure ulcers. The general demographic and clinical characteristics of the patients are presented in Table I.

Table I. Demographic and Clinical Characteristics (n=49)

Variables	n (%) or Median (IQR) [Min–Max]
Female, n (%)	25 (51)
Age (year), median (IQR) [Min-Max]	67 (55–75) [24–91]
Presence of comorbidity, n (%)	44 (89.8)
Charlson Comorbidity Index median (IQR) [Min-Max]	4 (2–6) [0–16]
History of immunosuppressive therapy, n (%)	14 (28.6)
History of intra-abdominal surgery, n (%)	22 (44.9)
History of surgical debridement, n (%)	10 (20.4)
Hospitalization within last 3 months, n (%)	33 (67.3)
Central venous catheter, n (%)	39 (79.6)
Total parenteral nutrition, n (%)	8 (16.3)
Prior antibiotic use, n (%)	47 (95.9)
Prior antifungal use, n (%)	28 (57.1)
ICU stay at time of isolation, n (%)	31 (63.3)
Ward admission at time of isolation, n (%)	18 (36.7)

IQR: Interquartile Range, ICU: Intensive Care Unit

At least one comorbidity was present in 89.8% of patients, with a median Charlson Comorbidity Index (CCI) of 4. The most frequent comorbidities were

hypertension (n=22, 44.9%) and diabetes mellitus (n=18, 36.7%), followed by solid organ malignancy (n=14, 28.6%), congestive heart failure (n=11, 22.4%), chronic renal failure (n=6, 12.2%), neurological disease (n=3, 6.1%), and hematological malignancy (n=2, 4.1%). Other less frequent comorbidities included chronic liver disease, rheumatological disease, history of solid organ transplantation, and chronic lung disease (each present in 1 patient, 2.0%).

The distribution of clinical specimens with *C. auris* growth is presented in Table II. During the study period, a total of 44 patients underwent screening, while five patients could not undergo screening because they died or were discharged before surveillance cultures could be obtained. Among the screened patients, skin swabs from 26 patients tested positive for *C. auris* growth.

Table II. Distribution of *C. auris* Isolates by Specimen Type*

Source	n (%)*
Skin swab	26 (53.1)
Blood	15 (30.6)
Urine	11 (22.4)
Wound	12 (24.5)
Catheter culture	9 (18.4)
Respiratory tract	7 (14.3)
Surgical specimen	6 (12.2)
Conjunctival swab	1 (2.0)

*Some patients had isolates from multiple specimen types.

*Percentages sum to >100% as some patients had positive cultures from multiple anatomical sites.

Overall, *C. auris* isolation was classified as colonization in 27 patients (55.1%) and as clinically significant infection in 22 patients (44.9%). Among infections, candidemia was the most common presentation (n=15, 68.2%). Other infection types included urinary tract infections (n=5, 22.7%), pneumonia (n=2, 9.1%), surgical site infections (n=2, 9.1%), and intra-abdominal infections (n=1, 4.5%). In some patients, multiple infection foci were observed. Candidemia was present concomitantly in two of five patients with urinary tract infection and in one patient with intra-abdominal infection. Additionally, *C. auris* was isolated from a catheter culture in a patient diagnosed with pneumonia, and in another patient with conjunctival isolation, candidemia was also present. Patients were categorized into three clinical groups: colonization (n=27), non-bloodstream infection (n=7), and candidemia (n=15). Trend analysis was performed to evaluate the stepwise changes in clinical variables across these groups. Significant differences were observed among the groups in terms of intensive care unit stay and central venous catheter presence (p=0.006 and p=0.03, respectively). Moreover, both variables demonstrated a significant increasing trend from colonization to candidemia (p for trend=0.01 and p for trend=0.04, respectively). Total parenteral nutrition was observed only in the candidemia group and showed a significant difference across groups (p<0.001), along with a marked increasing trend (p for trend <0.001). Although the Charlson Comorbidity Index increased from colonization to candidemia, this trend did not reach statistical significance (p=0.09; p for trend=0.07). No significant differences or trends were observed for other variables (Table III).

Table III. Comparison of Clinical Presentations Groups and Trend Analysis

Variable	Colonization (n=27)	Non-bloodstream infection (n=7)	Candidemia (n=15)	p	p (trend)
Age, median (years)	65	66	69	0.41	0.38
Female, n (%)	14 (51.9)	3 (42.9)	8 (53.3)	0.89	0.92
CCI score, median	3	4	5	0.09	0.07
Prior hospitalization (last 3 months), n (%)	17 (63.0)	5 (71.4)	11 (73.3)	0.72	0.65
ICU stay, n (%)	12 (44.4)	4 (57.1)	15 (100)	**0.006**	**0.01**
CVC presence, n (%)	17 (70.4)	7 (100)	15 (100)	**0.03**	**0.04**
TPN administration, n (%)	0	0	8 (53.3)	**<0.001**	**<0.001**
Prior antibiotic use, n (%)	26 (96.3)	7 (100)	14 (93.3)	0.81	0.77
Prior antifungal use, n (%)	13 (48.1)	5 (71.4)	10 (66.7)	0.472	0.28
Immunosuppressio n, n (%)	6 (22.2)	2 (28.6)	6 (40.0)	0.29	0.24
Intra-abdominal surgery, n (%)	10 (37.0)	3 (42.9)	9 (60.0)	0.17	0.15

CCI: Charlson Comorbidity Index, CVC: Central Venous Catheter, TPN: Total Parenteral Nutrition, ICU: Intensive Care Unit.

To evaluate factors associated with infection and candidemia, two complementary analyses were performed: colonization versus infection (including candidemia and non-bloodstream infection), and candidemia versus non-candidemia. Clinical and demographic characteristics were compared between these groups, and potential risk factors were evaluated using univariate logistic regression analysis (Table IV). Intensive care unit stay and total parenteral nutrition were found to be significantly associated

Table IV. Univariate Risk Factors for Infection and Candidemia in Patients with *Candidozyma auris* Isolation

Variable	Colonization (n=27)	Infection (n=22)	OR (95% CI)	*p*	No candidemia (n=34)	Candidemia (n=15)	OR (Candidemia)	*p*
Age, median (years)	65	68	—	0.32	65	69	—	0.21
Female, n (%)	14 (51.9)	11 (50.0)	0.93 (0.3 -2.9)	0.89	17 (50.0)	8 (53.3)	1.14 (0.3 - 3.8)	0.83
CCI, median	3	5	—	**0.03**	3	5	—	0.08
Hospitalization within last 3 months, n (%)	17 (63.0)	16 (72.7)	1.57 (0.5 -5.3)	0.48	22 (64.7)	11 (73.3)	1.50 (0.4 - 5.7)	0.57
ICU stay, n (%)	12 (44.4%)	**19 (86.4%)**	**7.91 (1.94 -32.3)**	**0.003**	16 (47.1)	**15 (100)**	**17.10 (1.45-201.20)**	**0.001**
CVC presence, n (%)	17 (63.0)	**22 (100)**	-	**0.002**	24 (70.6)	**15 (100)**	—	**0.020**
TPN administration, n (%)	0 (0)	**8 (36.4)**	**15.42 (1.81-131.2**	**<0.001**	0	**8 (53.3)**	**21.40 (2.34-195.40)**	**<0.001**
Prior antibiotic use, n (%)	26 (96.3)	21 (95.5)	0.81 (0.05-13.56)	0.87	33 (97.1)	14 (93.3)	0.42 (0.02-7.42)	0.556
Prior antifungal use, n (%)	13 (48.1)	15 (68.2)	2.31 (0.71 - 7.52)	0.165	18 (52.9)	10 (66.7)	1.78 (0.5-6.32)	0.374
Immunosuppression, n (%)	6 (22.2)	8 (36.4)	2.0 (0.6-6.9)	0.27	8 (23.5)	6 (40.0)	2.17 (0.6-7.8)	0.25
History of intra-abdominal surgery, n (%)	10 (37.0)	12 (54.5)	2.04 (0.6-6.5)	0.21	13 (38.2)	9 (60.0)	2.42 (0.7-8.5)	0.16
Surgical debridement, n (%)	3 (11.1)	7 (31.8)	3.73 (0.8-17.3)	0.09	5 (14.7)	5 (33.3)	2.90 (0.7-12.4)	0.14

OR (Infection): Odds ratio for infection (compared to colonization).
OR (Candidemia): Odds ratio for candidemia (compared to non-candidemia).
CCI: Charlson Comorbidity Index, TPN: Total Parenteral Nutrition, CVC: Central Venous Catheter, ICU: Intensive Care Unit.

*High OR values and wide confidence intervals for TPN and ICU stay reflect zero cell counts in reference subgroups, which were adjusted using Firth's penalized logistic regression.

with both infection and candidemia development. The Charlson Comorbidity Index was significantly associated with infection (p=0.03) but showed borderline significance for candidemia (p=0.08). Due to marked separation between groups for variables such as central venous catheter presence and total parenteral nutrition, some odds ratios could not be reliably estimated. Therefore, multivariate analysis for candidemia was performed using Firth penalized logistic regression. In this model, total parenteral nutrition use (adjusted OR 6.9, p=0.04) and intensive care unit stay (adjusted OR 4.2, p=0.03) were identified as independent risk factors for candidemia, whereas the Charlson Comorbidity Index was not independently associated (adjusted OR 1.2, p=0.14) (Table V).

Antifungal susceptibility profiles of 14 *C. auris* isolates obtained from blood cultures were evaluated, except for one patient, based on tentative breakpoints recommended by the CLSI[9] (Table VI). All isolates demonstrated high MIC values for fluconazole, corresponding to a resistance rate of 100%. Although low MIC values were observed for itraconazole, posaconazole, and voriconazole, clinical susceptibility could not be inferred because clinical breakpoints have not been established.

Table V. Multivariate Analysis for Predictors of Candidemia

Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval (CI)	*p*-value
Intensive care unit (ICU) Stay	**4.20**	**1.22 – 14.81**	**0.030**
Total parenteral nutrition (TPN) Use	**6.90**	**1.41 – 33.92**	**0.040**
Charlson comorbidity index (CCI)	1.20	0.91 – 1.58	0.140

*Multivariate analysis was executed using Firth's penalized logistic regression to eliminate small-sample bias and adjust for parameters exhibiting complete separation (zero cell counts in reference groups) in the baseline data. Variables with a p-value <0.10 in the univariate analysis and those considered clinically significant were included in the final multivariate model.

Table VI. Antifungal Susceptibility Profiles of Bloodstream *Candidozyma auris* Isolates (MIC, µg/mL) (n=14)

Isolate no	Fluconazole	Itraconazole	Posaconazole	Voriconazole	Anidulafungin	Micafungin	Amphotericin B
1	32	0.06	<0.05	0.125	0.25	ND	8
2	>64	>16	>16	0.25	0.5	ND	4
3	>64	≤0.03	≤0.03	0.125	0.06	≤0.015	4
4	>64	0.06	0.25	1	0.25	0.125	1
5	>64	0.125	0.125	1	0.25	0.125	1
6	>64	0.125	0.25	0.5	0.125	0.125	1
7	>64	0.06	≤0.03	0.25	0.06	0.125	4
8	32	≤0.03	≤0.03	0.25	0.25	0.125	4
9	>64	≤0.03	≤0.03	0.25	0.25	0.5	2
10	≥64	≥16	≥16	≥16	0.5	1	4
11	>64	0.125	0.06	0.06	2	0.25	1
12	32	0.06	≤0.03	0.25	0.25	0.03	4
13	>64	0.125	0.06	0.5	0.5	0.06	0.5
14	32	0.03	0.03	0.25	4	0.03	2

Values represent Minimum Inhibitory Concentrations (MIC) in µg/mL. ND: Not Determined.

Tentative CDC breakpoints used to define resistance were as follows: fluconazole ≥32 µg/mL, amphotericin B ≥2 µg/mL, anidulafungin ≥4 µg/mL, and micafungin ≥4 µg/mL. No interpretive breakpoints are currently available for itraconazole, posaconazole, or voriconazole; therefore, MIC values for these agents are presented descriptively.

For amphotericin B, high MIC values (≥2 µg/mL) were observed in 9 isolates (64.3%). Among echinocandins, resistance to anidulafungin was detected in only one isolate (7.14%), whereas, excluding two isolates for which micafungin susceptibility was not determined, all remaining isolates were susceptible to micafungin (100%).

The overall mortality rate was 46.9% (n=23). Among 40 patients with available follow-up data, the 30-day mortality rate was 37.2% (n=16), and the 90-day mortality rate was 51.2% (n=21). Mortality was higher in patients with clinically significant infection (68.2%, n=15) compared to those with colonization (29.6%, n=8). In univariate analysis, Charlson Comorbidity Index, intensive care unit stay, total parenteral nutrition use, immunosuppression, clinically significant infection, and presence of candidemia were associated with mortality. In multivariate analysis, Charlson Comorbidity Index (adjusted OR 1.35, p=0.04), total parenteral nutrition use (adjusted OR 6.9, p=0.02), and clinically significant infection (adjusted OR 3.8, p = 0.048) were identified as independent risk factors for mortality (Table VII).

Table VII. Risk Factors for In-Hospital Mortality: Univariate and Multivariate Analysis

Univariate Analysis		
Variable	**OR (95% CI)**	***p*-value**
CCI	1.48 (1.12-1.96)	**0.006**
ICU stay	3.60 (1.10 – 11.8)	**0.040**
TPN	10.50 (1.98 – 55.6)	**0.003**
Immunosuppression	4.30 (1.15 – 16.1)	**0.030**
Clinically significant infection	5.10 (1.47 – 17.7)	**0.010**
Candidemia	3.10 (0.95 – 10.1)	**0.050**
Multivariate Analysis		
Variable	**aOR (95% CI)**	***p***
CCI	1.35 (1.01 – 1.81)	**0.040**
TPN	6.90 (1.34 – 35.61)	**0.020**
Clinically significant infection	3.80 (1.02 – 14.12)	**0.048**

CCI: Charlson Comorbidity Index; ICU: Intensive Care Unit; TPN: Total parenteral nutrition OR: Odds Ratio; aOR: Adjusted Odds Ratio; CI: Confidence Interval.

Variables with $p < 0.10$ in univariate analysis were included in the multivariate model.

Multivariate analysis was performed using Firth penalized logistic regression due to the limited number of events.

Among the 15 patients with candidemia, central venous catheters were removed in 11 patients, while they were left in place in 4 patients. The mortality rate was 36.4% in patients whose catheters were removed. When analyzed according to timing, mortality was 14.3% in patients whose catheters were removed within ≤72 hours, compared to 75% in those with delayed removal or no removal. Although this difference did not reach statistical significance, early catheter removal showed a clear trend toward reduced mortality.

Discussion and Conclusion

Candidozyma auris has recently emerged as an important cause of healthcare-associated infections, particularly in critically ill patients and individuals exposed to invasive procedures[1,2]. In our study, most patients with *C. auris* isolation had underlying diseases, a history of invasive procedures, and healthcare-associated risk factors. The presence of central venous catheters and prior antibiotic use in a substantial proportion of patients is consistent with the healthcare-associated nature of *C. auris* infections.

Most patients were over 60 years of age, which is consistent with the typical risk group reported in the literature[11,12]. The fact that more than half of the isolates were classified as colonization and that the most common specimen type was skin swab indicates that *C. auris* has substantial colonization potential. This is particularly important in terms of hospital transmission and outbreak potential. Indeed, it has been reported that *C. auris* can persist on skin and environmental surfaces for prolonged periods and can be easily transmitted via contact[4,5]. In our study, the higher rate of candidemia development among colonization-positive patients, although not statistically significant, suggests that colonization may be a potential risk indicator for invasive infection. This finding supports the importance of contact precautions and active screening strategies.

Among clinically significant infections, candidemia was the most common presentation in our study, consistent with previous reports[1,6,11]. We observed a stepwise increase in disease severity from colonization to candidemia, accompanied by increasing frequencies of intensive care unit stay, central venous catheter use, and total parenteral nutrition. These findings are consistent with the literature indicating that *C. auris* infections occur more frequently in patients exposed to invasive procedures and those with more severe clinical conditions[1,2,11-14]. Intensive care unit stay and central venous catheter presence were strongly associated with both infection and candidemia. Notably, total parenteral nutrition was observed only in the candidemia group and was identified as an independent risk factor in multivariate analysis.

In addition, total parenteral nutrition was independently associated with in-hospital mortality, suggesting that it may represent a marker of greater clinical complexity and healthcare exposure rather than an isolated causal factor, although the underlying mechanisms cannot be established in this retrospective study. Although the Charlson Comorbidity Index was higher in the infection group, this difference did not reach statistical significance, suggesting that comorbidity burden may also contribute to infection development.

Our antifungal susceptibility results showed that fluconazole resistance is widespread in *C. auris* and that echinocandins remain the most effective agents. These findings are consistent with the existing literature[6,15,16]. Amphotericin B MICs ≥2 µg/mL were observed in 64.3% of isolates, a proportion higher than that reported in previous studies[16-19]. This difference may reflect variations in isolate numbers, study periods, or regional epidemiology. Although the clinical significance of elevated amphotericin B MICs has not been fully established, the high proportion observed in our cohort is noteworthy because amphotericin B remains one of the commonly available treatment options in many centers. These findings support continued local antifungal susceptibility surveillance and are consistent with current recommendations favoring echinocandins as first-line therapy whenever appropriate. Although resistance to echinocandins was low, increasing reports of resistance in the literature necessitate cautious use of these agents[17]. In contrast, despite generally low MIC values for azole antifungals, the absence of established clinical breakpoints limits interpretation, and previous studies have shown that low MICs do not necessarily predict favorable clinical outcomes[20]. Finally, the relatively small number of isolates and the lack of molecular resistance analysis should be considered when interpreting our susceptibility data. Nevertheless, our findings provide valuable real-world information on local antifungal susceptibility patterns.

The overall mortality rate in our study was 46.9%, consistent with rates reported in the literature[1,6,11,14]. Higher mortality among patients with clinically significant infection underscores the importance of distinguishing colonization from infection in routine clinical practice. In multivariable analysis, Charlson Comorbidity Index, total parenteral nutrition use, and clinically significant infection were independently associated with in-hospital mortality, suggesting that both comorbidity burden and disease severity contribute to poor clinical outcomes in this cohort. The association between clinically significant infection and mortality is consistent with the greater severity of invasive disease compared with colonization. However, this finding should be interpreted cautiously given the retrospective design and limited sample size of the study.

Although not statistically significant, early removal of central venous catheters in patients with candidemia showed a trend toward lower mortality. This observation is consistent with current clinical recommendations; however, the present study was not designed to evaluate the independent effect of catheter removal on mortality[21].

In our center, comprehensive infection control measures, including contact precautions, enhanced environmental cleaning with chlorine-based disinfectants, and active surveillance, were implemented following the detection of *C. auris*. However, the increase in the number of cases over time, particularly in intensive care units, may reflect the challenges of controlling transmission of this pathogen in healthcare settings. On the other hand, considering that our institution is a tertiary care center with a high volume of patient referrals, the number of detected cases appears to be relatively limited.

This study has several limitations. First, its single-center and retrospective design limits the generalizability of the findings. The relatively small

sample size may have reduced the statistical power, particularly in subgroup analyses. Another important limitation is the lack of evaluation of molecular resistance mechanisms in antifungal susceptibility testing.

Real-world clinical data on *C. auris* in Türkiye remain scarce, largely limited to isolated case reports, a recent national consensus statement addressing epidemiology, diagnostic standardization, and treatment recommendations,[22] and limited case-control data on candidemia risk factors.[13] Our two-year, single-center cohort complements the existing national literature by describing the clinical spectrum from colonization to non-bloodstream infection and candidemia, together with antifungal susceptibility and mortality outcomes. To our knowledge, represents one of the first real-world clinical cohorts from Türkiye evaluating these features within routine hospital practice.

In conclusion, among patients with C. *auris* isolation, infection and candidemia were associated with intensive care unit stay, total parenteral nutrition use, and greater comorbidity burden. The observed stepwise increase in ICU stay, central venous catheter use, and total parenteral nutrition across colonization, non-bloodstream infection, and candidemia suggests that increasing healthcare exposure accompanies more invasive clinical presentations, although causality cannot be inferred from this retrospective study. These findings highlight the importance of early recognition, infection control measures, and careful management of invasive procedures in high-risk patient groups. Further studies with larger patient cohorts are needed to better define the role of *C. auris* colonization in the development of invasive infections and to guide clinical management.

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