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Clinical Characteristics and trends in *Candida auris* infections: experience from a South Indian Tertiary Care Center

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ABSTRACT

Background: *Candida auris* has emerged globally as a multidrug-resistant pathogen associated with healthcare-associated outbreaks, particularly in intensive care units (ICUs) and neonatal settings[1-4]. Data from South India remain limited, particularly regarding clinical characteristics, neonatal involvement, and antifungal resistance patterns [5,6].

Methods: This prospective observational study was conducted at a tertiary care academic medical center in South India from 2019 to 2023. All patients with laboratory-confirmed *C. auris* isolation from any clinical specimen were included. Duplicate isolates from the same infection episode were excluded unless obtained from different anatomical sites or more than 30 days apart. Species identification was performed using MALDI-TOF mass spectrometry and confirmed by PCR. Clinical data, including demographics, comorbidities, ICU exposure, device use, antifungal therapy, and outcomes, were collected prospectively. Antifungal susceptibility testing was performed using CLSI broth microdilution, and resistance interpreted according to CDC tentative breakpoints.

Results: A total of 121 *C. auris* isolates were recovered from 114 unique patients. Bloodstream isolates accounted for 57.9% (70/121), followed by urine (33.9%), pus (6.6%), and respiratory specimens (1.6%). Neonatal cases comprised 12 isolates and were strongly associated with prematurity, prolonged NICU stay, total parenteral nutrition, and central venous catheter use. High resistance rates were observed for fluconazole (83.5%) and amphotericin B (80.2%). Echinocandin resistance was less frequent (5.8–10.7%). Multidrug resistance was identified in 71.9% of isolates. Compared with candiduria, candidemia was significantly associated with central venous catheterization, longer ICU stay, and echinocandin therapy, whereas urinary catheterization was more common among candiduria cases. 28-day survival rate was 33.3%.

Conclusions: *C. auris* infection in our center was predominantly ICU-associated and characterized by high azole and amphotericin B resistance, substantial multidrug resistance, and significant neonatal involvement. Device exposure and prolonged hospitalization were major risk factors. These findings underscore the need for robust infection control measures, routine susceptibility testing, and echinocandin-based empiric therapy in high-risk settings.

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INTRODUCTION:

Candida auris is an emerging multidrug-resistant fungal pathogen that has become a major global public health concern since its first identification in 2009[1]. It is frequently associated with healthcare-associated outbreaks, particularly in intensive care units (ICUs), and causes invasive infections with reported mortality rates ranging from 30% to 60% [3-5]. Owing to its high transmissibility, environmental persistence, and limited therapeutic options, *C. auris* has been designated an urgent antimicrobial resistance threat by the World Health Organization (WHO) [7].

A key challenge in the management of *C. auris* is its antifungal resistance profile. High levels of azole resistance—approaching 90% in some reports—along with emerging echinocandin resistance, significantly restrict treatment options [8]. In addition, the organism's ability to form biofilms, persist on environmental surfaces, and survive commonly used disinfectants facilitates prolonged transmission within healthcare facilities and complicates infection control efforts [9].

India is recognised as one of the major epicentres of *C. auris* infections, with multiple outbreaks reported from tertiary care hospitals, predominantly involving critically ill ICU patients (10-24). While most published studies focus on candidemia, *C. auris* is also increasingly isolated from urine specimens, raising important questions regarding its clinical significance, risk factors, and outcomes in candiduria [25,26]. Differentiating colonisation from true infection remains challenging, and comparative data examining differences in patient characteristics and healthcare exposures between candidemia and candiduria are limited [27].

Data from South India remain sparse, despite the region's high healthcare burden and tropical climate, which may influence fungal persistence and transmission. Region-specific analyses that explore both invasive and non-invasive *C. auris* infections are essential to better understand the spectrum of disease, identify high-risk patient groups, and guide targeted infection control interventions.
In this study, we conducted a prospective analysis of patients with laboratory-confirmed *Candida auris* infection in a tertiary care centre in South India. We aimed to describe the demographic and clinical profile, comorbidities, healthcare-associated risk factors, antifungal susceptibility patterns, and outcomes of *C. auris* infections, and to compare risk factors and comorbidity profiles between patients with candidemia and those with candiduria. By providing this comparative regional data, the study seeks to inform empirical therapy, infection prevention strategies, and ongoing surveillance efforts in high-burden healthcare settings.

Methods:

Study Design and Setting:
This prospective observational study was conducted at Sri Ramachandra Institute of Higher Education and Research, Chennai, South India, an approximately 1800-bedded tertiary care academic medical center with multiple adult and neonatal intensive care units (ICUs). The study was carried out from January 2019 to December 2023.

Study Population:
All hospitalized patients with laboratory-confirmed isolation of *Candida auris* from any clinical specimen during the study period were eligible for inclusion.

Duplicate isolates from the same infection episode were excluded unless obtained from different anatomical sites or more than 30 days apart.

Data Collection:
Clinical and demographic data were collected using a structured data collection form and supplemented by review of electronic medical records.

Variables collected included:
- Age and sex
- Diagnosis
- Comorbidities
- Length of hospital stay prior to isolation
- Length of ICU stay
- Exposure to medical devices and procedures
- Total parenteral nutrition
- Prior exposure to antibiotics and antifungals
- Antifungal treatment administered
- 28-day Survival

Microbiological Identification:
Clinical specimens were processed according to standard microbiological protocols. Species identification was initially performed using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight mass spectrometry (MALDI-TOF; bioMérieux). Confirmation was performed by polymerase chain reaction (PCR) using *Candida auris*-specific primers standardized and validated in

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our laboratory.

Antifungal Susceptibility Testing:
All isolates underwent antifungal susceptibility testing using the broth microdilution method according to Clinical and Laboratory Standards Institute (CLSI) M27-A3 guidelines.
The following antifungal agents were tested:

- Fluconazole
- Voriconazole
- Posaconazole
- Itraconazole
- Amphotericin B
- Caspofungin
- Micafungin
- Anidulafungin

In the absence of established CLSI clinical breakpoints for *C. auris*, tentative minimum inhibitory concentration (MIC) breakpoints recommended by the Centers for Disease Control and Prevention (CDC) were applied:

- Fluconazole ≥32 µg/mL
- Amphotericin B ≥2 µg/mL
- Caspofungin ≥2 µg/mL
- Micafungin ≥4 µg/mL

For other drugs, comparisons were obtained from standard references. Multidrug resistance (MDR) was defined as resistance to two or more antifungal classes. Quality control testing was performed using reference strains *Candida albicans* ATCC 22019 and *Candida krusei* ATCC 6258 in accordance with CLSI recommendations.

Statistical Analysis:
Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were expressed as frequencies and percentages.

For comparison between candidemia and candiduria, the patients with dual infections were excluded. Analysis was performed using Chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables, as appropriate. A two-tailed p-value <0.05 was considered statistically significant.

Ethical Considerations:
The study protocol was approved by the Institutional Ethics Committee of Sri Ramachandra Institute of Higher Education and Research. Given the observational design and use of routinely collected clinical data, informed consent was waived. Patient confidentiality was strictly maintained throughout the study.

RESULTS:

A total of 121 *Candida auris* isolates were recovered from 114 unique patients during the study period (Table 1). The majority of isolates were obtained from blood (70/121; 57.9%), followed by urine (41/121; 33.9%), pus (8/121; 6.6%), and respiratory specimens (2/121; 1.6%).

Seven patients had *C. auris* isolated from more than one anatomical site during the same admission. Among these, six patients had isolates from both blood and urine, while one patient had isolates originating from blood and pus.

The median age of patients with *Candida auris* infection was 51 years (IQR: 21–60 years). Of the 114 patients, 18 (15.8%) were neonates and young infants aged less than 1 year. The youngest patient was 9 days old. Among neonates, 14 isolates were identified, the majority of which were recovered from bloodstream infections (12/14). These neonates were admitted to the neonatal intensive care unit (NICU) and had underlying risk factors including prematurity, low birth weight, and exposure to invasive devices.

Seventy-six patients (66.7%) were male and 38 (33.3%) were female, yielding a male-to-female ratio of approximately 2:1.

Table 1: Demographic Characteristics, Clinical Risk Factors, and Outcomes Among Patients with *Candida auris* Infection

Parameter	**All Patients (n = 114)**	**Candidemia (n = 64)**	**Candiduria (n = 35)**
Demographics			
Gender	76 M (66.7%), 38 F (33.3%)	42 M (65.6%), 22 F (34.4%)	22 M (62.9%), 13 F (37.1%)
Age (mean ± SD)	55 ± 19	52 ± 18	63 ± 16
APACHE II (mean ± SD)	17.4 ± 7	17.3 ± 9.5	17.4 ± 6.3
Medical admission	81 (71.1%)	47 (73.4%)	23 (65.7%)
Prior LOS, days (median IQR)	11 (4–25)	7 (3–13)	15 (6–35)
Comorbidities	**All**	**Infected**	**Colonized**
COVID-19	35 (30.7%)	20 (31.3%)	10 (28.6%)
Cardiovascular disease	50 (43.9%)	26 (40.6%)	17 (48.6%)
Chronic pulmonary disease	17 (14.9%)	10 (15.6%)	5 (14.3%)
Neuropsychiatric disorder	42 (36.8%)	23 (35.9%)	13 (37.1%)

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Diabetes mellitus	30 (26.3%)	17 (26.6%)	9 (25.7%)
Chronic renal failure	8 (7.0%)	5 (7.8%)	2 (5.7%)
Malignancy	32 (28.1%)	20 (31.3%)	8 (22.9%)
Neutropenia	7 (6.1%)	5 (7.8%)	1 (2.9%)
Immunosuppressant therapy	16 (14.0%)	9 (14.1%)	4 (11.4%)
Cancer chemotherapy	11 (9.6%)	7 (10.9%)	2 (5.7%)
Health care exposure			
Variable	**All**	**Candidemia**	**Candiduria**
Recent hospitalization ≤1 month	30 (26.3%)	19 (29.7%)	8 (22.9%)
Surgery within 30 days	28 (24.6%)	18 (28.1%)	7 (20.0%)
Broad-spectrum antibiotics	80 (70.2%)	49 (76.6%)	24 (68.6%)
Corticosteroid use	46 (40.4%)	28 (43.8%)	11 (31.4%)
Prior antifungal exposure	29 (25.4%)	17 (26.6%)	8 (22.9%)
Days to diagnosis	12 (3–28)	22 (14–48)	4 (1–11)
Device associated			
Device	**All**	**Candidemia**	**Candiduria**
Central venous catheter	73 (64.0%)	50 (78.1%)	17 (48.6%)
Mechanical ventilation	60 (52.6%)	39 (60.9%)	15 (42.9%)
Tracheostomy	27 (23.7%)	15 (23.4%)	9 (25.7%)
Feeding tube	18 (15.8%)	11 (17.2%)	5 (14.3%)
Urinary catheter	69 (60.5%)	28 (43.8%)	30 (85.7%)
Total parenteral nutrition	15 (13.2%)	9 (14.1%)	3 (8.6%)
Hemodialysis	14 (12.3%)	9 (14.1%)	3 (8.6%)
Treatment			
Agent	**All**	**Candidemia**	**Candiduria**
Echinocandin	67 (58.8%)	48 (75.0%)	14 (40.0%)
Fluconazole	19 (16.7%)	5 (7.8%)	12 (34.3%)
Amphotericin B	8 (7.0%)	6 (9.4%)	1 (2.9%)
Outcome			
Variable	**All**	**Candidemia**	**Candiduria**
ICU LOS, days (median IQR)	25 (14–49)	45 (30–85)	18 (10–30)
Time to ICU discharge (mean ± SD)	26 ± 14	33 ± 16	15 ± 9
28-day survival	38 (33.3%)	22 (34.4%)	12 (34.3%)

Data are presented for 114 unique patients. For subgroup comparison, patients with concurrent blood and urine isolates during the same admission were excluded. The comparative analysis therefore includes 64 patients with candidemia and 35 patients with candiduria. Categorical variables are expressed as n (%), and continuous variables as mean ± SD or median (IQR), as appropriate.

Among all 114 patients with *Candida auris* infection, device exposure was observed in almost everyone. Central venous catheterization was present in 73 patients (64.0%), and urinary catheterization in 69 (60.5%). Mechanical ventilation was required in 60 patients (52.6%), and 14 (12.3%) underwent hemodialysis during hospitalization.

Broad-spectrum antibiotic exposure prior to isolation was documented in 80 patients (70.2%), while 29 (25.4%) had prior antifungal exposure. Following the first positive culture, echinocandin therapy was administered in 67 patients (58.8%), fluconazole in 19 (16.7%), and amphotericin B in 8 (7.0%).

The median ICU length of stay for the was 25 days (IQR 14–49). ICU survival was observed in 65 patients (57.0%).

Table 2: Antifungal Susceptibility Profile of *Candida auris* Isolates

Agent	**Blood (n=70)**	**%**	**MIC50**	**MIC90**	**Urine (n=41)**	**%**	**MIC50**	**MIC90**	**Total (n=121)**	**%**	**MIC50**	**MIC90**
Fluconazole	57	81.4	64	256	35	85.4	64	256	101	83.5	64	256
Amphotericin B	52	74.3	8	32	37	90.2	8	32	97	80.2	8	32
Caspofungin	9	12.9	0.5	1	3	7.3	0.5	1	13	10.7	0.5	1
Anidulafungin	5	7.1	1	2	2	4.9	1	2	7	5.8	1	2
Micafungin	6	8.6	1	2	1	2.4	1	2	8	6.6	1	2
MDR	48	68.6	—	—	33	80.5	—	—	87	71.9	—	—

This table summarizes antifungal susceptibility results of 121 Candida auris isolates recovered from blood (n = 70) and urine (n = 41) specimens. Percentages represent the proportion of resistant

isolates based on CDC tentative minimum inhibitory concentration (MIC) breakpoints. MIC_{50} and MIC_{90} denote the minimum inhibitory concentrations (µg/mL) required to inhibit 50% and 90% of isolates, respectively. Multidrug resistance (MDR) was defined as resistance to two or more antifungal classes.

On subgroup comparison between 64 blood isolates and 35 urinary isolates, patients with candidemia were younger than those with candiduria (mean age 53 ± 17 vs. 62 ± 15 years). Prior length of hospital stay was longer among patients with candiduria (median 16 days [IQR 6–36]) compared to candidemia (7 days [IQR 3–14]).

Echinocandin therapy following the first positive culture was significantly more common in candidemia (75.0%) than in candiduria (40.0%) ($p < 0.001$), whereas fluconazole use was more frequent in candiduria (34.3% vs. 7.8%).

Regarding device exposure, central venous catheter use was significantly higher among candidemia patients (78.1% vs. 48.6%, $p = 0.003$), while urinary catheterization was equally prevalent in both the groups.

Candidemia was also associated with prolonged ICU stay (median 45 days [IQR 30–85] vs. 18 days [IQR 10–30], $p = 0.002$) and longer time to ICU discharge following isolation (33 ± 16 vs. 15 ± 9 days, $p < 0.001$). No significant differences were observed in 28-day survival between the two groups. Sepsis was the predominant clinical presentation in bloodstream isolates, while only about half of the urinary isolates were associated with a diagnosis of urinary tract infection.

Eight patients had *Candida auris* isolated from pus specimens. Of these, 5 (62.5%) had recent surgical intervention within 30 days prior to isolation, and 4 (50.0%) had underlying diabetes mellitus. Soft tissue abscesses and bedsores were the most common clinical presentations. Six patients (75.0%) had prior exposure to broad-spectrum antibiotics, and 5 (62.5%) had a central venous catheter in situ at the time of isolation.

Two patients had *C. auris* isolated from respiratory specimens. Both were mechanically ventilated (100%) and admitted to the ICU with severe underlying pulmonary disease and prolonged hospitalization. Each had prior exposure to broad-spectrum antibiotics and central venous catheter placement. In both cases, isolation occurred after more than 10 days of hospitalization.

Fourteen *Candida auris* isolates were identified in neonates, of which 12 (83.3%) were from blood and 2 (16.7%) from pus specimens. The median gestational age was 30 weeks (IQR 28–33), and the median birth weight was 1,250 g (IQR 980–1,620). Eight neonates (66.7%) were preterm (<32 weeks), and 7 (58.3%) had very low birth weight (<1,500 g).

All neonates required NICU admission. The median duration of NICU stay prior to isolation was 21 days (IQR 14–34). Central venous catheterization was present in 11 neonates (91.7%), 9 (75.0%) received total parenteral nutrition and 10 (83.3%) had prior exposure to broad-spectrum antibiotics. Overall survival in the neonatal cohort was 66.7%.

The number of *Candida auris* cases was relatively low during 2020–2021, which may be attributable to heightened infection prevention practices implemented during the COVID-19 pandemic, including enhanced hand hygiene, environmental disinfection, and restricted patient movement. A marked increase in cases was observed in 2023. Notably, only 6 of the 114 patients (5.3%) had documented COVID-19 infection, indicating that the surge in C. *auris* cases was unlikely to be directly driven by active SARS-CoV-2 infection in that time period.

Among 121 Candida auris isolates (70 blood and 41 urine), resistance to fluconazole was high, observed in 101 isolates (83.5%), including 81.4% of blood and 85.4% of urine isolates. Amphotericin B resistance was detected in 97 isolates (80.2%), with higher resistance among urine isolates (90.2%) compared to blood isolates (74.3%). (Table 2)

In contrast, resistance to echinocandins was uncommon. Caspofungin resistance was identified in 13 isolates (10.7%), while anidulafungin and micafungin resistance were observed in 5.8% and 6.6% of isolates, respectively.

Overall, multidrug resistance was present in 87 isolates (71.9%), slightly more frequent among urinary isolates than blood isolates.

DISCUSSION:

In this single-center series we describe 114 unique patients (121 isolates) of *Candida auris* infection with a mixed-age cohort and a marked ICU/device-associated phenotype. Bloodstream infections comprised the largest proportion of isolates (70/121), urine was the second most common source (41/121), and resistance to first-line azoles and amphotericin B was high while echinocandin resistance remained relatively infrequent.

The temporal pattern in our dataset—low case counts during 2020–21 with a clear rise in 2022–

23—mirrors patterns described elsewhere where pandemic-era infection-control measures temporarily altered nosocomial transmission dynamics and case detection, followed by resurgence as restrictions relaxed and hospital pressures changed. Large surveillance series from the United States show rapidly increasing clinical isolate volumes in 2022–2023, underscoring a broader increase in reported *C. auris* activity [28].

Critically ill, device-exposed patients dominated this study—central venous catheters, urinary catheters, prolonged mechanical ventilation, and prior broad-spectrum antibiotic exposure were frequent. These features are consistent with global outbreak reports that identify prolonged ICU stay and invasive devices as the principal drivers of acquisition and invasive disease [23]. Neonatal cases in our cohort recapitulate the risk constellation reported in neonatal series: prematurity, very low birth weight, central lines and total parenteral nutrition are repeatedly implicated as predisposing factors and were highly prevalent in our neonatal group concordant with the literature [29,30].

Antifungal susceptibility patterns in our isolates showed very high fluconazole and amphotericin B resistance and relatively low but non-negligible echinocandin resistance; overall multidrug resistance (MDR) was common. These findings align with global summaries that report very high azole resistance (≈80–95%), variable amphotericin B resistance by region, and low but emerging echinocandin resistance—important because echinocandins are the recommended first-line therapy for invasive *C. auris*.[31]

Clinically, the high rates of azole and polyene resistance in our isolates reinforce current recommendations to initiate echinocandin therapy for suspected invasive *C. auris* and to perform susceptibility testing to guide escalation or switch (e.g., amphotericin B formulations or combination therapy) when echinocandin resistance or treatment failure is documented. The higher amphotericin-B resistance among urine isolates in our series emphasizes the importance of antifungal susceptibility results for non-blood isolates.

Neonatal mortality in published literature is substantial (pooled mortality ~40–45%), and our neonatal survival (8/12, 66.7% survival) is within the range of published series but on the more favorable side—possibly reflecting early recognition, aggressive supportive care, or small sample-size variation.

Compared with large national surveillance series and multi-center outbreak reports, our core messages are consistent: (1) *C. auris* has become a frequent ICU-associated pathogen where it is established; (2) antifungal resistance to azoles is pervasive and polyene resistance is regionally variable; (3) echinocandin resistance, while still uncommon, is being documented regularly—necessitating vigilance. Region-specific differences in amphotericin B resistance and the frequency of echinocandin resistance emphasize the importance of antifungal susceptibility testing to inform therapy.

The high device burden and frequent colonization/infection of skin and wounds support aggressive IPC measures: patient contact precautions, dedicated equipment, active environmental cleaning with agents effective against *C. auris* and targeted screening during outbreaks. Published outbreak-control reports emphasize rapid identification, cohorting, and environmental decontamination as keys to containment.

For clinicians and stewardship teams in similar tertiary settings we suggest:

- Treat suspected invasive *C. auris* with echinocandin pending susceptibility.
- Obtain species identification and AFST early;
- Consider source control (remove/replace central lines)
- For NICU cases, prioritize line-care bundles, TPN stewardship, and strict cohorting/screening during clusters.
- Regularly review institutional susceptibility data to update empiric protocols.

LIMITATIONS:

This is a single-center series with a mixed isolate and patient analysis that, while internally consistent, may not generalize to other geographic regions. Molecular clade typing was not reported here—clade differences can explain regional variability in resistance and transmission potential and should be included in future analyses.

CONCLUSIONS:

Our study contributes to the accumulating clinical evidence that *Candida auris* is an ICU-centered MDR pathogen with substantial neonatal relevance in centers that care for extremely preterm infants. High azole and polyene resistance and frequent MDR underline the necessity of echinocandin-led empiric therapy, robust local susceptibility monitoring, and strict infection control measures to prevent transmission.

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